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A STUDY OF PUPIL CYCLE TIME (PCT) IN ALTERED STATE OF NUTRITION IN INDIAN MALE

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Abstract : Pupil cycle time (PCT) is a simple way to measure the parasympathetic activity in the eye. This is a sensitive and specific test for the study of parasympathetic function. The cardiac parasympathetic tone is a good indicator to predict morbidity and mortality in an individual. The PCT is correlated with cardiac parasympathetic tone. In the present study we have aimed to look at the PCT in different nutritional status in human subjects. Sixty-three healthy adult male volunteers in the age group of 18–50 yrs were studied. They were divided in three groups based on their BMIs as undernourished, normal and preobese/obese. The mid-arm circumference (MAC) and waist- hip ratio (W:H) are incorporated as adjuvant to strengthen that they are divided into three different nutritional groups. The PCTs of undernourished (818±145 ms), normal control (904±63 ms) and overweight (991±106 ms) is expressed as mean and SD (P<0.001). A linear regression analysis was performed taking BMI, MAC, W:H and PCT as parameters, which shows a positive linear correlation. The results showed that the PNS activity in the eye is greatly modulated in different states of nutrition. Pupil cycle time is a simple, noninvasive investigative tool to assess and differentiate the PNS function in obese and chronic undernourished subjects.

Key words : autonomic function; pupil cycle time; body mass index; nutrition; mid arm circumference; waist hip ratio

INTRODUCTION

Nutritional health is maintained by a state of equilibrium when there is a balance between energy intake and expenditure. Loss of this equilibrium can lead to undernutrition i.e. negative energy balance (1, 2) and can/ or result in obesity i.e. positive energy balance (3, 4, 5, 6). This alteration in the energy balance which leads to malnutrition can cause changes in sympathetic (7) as well as parasympathetic activity in animals and human beings (8). Changes in the parasympathetic nervous system are evidenced by a decrease in Acetylcholinesterase in tissues (9) and cardiovascular parasympathetic

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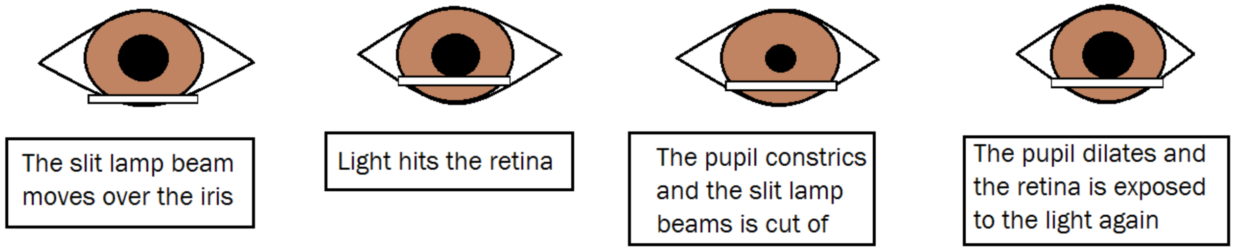

tone is increased in energy deficient subjects (10). Alteration of activity of the parasympathetic system has also been reported in obese humans (11).

The most commonly used tests for autonomic function are tests of cardiovascular system, which are well established (12). Another organ system that is tested for autonomic dysfunction is the eye. In the eye, pupil cycle time (PCT) is a sensitive measure of dysfunction of the parasympathetic efferent limb of the papillary light reflex arc (13) e.g. leprosy, diabetes etc. PCT is measured using slit-lamp that induces persistent oscillations of the pupil of the eye.

Autonomic dysfunction may be present in the eye without any clinical sign as has been shown in diseases affecting the eye e.g. Hansen disease and diabetes (14, 15). In 1990, Lanting et al showed that pupillary parasympathetic dysfunction occurred earlier than cardiovascular system when he considered darkness pupil diameter and pupil latency as ophthalmologic tests and response to standing and response to deep breathing as parasympathetic cardiovascular tests (13, 16). Martyn et al correlated well with the cardiac autonomic function test and opined that compared to CVS tests PCT is 59% sensitive and 70% specific (17).

It is well known that the nutritional status is a determinant of autonomic function may be an adaptation to the nutritional status of a subject and sympathetic tone is affected by the nutritional status (7, 17). Though pupillary oscillation is studied before using oscillometer and various drugs affecting ANS in the eye to establish parasympathetic dysfunction in obesity but PCT was not used before to investigate the effects of nutritional status, especially in Indian male subjects.

MATERIALS AND METHODS

Sixty-three males between the ages of 18 and 50 years were studied. They were recruited from general population and male staffs and students of St. Johns' Medical College. A brief history, including a system review and clinical examination was performed. The subjects who had history of diabetes, hypertension, hypotension, asthma, other cardiac and ophthalmologic diseases like cataract, optic neuritis, on chronic medication were excluded from the study. All of them were non-smoker, non-alcoholic and weight stable: those with a noticeable weight gain or loss over the preceding six months were also excluded (10). This was judged by taking detailed past history. They were instructed to have their last meal at 8 pm, the night before and avoid caffeinated beverages for 12 hours prior to the study. Detail of the experimental procedure was outlined to the participants and an informed written consent was obtained. The ethics committee of St. Johns' Medical College approved the study.

Anthropometric measurements

Body mass index (BMI): Body weight of the subjects was measured to the nearest 0.001 kg using a sensitive electronic scale (Fitness, Edryl, India) and height was measured using a stadiometer (Nivostise Brivete Depose). Body mass index (BMI) was calculated using Quetlet's index (weight in kilogram/height in meter squared).

Now, Sixty – three healthy male subjects were divided in three groups according to their BMI as undernourished (N=22, BMI<18.5 kg/m^2), normal (N=21, BMI = 18.5 kg/m^2–24.9 kg/m^2) and preobese/obese (N=20, BMI > 24.9 kg/m^2).

Mid arm Circumference (MAC)

Mid arm circumference (MAC) was measured in the right arm. Firstly measurement was taken from tip of the coracoid process to the tip of the olecrenon process as the anatomical landmark and the midpoint was decided on the lateral side. Mid arm circumference was measured on the midpoint around the arm by a simple measuring tape (18).

Waist Hip ratio (W:H)

The midpoint was selected between lowest point of the costal cartilage and the highest point of the iliac crest on the midaxillary line in standing position in the right side (18). The circumference was measured around the point by a simple measuring tape. Hip was considered as the maximum bulge over the gluteus maximus muscle at the levels of the trochanters. The ratio between these two is calculated as W:H.

Mid arm circumference and W:H was measured to differentiate the nutritional status more accurately to avoid the bias of regional or uneven distribution of body fat as they are considered as adjuvant to assess malnutrition.

Slit-lamp

A Haggstreit-type of slit-lamp was used to measure the PCT, in the Department of Ophthalmology at St. Johns' Medical College Hospital. The same lamp was used for all the subjects studied. The subjects placed their chin on the chin rest. The height of the chin-rest from the base of the table is adjusted in order to view the eye adequately for all the subjects with different heights. The slit beam was horizontal axis and a thickness of 1mm as depicted in the picture below. The white diffuse horizontal light was used.

Measurement of pupil cycle time

The subject was made to sit in a dimly lit room and stopwatch with a least count of 1/1000. Pupil cycle time was measured in a dimly lit room to get maximum dilatation of pupil before starting of the study. The subjects are asked to gaze at a fixed point to get accurate measurement. A horizontal beam of light of width of 1 mm was projected on the edge of the pupil. As soon as the light falls, the pupil constricts and again dilates to original position; when it dilates the beam of light again hit the pupil and pupil constricted. The time the pupil takes to constrict and dilate once is measured using a 'timed counter' with accuracy of 0.001 secs. The time taken for 90 cycles in 3 sittings with a gap of 15 minutes between them and PCT is calculated.

The stopwatch has an oscillator of 1 kHz, which gives an accuracy of 1 millisecond. The counter started the stopwatch at the beginning and at the end of the preselected number of cycles; which reduced human error to a minimum. The PCT is measured in both the eyes and the longer cycle is considered (measurements is obtained in both the eyes). The PCT which was of longer duration was in the two eyes were taken into consideration for analysis (20). Data is rejected if there was blinking more than 2 times in one sitting or too much of watering in the eye due to intensity of light.

Statistical analysis

Data were expressed as mean±SD (Table I) only. Fig. 1 depicts the true value of BMI and PCT in various data points and $P<0.05$ as criteria for statistical analysis with 95% confidence interval (Fig. 2, 3, 4). Statistical analysis is performed by linear regression analysis.

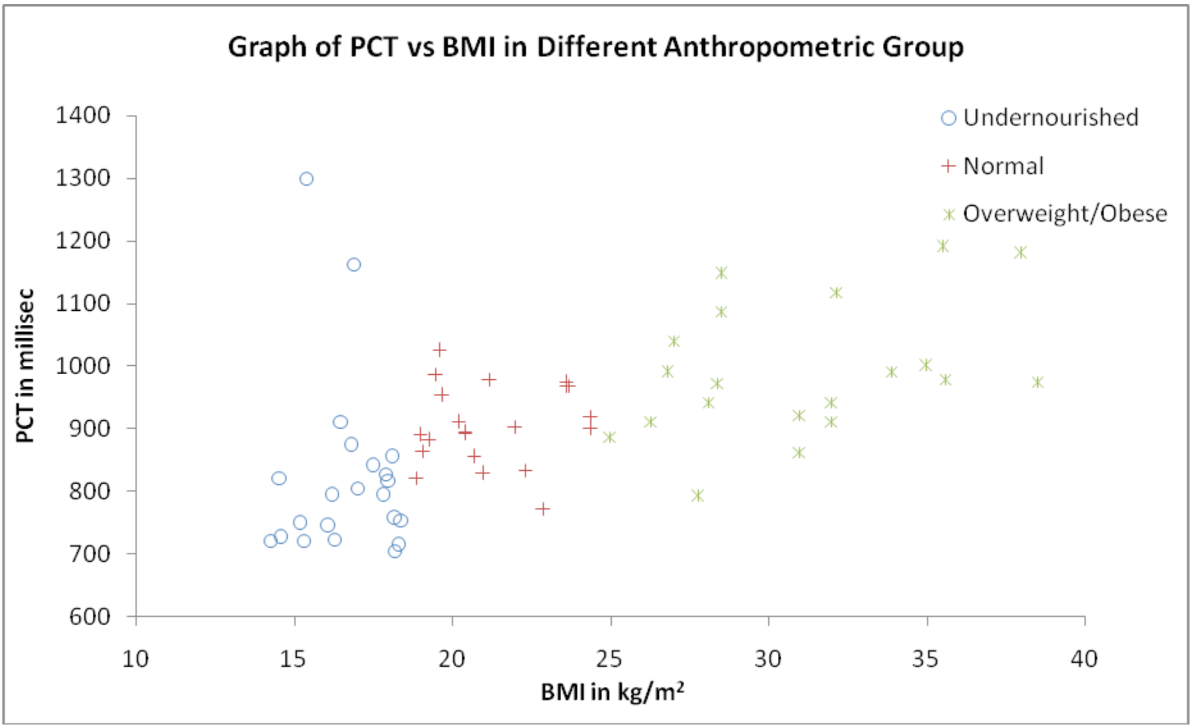

Fig. 1: Graph showing the true values of PCTs and BMIs.

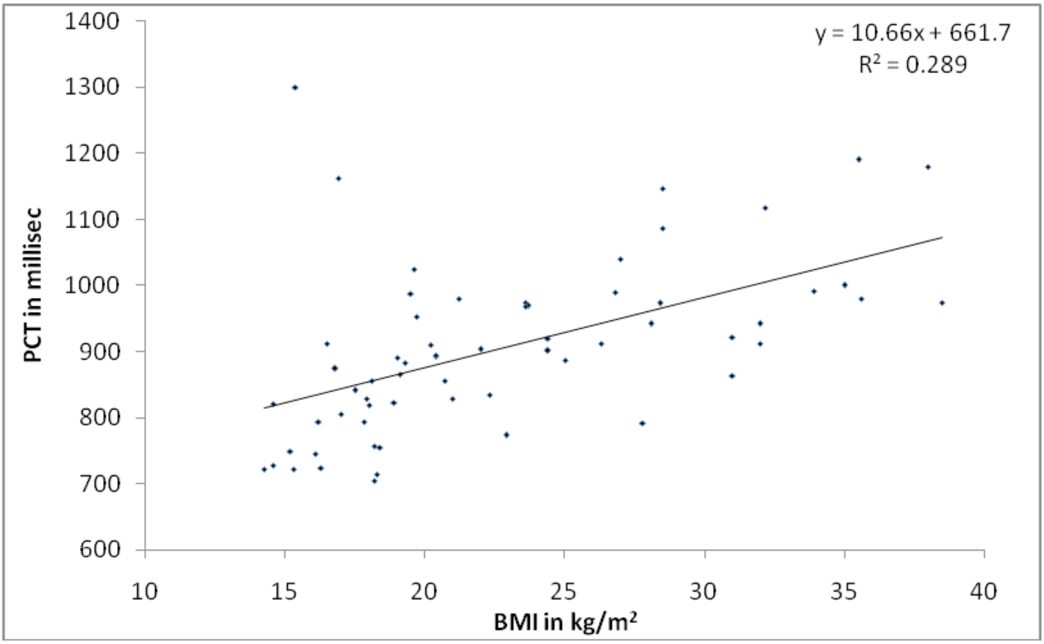

Fig 2 : A graph of statistical fitment is carried out through linear regression analysis to establish existence of linear relation between BMI and PCT in all three groups namely undernourished (BMI <18.5 kg/m²), normal (18.5-24.9 kg/m²) overweight/obese (24.9 kg/m²).

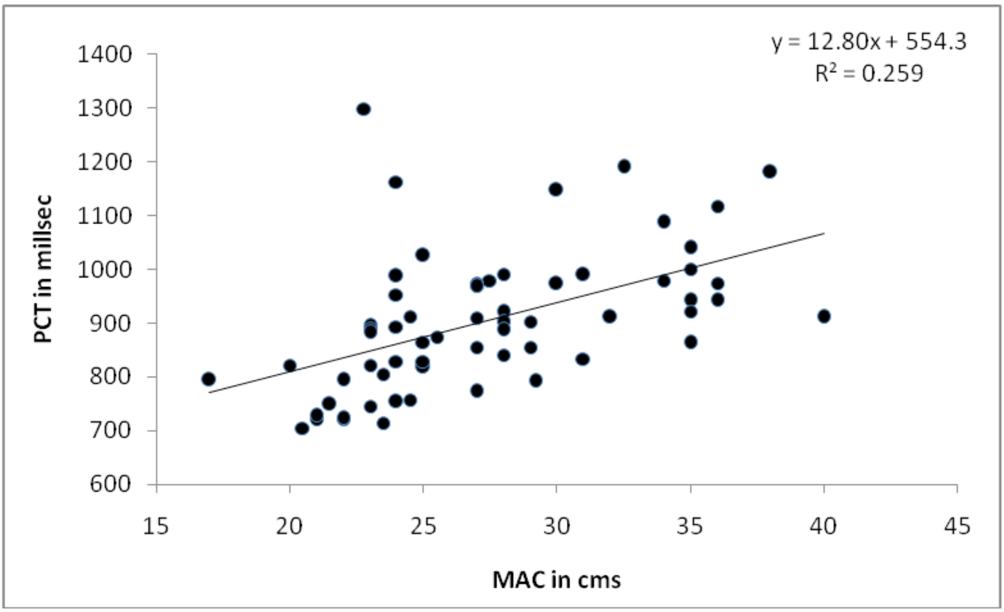

Fig 3 : A graph of statistical fitment is carried out through linear regression analysis to establish existence of linear relation between MAC and PCT in all three groups namely undernourished (23±2.61 cm), normal (25.8±2.20 cm) overweight/obese (33.4±3.39 cm).

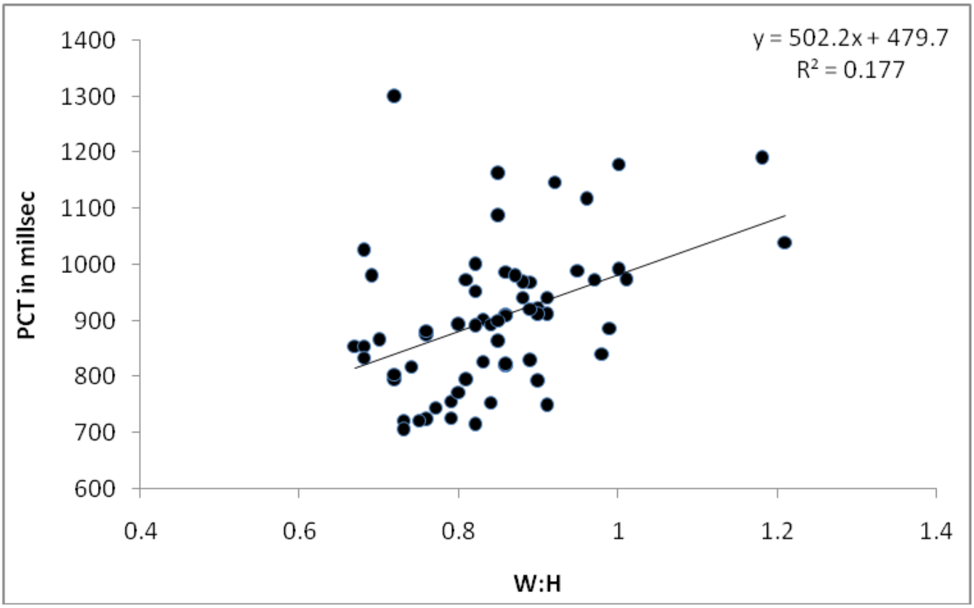

Fig 4: A graph of statistical fitment is carried out through linear regression analysis to establish existence of linear relation between W:H and PCT in all three groups namely undernourished (o.79±0.07), normal (0.80±0.07) overweight/obese (0.94±0.1).

RESULTS

TABLE I: Subject characteristic of the three study groups with pct (Data is expressed as mean±SD).

Subject characteristic	*Under-nourished (n=22)*	*Well-nourished (normal, n=21)*	*Overweight/Obese (n=20)*
Age (yr)	26±7.60	33±9.30	27±8.70
Weight (kg)	44.9±4.87	59.63±7.46	88.7±12.10
Height (M)	1.63±0.05	1.67±0.06	1.68±0.47
BMI (kg/M^2)	16.7±0.02	21.2±1.83	31±4.00
MAC (cm)	23.1±2.61	25.8±2.20	33.4±3.39
Waist : Hip	0.79±0.07	0.80±0.07	0.94±0.10
PCT (milli sec)	818±145	904±63	991±101

DISCUSSION

In this cross sectional study we found that the PCT is directly and positively correlated with BMI; that means there is an increase in the duration of PCT with increase of BMI (16). In 1986, functional correlates of PCT were studied by Martyn and Ewing (19). Miller and Thompson were among the first to investigate the method of PCT in 1978 (20). They incorporated a method that we have followed closely in our study. We have used more accurate timer which can measure the duration with 0.001-second accuracy against 0.01-second used by them. Our study required 2 minutes as against 5 minutes taken by the earlier studies. Thus the ambient light is maintained in the same subject and we have conducted the study in same time (24). In 1993, again interest in PCT has also been raised by the exploration of the hypothesis that open angle glaucoma (OAG) has an autonomic neuropathy component which also investigated the cardiovascular autonomic function and found that there was presence of prolonged PCT in patients with OAG compared to normal people without OAG and that is comparable with the cardiovascular autonomic function test (22). Using this approach, PCT measurements have since been made in wide variety of optic neuropathies (optic neuritis, compressive optic neuropathy, glaucoma, atrophic papilloedema, traumatic optic neuropathy, and ischaemic optic neuropathy) (24). So, we have taken care to choose the subject devoid of any of these diseases.

It is well known that quantifying the autonomic function is very difficult though lots of autonomic function tests are available. In contrast to that, PCT is a quantifiable test and can be conducted easily if some precautions can be taken as other CVS tests to investigate undernutrition (9). In the present study, we have taken measures, as far as possible, that minimal confounding factor would not interfere with the result. The physiological factor such as physical activity (ongoing study), gender (21) age (23) and pathological, such as diseases affecting autonomic nervous system, can affect PCT also. The PCT represent the only parasympathetic component of the autonomic nervous system in the eye. It was evidenced by blocked study or the sympathetic stimulation does not affect the PCT by Martyn et al (18). When the PCT increases the parasympathetic tone in the eye decreases and opposite happens when PCT decreases. As PCT is well correlated with the other autonomic function tests and we concluded that the ocular parasympathetic tone is increased in undernourished state and decreased in obesity.

As PCT is a quantitative index it would definitely assess the parasympathetic change and its extent in altered state of nutrition as other studies suggested (10). We have observed though two of the subjects were undernourished but they have very long PCT of 1162 millisecs and 1299 millisecs. This is considered long in terms of normal PCT which ranges from 800 millisecs – 900 millisecs (21). Though they are outliers we have included those data in the study. Except the fact that they were over 40 years of age they are fit to be included otherwise. The PCT becomes longer after 50 years of age (23) and age range of our study is 18-50 years. As Bremmer FD suggests that the measurement of pupil cycle time is the only clinical test that does not rely on comparison with the fellow eye, but it can only be measured in mild to moderate optic nerve dysfunction (24). But then also optic neuropathy can occur in chronic undernutrition. So, we have chosen carefully the subjects those who do not have the mildest form of optic neuritis. The caveat of the study may be, we did not consider the pupil size to measure the 'edge-light pupil cycle time' as described by Howarth et al (25). But, they have recruited only 22 subjects (10 male, 12 female) and intra-individual variation can occur especially in females. In female, there is a difference in PCT values in different phases of menstrual cycle as studied by Moodithaya et al. That is another reason that we have chosen the male subjects only to investigate the effect of nutrition on pupil cycle time (21). Our data was collected from the same setting and laboratory and same technique is quoted (25).

We could not depend on any available data, which had investigated directly the nutritional status by this simple but specific test. We have observed in our study, PCT is reduced in undernourished subjects (818±145 ms) whose BMI ranged from 14.26 kg/m^2 to 17.5 kg/m^2 (average 16.7 kg/m^2) compared to normal with BMI range of 18.5 kg/m^2 to 24.9 kg/m^2 (average 21.2 kg/m^2). On contrary to that fact, PCT of the preobese/obese subject has increased with a BMI range of 25 kg/m^2 to 38 kg/m^2 (average being 31 kg/m^2)(Fig. 1). Through linear regression analysis we got that a fitment line can be drawn easily with BMI and PCT as parameter and they are positively correlated with $R^2 = 0.29$ (Fig. 2). In order to reduce the error of misclassifying individuals as undernourished or overweight/obese the assessment of mid-arm circumference and waist-hip ratio was carried out. The cut-offs for MAC in men is 24 cm which is considered normal (3). In our cross sectional study we have the MAC value averaging 23.1±2.61 cm for the undernourished, 25.8±2.20 cm for the normal, and 33.4±3.39 cm for the overweight/obese subjects. The MAC value can change dramatically also within small range of change of BMI (5). A regression analysis is run with MAC and PCT as parameter and a linear positive correlation is obtained with $R^2 = 0.26$ and a fitment is drawn easily (Fig. 3).

Abdominal fat mass can vary dramatically within narrow range of body fat or BMI. Our data suggest that there is an increase of W:H with increase of BMI with a result of undernourished 0.79±0.07, normal0.80±0.07 and preobese/obese 0.94±0.1 which is directly correlated with cardiovascular risk factor where the cardiac parasympathetic activity is altered (5, 6). A linear fitment can be drawn easily with the W:H and PCT as parameter with $R^2 = 0.18$ which proves the linear positive correlation between the two (Fig. 4).

Summary and conclusion

In conclusion, the present finding demonstrate that in obesity, the ocular parasympathetic tone is decreased and there is an enhanced tone in undernourished people and this increase follows a steady rate supported by data for the first time in Indian males. As this result is corroborating the finding of cardiac parasympathetic tone, measurement of pupil cycle time can be tested as parasympathetic alteration in the eye in altered state of nutrition although further study is required to compare both of them in these particular conditions.

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