ABSTRACT

Background: Edge light pupil cycle time (ELPCT) is one of the eye’s light reflexes. Studies have shown ELPCT to be a measurable constant, unaffected by visual acuity, refractive error, eye color, pupil size, or sex. Control of this reflex occurs through the autonomic nervous system. Researchers have postulated that manual medicine procedures produce remote effects by influencing the autonomic nervous system (ANS)

Objective: The study aimed to investigate the effects of a C1-2 high-velocity, low-amplitude manipulation on ELPCT.

Methods: Thirteen men (mean age 24.2 years) without a history of eye disease or central or autonomic nervous system pathologic conditions had their ELPCT measured before and after manipulation. The manipulation comprised a high-velocity, low-amplitude rotatory thrust, localized to the C1-2 joint on the left (n = 6) or right (n = 7) eye, determined randomly.

Results: ELPCT measures demonstrated a significant difference for both eyes before and after manipulation (P = 0.027; the left eye, P = 0.046). This suggests that ELPCT, which is mediated through the autonomic nervous system, can be directly influenced by high-velocity manipulation to the upper cervical spine. (J Manipulative Physiol Ther 2000; 23:465-69)

Conclusion: This suggests that ELPCT, which is mediated through the autonomic nervous system, can be directly influenced by high-velocity manipulation to the upper cervical spine. (J Manipulative Physiol Ther 2000; 23:465-69)

Key Indexing Terms: Eye; Chiropractic Manipulation; Autonomic Nervous System

INTRODUCTION

High-velocity low-amplitude (HVLA) manipulation of the cervical spine is a common treatment modality used in a variety of manual medicine disciplines. HVLA techniques are those that use high-velocity and low-amplitude force on a specific spinal segment and are ordinarily associated with an audible “crack,” which is widely accepted as representing cavitation of a spinal zygapophyseal joint. Researchers have investigated the potential remote effects of manual medicine procedures applied to the cervical spine on distal skin temperature, electrical skin conductance, and digital blood flow. Others have investigated the remote effects of spinal manipulation in women with primary dysmenorrhea and asthmatics. Various authors believe that manual medicine procedures produce remote effects by influencing the activity of the autonomic nervous system (ANS). Kuchera and Kuchera maintain that manual medicine techniques have a definite impact on the sympathetic nervous system and outline specific techniques they believe produce a direct effect on the sympathetic nervous system. They suggest that the sympathetic ganglia in the cervical region are closely related to the cervical joints, primarily through fascial connections, and propose that somatic dysfunctions of the cervical region can express symptoms of ganglia involvement in the ears, eyes, and cardiac tissues. They assert that these may be corrected by addressing underlying problems in the cervical spine. Celandron at al suggest that manipulation has a positive role to play in the treatment of hypertensive patients through “shifting the autonomic tone in the direction of the sympathetic nervous system.” In a review of the efficacy of chiropractic treatment in hypertensive disease, Crawford et al similarly propose that chiropractic treatment can aid the control of hypertension by influencing the sympathetic nervous system.

Researchers have postulated that manual medicine interventions may produce measurable changes in distal skin temperature, electrical conductance, and digital blood flow and that these changes are mediated by way of the ANS. Harris and Wagnon studied the effects of chiropractic adjustments on distal skin temperature and reported that blood flow through the fingertips can be affected by specific manipulative adjustments to the spine. Chiu and Wright reported a small magnitude reduction in skin temperature after the
application of nonthrust cervical mobilization techniques. Purdy et al\textsuperscript{13} investigated the effects of suboccipital soft-tissue manipulation on digital blood flow. Although this study did not use direct joint mobilizing technique, we suggest that the significant changes found in digital blood flow may be attributed to an influence on the ANS, possibly the sympathetic division, because it supplies the vasculature in this area.

Although various authors support the concept that manual medicine procedures applied to spinal joints can produce measurable remote effects mediated through the autonomic nervous system,\textsuperscript{10-15,16-18} convincing evidence of a direct effect on the ANS is limited, and evidence that these effects can be systematically harnessed to produce a positive therapeutic outcome is lacking.

Ongoing research is needed to test the hypothesis that manual medicine techniques applied to the spine can produce remote effects and that these effects are mediated by the ANS. Pupillary light reflexes are mediated through the ANS and are measurable and reproducible. The edge light pupil cycle time (ELPCT) is the time taken for constriction and redilation of the pupil when exposed to light, usually a thin beam of light from a slit lamp. ELPCT in normal subjects is 822 ± 69 ms.\textsuperscript{19} Stability tests show variations in ELPCT over time to be approximately 3%.\textsuperscript{19} This suggests that ELPCT is a reliable and readily reproducible reflex. Sex, iris color, visual acuity, refractive error, pupil size during the examination, pupil unrest, oscillation amplitude and regularity, and light adaptation do not significantly affect ELPCT.\textsuperscript{19} Martyn and Ewing\textsuperscript{20} confirmed that ELPCT is not influenced by the width of slit light, the time of day the measurement is taken, or the eye side measured, with no evidence that ELPCT became prolonged with repeated measurements. The only variable Miller and Thompson\textsuperscript{19} tested that proved to be significant was age, with a small but significant increase in ELPCT occurring with increasing age.

ELPCT occurs by way of the pupillary light reflex arc.\textsuperscript{19} The pupillary light reflex arises from the stimulation of the 2 iris muscles, the sphincter iridis supplied by the parasympathetic division of the ANS, and the dilator pupillae innervated by the sympathetic division of the ANS. Parasympathetic control arises from the Edinger-Westphal nucleus, the subsnucleus of the oculomotor nucleus which is located in the mid-brain.\textsuperscript{21} It consists of 3 divisions, the functions of which are not completely known. The nucleus is divided into a rostral accommodative area and a caudal pupillary constrictor region. The middle section can produce both accommodation and constriction.

The sympathetic nerves arise from the hypothalamus and descend in the brainstem tegmentum into the intermediolateral gray cell column of the spinal cord.\textsuperscript{21} Synapse occurs at C8, T1, and T2 levels, and a second order neuron is given off. This exits the spinal cord through the white rami communicantes, over the apex of the lung, and under the subclavian artery. The fibers then ascend in the sympathetic chain and synapse in the superior cervical ganglion. A third order neuron then travels in the pericarotid sheath to the cavernous sinus, where it closely approximates the fifth and sixth cranial nerves. Fibers enter the eye through the superior orbital fissure and travel with the long and short posterior ciliary nerves to the dilator muscle.

ELPCT has in the past shown a prolonged cycle time in whiplash patients,\textsuperscript{22} optic neuritis and multiple sclerosis,\textsuperscript{23} optic nerve compression,\textsuperscript{24} oculomotor nerve palsy,\textsuperscript{25} and Horner’s syndrome.\textsuperscript{26} Control of ELPCT involves a complex interaction between the parasympathetic and sympathetic nervous systems, with evidence that specific diseases may interfere with either of these components of the reflex and can alter ELPCT. Nonetheless, in normal individuals ELPCT is a reproducible and easily measured reflex response. The purpose of this pilot study was to establish whether an HVLA thrust technique applied to the atlanto-axial joint could influence ELPCT in normal individuals and if the direction of thrust would be associated with ipsilateral, contralateral, or bilateral changes.

**MATERIALS AND METHODS**

**Subjects**

Thirteen healthy male subjects aged 18 to 29 years (mean age, 24.2 years) were recruited from a volunteer list at Victoria University, Melbourne. Exclusion criteria included a history of eye disease or central or autonomic nervous system pathologic conditions. The Victoria University Human Research Ethics Committee granted ethical approval. All subjects signed an informed consent form and were free to withdraw from the study at any time.

**Procedure**

A researcher trained and competent in the measurement of ELPCT collected data with the method previously described by Miller and Thompson.\textsuperscript{19} Measurement was undertaken in a dimly lit examination room, and the ELPCT was measured in both eyes, with a Hag-Streit Bern slit lamp (Hag-Streit, Bern, Switzerland) and hand-held stopwatch.

The subject was seated comfortably in front of the slit lamp. A vertical slit beam of light of moderate intensity (.5-mm thick) was directed perpendicular to the plane of the iris at the lateral limbus. The beam was slowly moved medially until it overlapped the margin of the pupil, which then constricted. The beam was held in this position so that the constricted iris blocked the light from entering the eye and reaching the retina. With the retina in darkness the pupil dilated, overlapped the edge of the light beam, and allowed light to again reach the retina, producing another pupil constriction. This sets up a persistent oscillation measured in milliseconds (ms) (Fig 1).

All subjects underwent an initial slit lamp examination of ELPCT to familiarize them with the measuring protocol. Subjects were instructed to blink as little as possible. Once the familiarization process was complete, the subjects were escorted to a treatment room and asked to lie quietly on a treatment table. Subjects then returned to the examination room for formal measurement of their ELPCT.

On completion of measurement of the ELPCT each subject returned to the treatment room for atlanto-axial (C1-2) manipulation. Each subject was tested for vertebro-basilar artery insufficiency\textsuperscript{27} before manipulation; all subjects had negative test results, and all 13 subjects received C1-2 manipulation.

The subject lay in a supine position on the treatment table.
A medically qualified osteopath with 25 years’ experience in the application of HVLA technique delivered an HVLA rotatory thrust, localized to the C1-2 joint on the left (n = 6) or right (n = 7), determined randomly. The practitioner then recorded if cavitation was achieved, which was characterized by an audible “pop” or “crack” associated with the thrust.28 The same practitioner applied all HVLA manipulations to limit variability in technique. As soon as the HVLA manipulation was complete, the subject returned to the examination room and his ELPCT technique. The same practitioner applied all HVLA manipulations to limit variability in technique. As soon as the HVLA manipulation was complete, the subject returned to the examination room and his ELPCT was measured again for both eyes. The researcher measuring ELPCT was blind to both the manipulation direction and whether cavitation had occurred during the manipulation.

Statistical Methods

A paired sample Student t test was used to measure the differences between ELPCT in the pre-manipulation and post-manipulation groups (SPSS for Windows, SPSS Inc, Chicago, Ill.). A P value of .05 was considered significant. Results are reported as mean ± standard deviation for all measured values.

RESULTS

The results have been divided into 2 sections. Comparison of ELPCT looks at each eye as an individual entry, giving 26 separate measurements of ELPCT and examining the results when the data are broken into their matched subject pairs (ie, results are separated into left eyes and right eyes). The second section incorporates results that account for the direction of manipulation (ie, to the left or to the right).

Comparison of ELPCT

Each individual measurement of ELPCT was treated as if it had come from a separate subject. Therefore each subject contributed 2 ELPCT readings, 1 from each eye. Ostensibly, this provides a larger sample size. The results (Table 1, Fig 2) demonstrate a significant difference in the mean ELPCT between the pre-manipulation and post-manipulation group when measured for all eyes (P = .002). Significance was also found between the mean pre-manipulation and post-manipulation groups when measuring for both the left (P = .046) and right eye (P = .027) individually.

Side of Manipulation

In an attempt to identify whether the side of thrust was an important factor affecting ELPCT, measurements of ELPCT were grouped for left and right eyes according to the side of manipulation. Therefore each subject had one measurement in each group, 1 left eye measurement and 1 right eye measurement. These results (Table 2, Figs 3 and 4) represent the effects of the manipulation either to the left or to the right C1-2 joint.

All estimated post-manipulation values were lower than the pre-manipulation values. The estimated difference between pre- and post-manipulation ELPCT was higher on the ipsilateral side of manipulation. However, only the values for right HVLA thrust and the readings for the right eye were statistically significant (P = .047).

DISCUSSION

The results of this pilot study indicate that manipulation of the atlanto-axial joint can produce a significant measurable difference between manipulation before and after ELPCT, with the ELPCT becoming significantly faster after manipulation. Significance is demonstrated for all eyes taken as individual measures and also when separated for both left and right eye. The direction of manipulation showed a significant association between the right eye and manipulation of the right C1-2 joint (P = .047), but only a trend toward significance for the left eye when the manipulation was directed to the left C1-2 joint. Reproduction of this study with a greater number of subjects and inclusion of a control group needs to be undertaken to identify whether the trend on the left side could reach significance.

Unilateral manipulation has been shown to produce unilateral effects. Nansel et al29 found that unilateral manipulation to the side of restriction improved asymmetry for at least 30 to 45 minutes in otherwise asymptomatic subjects who exhibited cervical lateral-flexion asymmetry. When manipulating the
right C1-2 joint, there was a significant difference in ELPCT in
the right eye after manipulation \((P = .047)\), but no significant
change in the left eye \((P = .204)\). Although the same result
was not demonstrated for the left eye with a left C1-2 joint manipu-
lation, there was a trend toward significance \((P = .173)\). This
may indicate that ANS changes have the potential to occur on
the same side as the manipulation (ie, unilateral manipulation
may produce unilateral physiologic changes). The significance
demonstrated for the right C1-2 thrust affecting right eye
ELPCT may be a result of different forces and velocity being
applied to the right when compared with the left C1-2 joints
because the person performing the manipulation was right-
handed. Future studies may benefit from the inclusion of force
and amplitude measurement in an attempt to ensure that thrust
techniques are applied equally to both sides of the neck.

Miller and Thompson\(^1\text{9}\) reported ELPCT in normal subjects
\((n = 116)\) as 822 ± 69 ms. Results of this study demonstrated
mean ELPCT before manipulation for normal subjects \((n =
13)\) of 1031 ± 120 ms. Although the method for measuring
ELPCT replicated that of an earlier study,\(^1\text{9}\) our ELPCT mea-
surements were higher than reported in their study. This may
reflect larger variability within the restricted pilot study sample
size, variation in the sampled population, and differences in
conditions used in this investigation before measurement.

Mechanisms for the documented changes in ELPCT have been
postulated by various authors as being mediated by the ANS,\(^2\text{2}\)
specifically either the parasympathetic,\(^1\text{9},2\text{0},2\text{3},2\text{4}\) or sympathetic\(^2\text{6}\)
branch. The extent of interaction between the 2 divisions of the
ANS on the pupillary reflexes remains an area of debate. Certain
authors\(^2\text{0},2\text{5},2\text{6},2\text{9}\) have been more assertive about possible mecha-
nisms when discussing specific medical conditions or results from
trials with ANS activating or blockading drugs.

Martyn and Ewing\(^2\text{0}\) undertook a study of ELPCT with parasympathetic and sympathetic blocking drugs. Parasympathetic blockade with intraocular homatropine (0.4%) or tropicamide (1%) produced a lengthening in ELPCT within a few minutes. After 10 to 15 minutes, the oscillations of the pupil were abolished. Sympathetic block-
ade with intraocular instillation of guanethidine monosulfate
(4%) had no significant effect on ELPCT, despite a marked
degree of miosis. Phenylephrine (10%), a sympathomimetic,
had no effect on ELPCT. We made the inference that from a
clinical perspective, the ELPCT was more likely to be pro-
longed when lesions were present in the parasympathetic
efferent limb of the pupillary light reflex, which was support-
ded by Blumen et al.\(^2\text{5}\) They inferred that the increase in
ELPCT in people with oculomotor nerve palsy suggests that a
subclinical involvement of the parasympathetic component of
the oculomotor nerve contributed to alterations in the ELPCT.

An earlier study by Blumen et al\(^2\text{6}\) concentrated on the sympa-
thetic component in ELPCT. They studied ELPCT in 12 patients
with Horner’s syndrome, a condition that results from paralysis
of the cervical sympathetic nerves. Their results showed signifi-
cantly prolonged ELPCT in the affected eye of all patients when
compared with their own normal eye and a normal control group.
They suggest that the sympathetic nervous system controls the
redilation phase in the ELPCT by virtue of their innervation to
dilator pupillae. These findings in patients with Horner’s syn-
drome strongly suggest that sympathetic innervation is essential
for a normal ELPCT. This appears to contradict the findings
of Martyn and Ewing,\(^2\text{0}\) who found that both sympathetic blockade
and the use of a sympathomimetic agent did not significantly
alter ELPCT. Thompson\(^2\text{9}\) argues that alteration of normal func-
ction of either sympathetic or parasympathetic pre- or post-gan-
glionic neurons may prolong ELPCT. He suggests that the loss of innervation of the dilator muscle and the adrenergic inhibitory impulses to the sphincter muscle might be an explanation for the prolonged ELPCT in patients with Horner’s syndrome.

Although there appears to be no strong agreement between researchers in relation to the balance of the parasympathetic and sympathetic activity in the control of ELPCT, there is agreement that alterations in ELPCT do reflect changes within the ANS.

It has been postulated that somatic dysfunction and the ANS are interrelated. A study by Brown lends further support to the concept that somatic disorders may affect autonomie function. In an investigation of the effect of whiplash injuries on various ocular functions, Brown reported a significant difference in ELPCT between left and right eyes in those subjects who had sustained whiplash injuries. The postulated mechanism for these findings related to effects on the ANS.

The results of this study on manipulation and ELPCT found that an HVLA thrust applied to C1-2 produced a significant effect on the autonomically mediated ELPCT (P = .002). These results suggest that there may be an interrelation between somatic and autonomic function and that autonomic function might be altered by manual intervention. However, this was a preliminary study comprising small subject numbers and no control group. Caution should therefore be exercised in the interpretation and extrapolation of the results of this study.

CONCLUSION

Cervical manipulation at the atlanto-axial joint appears to have an effect on ELPCT, in that it decreases the time to complete a cycle. The exact neurophysiologic mechanism by which this change is mediated remains unknown, although there is a clear indication of ANS involvement. Examining the association between direction of the manipulation and changes in ELPCT produced variable results for the left and right side, thus warranting further investigation.

Attempts have been made by different researchers to quantify the remote effects of manual interventions by measuring autonomically mediated responses, such as electrical skin conductance and skin temperature. Measurement of ELPCT may provide a further quantifiable measure of the effects of somatic intervention on autonomic function. This pilot study has demonstrated that the use of manipulation directly influences the autonomically mediated ELPCT. These findings warrant further study that includes a control group and a greater number of subjects.

REFERENCES