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Original Article

Autonomic nervous system function in childhood migraine

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Abstract

***Background*:** Although the pathogenesis of migraine is controversial, autonomic nervous system (ANS) dysfunction has been reported in patients with adult migraine in recent years. The present study was planned to investigate ANS function in childhood migraine.

***Methods*:** The migraine and control groups consisted of 25 migraineur and 30 healthy children, respectively. Orthostatic test, sustained handgrip, Valsalva ratio, 30/15 ratio and heart rate responses to deep breathing were used as non-invasive ANS function tests in both groups.

***Results*:** In the orthostatic test, systolic (SBP) and diastolic blood pressures (DBP) were higher in the upright than the supine position in the migraine group, but were higher in the supine than upright position in the control group. In the sustained handgrip test, the mean difference in SBP was higher in the migraine than the control group ($P = 0.0278$), but there was no significant difference in DBP between migraine and control groups ($P = 0.107$). The Valsalva ratio was higher in the migraine than the control group ($P = 0.0002$), as was the 30/15 ratio ($P = 0.0108$). Heart rate responses to deep breathing were not different between the migraine and control groups ($P = 0.749$).

***Conclusions*:** Our results demonstrate ANS dysfunction, with hyperactivity of both the sympathetic and parasympathetic nervous system, in children with migraine.

Key words autonomic nervous system, childhood, handgrip test, migraine, orthostatic test, Valsalva maneuver.

The function of the autonomic nervous system (ANS) in patients with migraine has been investigated for many years. The results of these studies, which have been performed on adult migraine in particular, are controversial. Some studies have reported normal ANS function,[1,2] whereas others have reported sympathetic nervous system (SNS) dysfunction[3–17] or both SNS and parasympathetic nervous system dysfunction.[18–21] Studies regarding ANS function in childhood migraine are limited.[22] The present study was planned to investigate ANS function in childhood migraine.

Methods

The migraine group consisted of 25 children (16 boys and nine girls) with migraine (with no concomitant disease), while there were 30 healthy children (18 boys and 12 girls) in the control group. The mean (± SEM) ages of the migraine and control groups were 10.0 ± 1.1 (range 8–12) and 10.1 ± 1.8 years (range 7–13), respectively. The mean weight and height of the migraine and control groups were 32.4 ± 1.3 kg and 135 ± 2.7 cm and 33.7 ± 1.4 kg and 137 ± 3.2 cm, respectively. The diagnosis of migraine was made according to criterion of the Headache Classification Committee of the International Headache Society.[23] A detailed history was taken and neurologic examinations were performed in both groups. Children in the migraine group had no migraine attack during the study and had not received any medication during the past 10 days. All children in the migraine group had migraine without aura. After obtaining written consent from the parents, the five non-invasive ANS function and visual acuity tests were performed on each child in both groups.[24]

All studies were performed in the morning in an outpatient clinic. All five tests for each subject were performed in one day. After each test, children were allowed to rest for 2 min unless otherwise stated. All tests (with the exception of the orthostatic test) were performed with the subject in the supine position. Blood pressure (BP) measurements were performed by an automatic sphygmomanometer.

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Test 1: Orthostatic test

Blood pressures were recorded with a proper arm sphygmomanometer in the supine position and while standing after 15 min rest. The BP was recorded just before and immediately after standing, as well as during standing at 1 min intervals. After a 5 min rest period in the supine posture, the whole procedure was repeated. The higher orthostatic ratio and the change in BP immediately after standing that went with it were recorded as the results of the test.

Test 2: Sustained handgrip

Each child was asked to exert 30% of maximal voluntary contraction for 3 min on a handgrip dynamometer using the dominant arm. Blood pressure was measured in the non-exercising arm at rest and at 60 s intervals during the contraction.

Test 3: Valsalva ratio

Each child was trained and instructed to maintain an expiratory pressure of 40 mmHg for 10 s by blowing through a mouthpiece attached to an aneroid manometer. The electrocardiogram (ECG) at 50 mm/s was continuously recorded during the Valsalva maneuver and for 30 s after release of pressure. The Valsalva ratio was calculated as the ratio of the longest R-R interval after the maneuver, to the shortest R-R interval during the maneuver. All children completed the test successfully.

Test 4: Heart rate responses to deep breathing

Each child was trained to breathe deeply at a rate of 6 breaths/min while sitting. After a rest period of 5 min, the heart rate (HR) was monitored continuously on a standard ECG at a paper speed of 50 mm/s for at least 1 min. The change in HR with breathing was expressed as the mean of the differences between the maximal and minimal HR in at least six cycles.

Test 5: 30/15 ratio

After 15 min of supine rest, each child was asked to stand while HR was continuously monitored. The 30/15 ratio was calculated as the ratio of the R-R interval at beat 30 after standing to the R-R interval at beat 15 after standing (50 mm/s chart speed). The test was repeated twice and the highest ratio obtained was accepted as the 30/15 test value.

Results are presented as the mean ± SD. The Mann–-Whitney *U*-test and Student's *t*-test were used for statistical analysis. Variables were considered to be significantly different if $P < 0.05$.

Results

All children performed the five ANS function tests, including the Valsalva maneuver, perfectly. The results of tests performed in both groups are shown in Table 1. The following points are of note.

Orthostatic test

In the migraine group, systolic and diastolic BP (SBP and DBP, respectively) were higher in the upright than supine position. The mean difference in SBP between the supine and upright positions was significant ($P = 0.0114$), but the mean difference in DBP between the two positions was not ($P > 0.05$). In the control group, SBP and DBP were higher in the supine than upright position, but the mean difference in SBP and DBP between the two positions was not significant ($P > 0.05$; Fig. 1). We did not encounter any impending syncope in any children.

Sustained handgrip test

In the migraine group during the sustained handgrip test (SHGT), SBP and DBP increased 12.4 ± 4.9 and 8.8 ± 5.5 mmHg, respectively. In the control group during SHGT, SBP and DBP increased 8.9 ± 6.0 and 11.6 ± 6.2 mmHg, respectively. The mean difference in SBP was higher in the migraine group compared with the control group ($P = 0.0278$). There was no significant difference in DBP between the migraine and control groups ($P > 0.05$; Fig. 2).

Valsalva ratio

The Valsalva ratio was higher in the migraine than the control group ($P = 0.0002$).

The 30/15 ratio

The 30/15 ratio was higher in the migraine group than the control group ($P = 0.0108$).

Heart rate responses

Heart rate responses to deep breathing were not different between the migraine and control groups ($P = 0.749$).

Visual acuity

All children had 20/40 or better spectacle-corrected visual acuity.

Table 1 Autonomic nervous system function tests in children with and without migraines

Function tests	Control	Migraineur group
Orthostatic test		
SBP (mmHg)		
Supine	101.5 ± 10.9	97.4 ± 16.7
Standing	98.6 ± 11.2	110.2 ± 16.7
Difference	–4.3 ± 4.9	+ 17 ± 11.3
DBP (mmHg)		
Supine	63.1 ± 8.4	62 ± 11.8
Standing	60.3 ± 8.2	67.4 ± 12.9
Difference	–3.4 ± 4.8	+ 10.7 ± 6.9
SHGT		
SBP (mmHg)		
Before SHGT	107 ± 13.3	100.6 ± 16.1
After SHGT	108 ± 12.9	106.9 ± 13.3
Difference	8.9 ± 6	12.4 ± 4.9
DBP (mmHg)		
Before SHGT	63.3 ± 12.4	62.4 ± 16.1
After SHGT	65.1 ± 11.8	64.9 ± 16.1
Difference	11.6 ± 6.2	8.8 ± 5.5
Valsalva ratio	1.28 ± 0.08	1.27 ± 0.21
HRDB (pulse/min)	14.7 ± 4.21	15.28 ± 8.32

Data are the mean ± SEM. SBP, DBP, systolic and diastolic blood pressure, respectively; SHGT, sustained handgrip test; HRDB, change in heart rate responses to deep breathing.

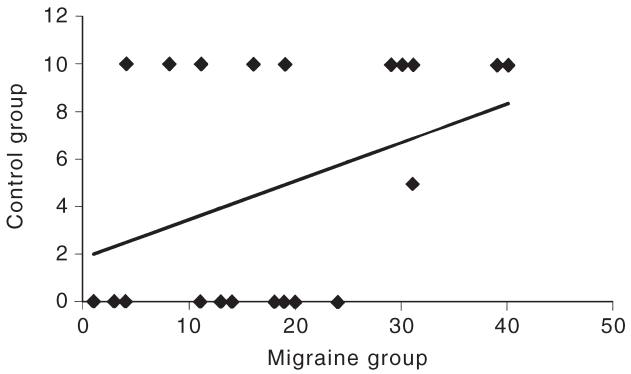

Fig. 1 Relationship between orthostatic test and systolic blood pressure. $y = 0.1639x + 1.814$, $R^2 = 0.1402$.

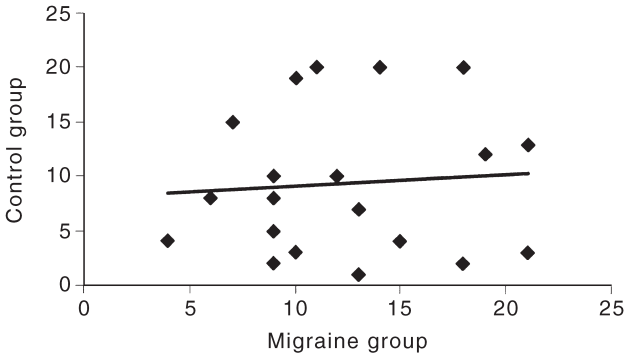

Fig. 2 Relationship between sustained handgrip test and systolic blood pressure. $y = 0.111x + 7.9234$, $R^2 = 0.0069$.

Discussion

In the migraine group during the orthostatic test, SBP and DBP were higher in the upright than the supine position. These results demonstrate hyperactivity of the SNS in the migraine group. In the control group, as expected, SBP and DBP tended to be lower in the upright than the supine position. In the SHGT, the mean difference in SBP was higher in the migraine group than in the control group. The mean difference in DBP was not different between the two groups. These results indicate minimal hyperactivity of the SNS. The Valsalva and 30/15 ratios, tests for evaluating the parasympathetic nervous system, were significantly higher in the migraine group than the control group (Fig. 3). These results demonstrate parasympathetic nervous system dysfunction characterized as hyperactivity. Heart rate responses to deep breathing were not different between the two groups. As a result, these five ANS function tests demonstrate ANS dysfunction with hyperactivity of both SNS and parasympathetic nervous system in children with migraine.

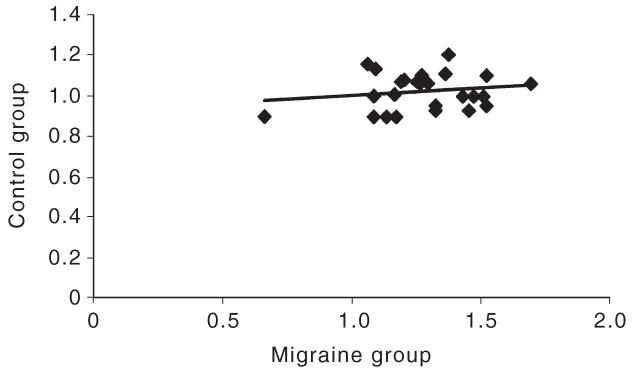

Fig. 3 Comparison of Valsalva ratio between groups. $y = 0.0765x + 0.9254$, $R^2 = 0.0336$.

In the literature, there are many reported studies on ANS function in adult migraine, but few studies of ANS function in childhood migraine.[22] In most of these published studies, ANS dysfunction was determined. Some studies reported SNS hyperactivity,[3–5,9,10,17] while others reported SNS hypoactivity.[6,8,13–15,18–21] All these studies were performed between migraine attacks. Two of the studies performed during a migraine attack reported hypoactivity[11,12] and one study reported hyperactivity of the SNS.[7] Three of the studies, performed during a migraine attack in an adult, reported hypoactivity[19–21] and one study reported mild hyperactivity of the parasympathetic nervous system.[18] The discrepancies in the results of ANS function studies performed in adult migraine may be due to the use of different methods for the evaluation of ANS function. Autonomic nervous system dysfunction was demonstrated in almost all the studies in adult migraine.

The mechanism of migraine has been presented as an unstable trigeminovascular reflex with a segmental defect in the pain control pathway. This defect permits excessive discharge of part of the spinal nucleus of the trigeminal nerve and its thalamic connections in response to excessive afferent input or corticobulbar drive. The end result is the interaction of brain stem and cranial blood vessels, with the afferent impulses from the latter creating the throbbing (pulsating) character of the headache. Brain stem mechanisms may be triggered from the cerebral cortex in response to emotion or stress, from thalamus in response to excessive afferent stimulation (e.g. glare, noise or smells), from the hypothalamus in response to 'internal clocks' or to changes in the internal environment. Warning signs of an oncoming migraine attack, such as changes in mood, thirst and appetite, and somnolence and libido, have been related to hypothalamic dysfunction.[25] It is postulated that factors such as stress, hormonal levels and dietary substances that can influence the brain by decreasing the cortical threshold may change hypothalamic and, subsequently, brainstem activity.[26] The central role of the hypothalamus in the initiation and regulation of autonomic activity is now generally recognized.[27] It is probable that hypothalamic dysfunction causes both ANS dysfunction and migraine headache as a result of the mechanisms mentioned above. Determining the cause(s) of hypothalamic dysfunction in patients with migraine may enlighten this subject further.

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