J Neurol (2010) 257:1642–1647
DOI 10.1007/s00415-010-5582-8

ORIGINAL COMMUNICATION

Painful scalp arteries in migraine

Carlo Cianchetti · Maria Giuseppina Ledda · Maria Celeste Serci · Francesco Madeddu

Received: 21 January 2010 / Revised: 27 March 2010 / Accepted: 27 April 2010 / Published online: 9 May 2010

Abstract Previous studies suggest a role of scalp perivascular structures in at least a substantial number of migraineurs. This study aimed to evaluate the presence of pressure-painful scalp arteries in patients with migraine. Pressure-painful points on scalp arteries were searched for in 100 consecutive patients affected with migraine, 84 females (F) and 16 males (M), 83 without aura (70 F) and 17 with aura (14 F), and in 30 healthy matched subjects. The examined arteries were, bilaterally, the superficial temporal and its frontal branch, the zygomatico-orbital, the occipital and the posterior auricular. We examined 75 patients interictally: 60 (80.0%) reported one or more (mean per subject 3.7 ± 1.9) pressure-painful arteries and 15 (20.0%) reported none. In the 30 controls, pressure-painful arteries were present in only nine (30.0%, mean per subject 1.3 ± 0.7), with highly significant differences ($p < 0.001$). During a migraine attack, of the 51 patients examined, 45 (88.2%, 38F) reported one or more (mean 3.8 ± 2.1) pressure-painful arteries and six (11.8%) reported none. Both when during an attack and interictally, the arteries most frequently involved were the occipital, the frontal branch, and the temporal. Scalp arteries are frequently painful to pressure in migraineurs, especially in females, both during headache and interictally. Painful arteries suggest hypersensitivity of periarterial nociceptive afferents, which is perhaps due to the local presence of endogenous algogenic products, as suggested by our previous studies.

C. Cianchetti (✉) · M. G. Ledda · M. C. Serci · F. Madeddu
Neuropsichiatria Inf., Università di Cagliari, Azienda Ospedaliero-Universitaria, Via Ospedale 119, 09124 Cagliari, Italy
e-mail: cianchet@unica.it

Keywords Migraine · Scalp arteries · Tender · Trigger · Pain

Abbreviations

STA	Superficial temporal artery
F	Female/s
M	Male/s
GON	Great occipital nerve

Introduction

Muscular or myofascial tender and trigger points, both pericranial and in the neck-shoulder region, have been extensively studied in migraine [1–8]. Although migraine is considered to be a neurovascular disorder, evaluation of pressure-painful scalp arteries has never been reported, probably due to the prevailing opinion that only intra-cranial neurovascular structures are involved in migraine.

Immunohistochemical studies [9, 10] showed that perivascular afferent fibers of the superficial temporal artery (STA) contain algogenic peptides. We recently showed that normal saline, when injected around pressure-painful scalp arteries, may attenuate or block a migraine attack in a substantial number of patients [11], which support a role for extracranial neurovascular structures in migraine.

In the present study we aimed to verify, in a larger number of subjects, the prevalence of pressure-painful scalp arteries both during migraine attacks and interictally. As secondary aims, its characterization and relation to some clinical aspects of migraine.

Materials and methods

Subjects

Successive ambulatory patients affected with migraine without and with aura according to ICHD-II criteria [12] were studied.

We examined 100 patients, 84 females (F) and 16 males (M), 83 without aura (70 F) and 17 with aura (14 F). Their ages ranged from 18 to 59 years (mean 40.5 ± 10.9 years). Their history of headache ranged from 1 year to 48 years (mean 22.7 ± 12.6 years). Attack frequency ranged from 1 month to 27 months, with a usual attack duration ranging from 3–4 h to more than 1 day.

Of the 100 patients, 49 (43 F) were examined only interictally, 25 (18 F) only during headache and 26 (23 F) both during headache and interictally; in total, 75 examinations (on 66 F) were carried out interictally and 51 (on 41 F) during headache. As a control, a population of 30 subjects (25 F, 5 M), not suffering from headache and of comparable age to that of the patients examined interictally (18–61 years old, mean 43.0 ± 13.7), were subjected to the same procedures. All the examined subjects gave their informed consent.

Procedures

According to our recent protocol of routine examinations of headache patients, each patient was examined to detect pressure-painful points on scalp arteries. The examination included the following arteries: STA, its frontal branch, zygomatico-orbital, occipital and posterior auricular (all deriving from the external carotid artery), on both sides (Fig. 1). This was done both when headache was present and absent. Here we do not report data on the parietal branch of STA (evaluation frequently difficult, due to the thickness of hair impeding pulse perception) and on supraorbital and supratrochlear arteries (for which it is practically impossible to establish whether pressure is also exerted on the homonymous nerves lying in close contact). The greater occipital nerve (GON) and the occipital artery also frequently cross each other in the occipital subcutaneous layer, but are usually clearly separated in their suboccipital tract.

The localization of the arteries was carried out by detecting their pulse with the light pressure of one or more fingertips, preferably two or three (2nd to 4th fingers) for the STA and its branches; comparison with the patient's radial pulse and with the examiner's own pulse was performed in dubious cases; in a few cases, a phono-Doppler or a portable Doppler apparatus was used in order to confirm the correct location of the artery. Except for the pulse of the STA, always clearly perceptible, perception of the pulse of the other arteries required a very slight finger pressure. Once the artery was clearly localized, compression in order to detect arterial pain was exerted using the same fingertips, preferably two or three (2nd to 4th fingers). With this procedure, guided by the pulsation, it was possible to localize the artery precisely. Therefore, only in a minority of cases and only for comparison with finger pressure, was an algometer (Wagner FDN 50 with a 1-cm^2 rubberized applicator tip) used. As the examiner (always CC) has a good deal of experience in carrying out this test, the intensity of fingertip pressure applied occurred within a narrow range. This range of intensity, according to comparative evaluation with the algometer, was between 1.0 and 2.0 kg/cm^2 on temporal, frontal, and zygomatico-orbital arteries and between 1.5 and 2.5 kg/cm^2 on occipital and auricular arteries. This pressure intensity is lower than that employed in other studies concerning myofascial pressure pain [5, 7, 8].

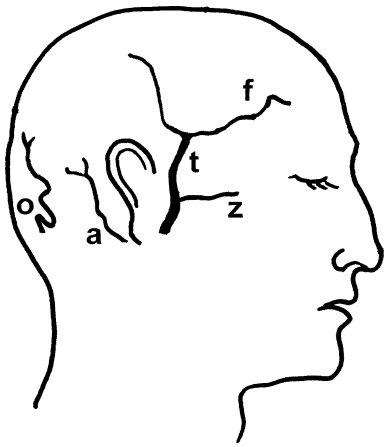

Fig. 1 Arteries compressed during the study: *t* temporal, superficial (STA), *f* frontal branch of STA, *z* zygomatico-orbital, *o* occipital, *a* auricular, posterior

For each compressed artery, pain evaluation was rated on a four-point scale: patients were asked to state whether they felt pain or not, and to rank the pain level from 1 to 3. In practice, bilateral compression on the homonymous arteries was performed with the examiner standing behind the seated subject; the latter answered by extending one (if mild pain) to three (if strong pain) fingers of the closed hand on the corresponding side, or maintaining the fist closed if he/she did not feel pain.

If the patient experienced pain on the compression of an artery, in order to be sure that the pain originated from the artery and not from the underlying muscle or soft tissues, as a control, compression of the same intensity was applied to the adjacent tissues, 0.5 to 1.5 cm distant from the arterial pulse. The patient was asked to compare the pain intensity between the different points.

When the examination was carried out during an attack, a comparison was made between the painful arteries and the present location of headache pain.

A few patients were examined on more than one occasion; since it sometimes happened that arterial tender points varied in subsequent examinations of the same patient, only the results of the last examination were taken into account for the statistical analysis in the present study.

The main parameters evaluated were: 1. The number of pressure-painful arteries. 2. The "severity", a term used to indicate the sum of the degree of intensities (1–3) found for each painful artery.

Statistical analysis

The following tests were used: χ^2 for the comparison between the presence/absence of painful arteries in patients and in controls; nonparametric test U (Mann–Whitney) for the several comparisons involving independent samples with continuous data; linear regression (Pearson's r) to correlate the number of painful arteries and frequency and duration of migraine. Calculations were done using GraphPad Prism software.

The research was approved by the local human research committee. All subjects gave their informed consent.

Results

No headache during examination

Of the 75 patients examined interictally, 60 (80.0%; 56 F) reported one or more pressure-painful arteries, and 15 (20.0%; 10 F) reported none (Table 1). Painful arteries were more frequent in F (84.8%) than in M (44.4%), with a significant difference ($\chi^2 = 8.1$, $p < 0.01$).

Each of the 60 patients had one or more painful arteries as follows: one in eight, two in 12, three in six, and four or more in 34 (in this computation, when tenderness involved the same artery bilaterally this was considered as two points), with a mean of 3.7 ± 1.9 painful arteries. Considering the severity (sum of the degrees of intensity of each painful point), the 60 migraineurs showed a mean value of 5.3 ± 3.3.

In the 30 subjects of the control population, nine (30.0%, all F) presented with painful arteries (Table 1), with pain intensity never higher than one (therefore severity coincides with the number of painful arteries); six had only one painful artery, and three had two painful arteries.

Table 1 shows a comparison between migraineurs and controls. A highly significant prevalence ($\chi^2 = 23.8$, $p < 0.0001$) is found in migraineurs with regard to the number of subjects with at least one painful artery. A similar highly significant prevalence is found in the mean number of painful arteries for each subject (3.7 ± 1.9 $n = 60$ vs. 1.3 ± 0.7 $n = 9$; $U = 65$, $p < 0.001$) and in the severity (5.3 ± 3.3 $n = 60$ vs. 1.3 ± 0.7 $n = 9$; $U = 46$, $p < 0.0001$).

The location of the painful arteries is shown in Table 2. For reasons of space, no distinction was made in the table between unilateral and bilateral location on the same artery. The occipital, frontal, and temporal are the most frequently painful arteries, considered both individually and in association.

It should be underscored that arterial pain was frequently localized in a segment and not on the whole palpable artery.

No significant difference was found between those suffering migraine with aura (ten patients) and those without aura (50 patients) in the number of painful arteries (with aura mean 3.3 ± 1.8, without aura mean 3.8 ± 1.9; $U = 218$, $p = 0.52$) and in severity (with aura 4.4 ± 2.5, without aura 5.4 ± 3.4; $U = 207$, $p = 0.40$).

No correlation was found in the whole population examined (75 patients), between the number of painful arteries and the headache frequency in the last month (Pearson's $r = 0.001$, $p = 0.74$) and the years of duration of the disorder ($r = 0.000$, $p = 0.88$). Correlation was also absent when we excluded the 15 patients not showing painful arteries (respectively $r = 0.000$, $p = 0.96$ and $r = 0.006$, $p = 0.55$).

We had the opportunity to examine 16 patients on different occasions interictally and found that in 13 both the location and/or side of painful arteries changed: in five patients the location changed completely, while in eight patients only one or two points were confirmed.

Table 1 Painful arteries in migraineurs and controls

	No. of subjects with at least one painful artery	Painful arteries in each positive subject (mean ± SD)	Severity (sum of painful arteries and pain intensity in each subject) (mean ± SD)
Migraineurs in absence of headache ($n = 75$)	60 (80%) (56 F)*	3.7 ± 1.9**	5.3 ± 3.3***
Controls ($n = 30$)	9 (30%) (9 F)*	1.3 ± 0.7**	1.3 ± 0.7***

Comparison between migraineurs and controls: * $\chi^2 = 23.8$, $p < 0.0001$; ** $U = 65$, $p < 0.001$; *** $U = 46$, $p < 0.0001$

Table 2 Painful arteries in absence of headache in 60 patients (of 75 examined)

t = 29 (48.3%)	f = 41 (68.3%)	z = 14 (23.3%)	o = 46 (76.7%)	a = 15 (25.0%)	Total no. of painful arteries: 145 (241.7%)
t + o = 5 (8.3%)	f + o = 10 (16.7%)	o + a=5 (8.3%)	t + f + o = 9 (15.0%)	Other associations = 18 (30.0%)	Patients with pain on a single artery = 11 (18.3%)

The upper part of the table shows the total number arteries found painful, monolaterally or bilaterally. The lower part shows more frequent associations of painful arteries, mono- or bi-laterally, in the same patient

t STA, *f* frontal branch, *z* zygomatic, *o* occipital, *a* auricular, posterior

Table 3 Painful arteries during headache in 45 patients (of 51 examined)

t = 24 (53.3%)	f = 27 (60.0%)	z = 14 (31.1%)	o = 32 (71.1%)	a = 9 (20.0%)	Total no. of painful arteries: 106 (235.5%)
f + o = 6 (13.3%)	z + o = 4 (8.9%)	t + f + o = 6 (13.3%)	t + f + o + a = 4 (8.9%)	Other associations = 13 (28.9%)	Patients with pain on a single artery = 12 (26.7%)

The upper part of the table shows the total number of arteries found painful, monolaterally or bilaterally and the lower part shows more frequent associations of painful arteries, mono- or bi-laterally, in the same patient

Headache during examination

Of the 51 patients examined during a migraine attack, 45 (88.2%; 38 F) reported one or more pressure-painful arteries, and six (11.8%; 3 F) reported none. Painful arteries were more frequent in F (92.7%) than in M (70.0%), with a significant difference ($\chi^2 = 3.9$, $p < 0.05$).

Each patient of the 45 had one or more painful arteries as follows: one in eight, two in 12, three in five, and four or more in 20 (again in this case, when tenderness involved the same artery bilaterally this was considered as two points), with a mean of 3.8 ± 2.1 painful arteries and a mean 5.8 ± 3.7 severity.

The location of tender points is shown in Table 3. As in Table 2, for reasons of space, no distinction was made between unilateral and bilateral location on the same artery. As occurred interictally, the occipital, frontal, and temporal arteries were the most frequently painful.

As occurred interictally, arterial pain was frequently localized in a segment and not on the whole palpable artery.

No significant difference was found between those suffering from migraine with aura (eight patients) and those without aura (37 patients) in the number of painful arteries (with aura mean 4.5 ± 2.0, without aura mean 3.7 ± 2.0; $U = 85$, $p = 0.06$) and in the severity of the pain (with aura 6.9 ± 3.6, without aura 5.6 ± 3.6; $U = 93$, $p = 0.10$).

At the time the procedures were performed, the headache was of moderate intensity.

No correlation was found between the number of painful arteries and the headache frequency in the previous month (Pearson's $r = 0.019$, $p = 0.41$) and the years of duration of the disorder ($r = 0.010$, $p = 0.48$) in the whole population examined (51 patients). Correlation was also absent when we excluded the six patients who did not have pressure-painful arteries (respectively $r = 0.008$, $p = 0.62$, and $r = 0.052$, $p = 0.14$).

Pressure-painful arteries were located in the territory of referred spontaneous headache pain in 34 patients (75.5%). On the contrary, they were outside the territory in 11 patients (24.4%) as follows: during intraorbital pain, occipital artery tenderness in four cases (with orbital irradiation of pain during pressure) and temporal-frontal-zygomatic artery tenderness in three cases; during fronto-temporal pain, occipito-auricular tenderness in two cases; during pain at the vertex, temporal and occipital tenderness in two cases (in one of the two also frontal).

Discussion

Our data show that scalp arteries are frequently painful to pressure in migraineurs, with a higher prevalence in females, both during headache and interictally. Often more than one artery is painful in the area of spontaneous headache pain. This study extends our previous data [11] on arterial tenderness in migraine, which were derived from a limited population without controls, since the focus of that study was the evaluation of the possibility of blocking headache using a local intervention.

No other studies on arterial tenderness in migraine are found in the literature.

Tender points (points with reduced pain threshold to pressure, pain remaining localized to the point of pressure) are differentiated from trigger points, in which the

pressure "triggers" spontaneous pain that also refers to remote locations. Many studies have evaluated pressure-pain threshold or tenderness or trigger points in pericranial muscles [1–8] and nerves [13]. Surprisingly, the most frequent "trigger" (not only "tender") points detected by Calandre et al.[5] are located in the same areas ("anterior temporal" in 42.6% and "suboccipital" in 33.4%) of the arteries we found to be most frequently painful. Since they did not determine whether they were exerting pressure on an artery (they report no search for pulsation), there is a possibility that they actually may have done so, without being aware of it. The same might have happened for at least some of the frontal and anterior temporal tender points tested by Fernandez-de-las-Peñas et al. [7, 8].

Calandre et al. [5], in absence of headache, found more frequent "trigger" points than we did. This could be due to the greater pressure they applied to detect the points, since they say "not more than 4 kg", as opposed to our 1.0–2.5 kg/cm^2. A similar difference in pressure intensity might also explain the more frequent muscle tender points found in other studies [7, 8]; moreover, the application of pressure on suboccipital muscles against the vertebrae causes pain more easily.

The frequency of migraine attacks and the duration of the disorder did not correlate with the number of painful arteries in our migraineurs, while Calandre et al. [5] did find such correlation in relation to the number of muscle trigger points, and Fernandez-de-las-Peñas et al. [13] found a negative correlation with pressure pain threshold in the supraorbital nerve. Our data suggest that arterial pain is often inherent in migraine, while attack frequency and duration of the disorder are regulated by other factors, most probably hypersensitivity of pain-regulating centers.

A causative role of cephalic cutaneous allodynia in our results seems improbable, since allodynia is characterized by a more superficial and less precisely localized pain sensation.

The presence of slight (never superior to one point of three) pain at pressure in about 1/3 of the controls (all F) fits well with similar results in other studies on pressure-painful extracranial structures [5, 7], and is probably due to varying hypersensitivity in some subjects, particularly females.

Painful arteries suggest hypersensitivity of periarterial nociceptive afferents, which is perhaps due to the presence locally of endogenous algogenic products. Dilution of these products could explain the effect of the periarterial injection of simple saline [11]. Alternatively, a local hypersensitivity of pain receptors located in the periarterial afferent fibers could be involved. This fits with the beneficial effects of the injection of a local anesthetic [14] and of topical administration of a capsaicin cream [15].

Neuroapraxia could explain the effect of a prolonged compression on the main trunk of those arteries [16–18]. Superficial scalp arteries identified as the source of headache pain were cauterized by Shevel [19] with a beneficial effect.

The higher prevalence of painful arteries in female migraineurs corresponds to a similar sex prevalence in controls, and might be due to differences in sensitivity between the sexes.

A surprising datum is that in a few cases, the painful artery is not included in the area of spontaneous pain. This occurs particularly for occipital artery tenderness during (intra)orbital headache, with an increase of orbital pain during pressure on the artery. The proximity of central pathways coming from the two areas causing an ephaptic interaction could be hypothesized. It should be noted that it is difficult to exclude a pressure on the GON when pressing on the occipital artery, due to their close anatomical relationships (for a review see Pearce [20]), although one would expect pressure on the nerve to cause pain in the area supplied by the GON, i.e., the occiput and the posterior parieto-temporal scalp. The effect of GON block with lidocaine [21] could also be due to an unintentional block of periarterial nociceptive afferents.

In the smaller percentage of patients who felt no pain on arterial pressure both during headache and interictally, only intracranial neurovascular structures might be involved. The evaluation of the clinical, prognostic, and therapeutic differences between these two populations is the object of an ongoing study.

In conclusion, this study shows that:

In a large percentage of patients suffering from migraine, pressure-painful arterial points are present both during a headache attack and interictally, with a very highly significant difference compared to controls.

This suggests a role for neurovascular scalp structures in migraine.

However, a lesser percentage of migraineurs do not present painful scalp arteries, suggesting that in those cases other structures, such as the intracranial neurovascular structures, are involved in the pain process.

Although we found no major clinical differences between these two populations, further studies are suggested in order to determine the presence of possible differences in clinical features, evolution, and therapeutic responses.

The presence of pressure-painful scalp arteries did not differ in relation to the presence of aura, migraine frequency, or disease duration.

The presence of pressure-painful scalp arteries suggests the presence of algogenic substances acting on periarterial nociceptive fibers. Since scalp arteries are accessible to local therapeutic modalities, this could lead to new ways of treatment, as recently reported [15].

Limitations of the study:

The study was not blinded, since the examiner was aware of the diagnosis.
The population examined has a high prevalence of females, who appear more sensitive to pain (although the control population had a similar F/M proportion).
Only some of the patients were examined both during a headache attack and interictally for a comparison.
A clinical comparison (symptoms, evolution, response to therapy) between those with and those without painful scalp arteries will be useful.

Acknowledgments Dr. Mary Groeneweg revised the English language of the manuscript.

Conflict of interest statement None.

References

1. Jensen K, Tuxen C, Olesen J (1988) Pericranial muscle tenderness and pressure-pain threshold in the temporal region during common migraine. Pain 35:65–70
2. Göbel H, Weigle L, Kropp P, Soyka D (1992) Pain sensitivity and pain reactivity of pericranial muscles in migraine and tension-type headache. Cephalalgia 12:142–151
3. Jensen K (1993) Extracranial blood flow, pain and tenderness in migraine: clinical and experimental studies. Acta Neurol Scand Suppl 147:1–27
4. Anttila P, Metsähonkala L, Mikkelsson M, Aromaa M, Kautiainen H, Salminen J, Viander S, Jäppilä E, Sillanpää M (2002) Muscle tenderness in pericranial and neck-shoulder region in children with headache: a controlled study. Cephalalgia 22:340–344
5. Calandre EP, Hidalgo J, García-Leiva JM, Rico-Villademoros F (2006) Trigger point evaluation in migraine patients: an indication of peripheral sensitization linked to migraine predisposition? Eur J Neurol 13:244–249
6. Giamberardino MA, Tafuri E, Savini A, Fabrizio A, Affaitati G, Lerza R, Di Ianni L, Lapenna D, Mezzetti A (2007) Contribution of myofascial trigger points to migraine symptoms. J Pain 8:869–878
7. Fernández-de-las-Peñas C, Cuadrado ML, Arendt-Nielsen L, Pareja JA (2008) Side-to-side differences in pressure pain thresholds and pericranial muscle tenderness in strictly unilateral migraine. Eur J Neurol 15:162–168
8. Fernández-de-las-Peñas C, Madeleine P, Cuadrado ML, Ge HY, Arendt-Nielsen L, Pareja JA (2009) Pressure pain sensitivity mapping of the temporalis muscle revealed bilateral pressure hyperalgesia in patients with strictly unilateral migraine. Cephalalgia 29:670–676
9. Jansen I, Uddman R, Hocherman M, Ekman R, Jensen K, Olesen J, Stiernholm P, Edvinsson L (1986) Localization and effects of neuropeptide Y, vasoactive intestinal polypeptide, substance P, and calcitonin gene-related peptide in human temporal arteries. Ann Neurol 20:496–501
10. Jansen I, Uddman R, Ekman R, Olesen J, Ottosson A, Edvinsson L (1992) Distribution and effects of neuropeptide Y, vasoactive intestinal peptide, substance P, and calcitonin gene-related peptide in human middle meningeal arteries: comparison with cerebral and temporal arteries. Peptides 13:527–536
11. Cianchetti C, Hmaidan Y, Finco G, Ledda MG (2009) Scalp periarterial saline effect on migraine attacks: percentage of positive responses and relation to type of pain. J Neurol 256:1109–1113
12. International Headache Society (2004) The international classification of headache disorders: 2nd edition (ICHD-II). Cephalalgia 24(suppl 1):1–160
13. Fernández-de-las-Peñas C, Arendt-Nielsen L, Cuadrado ML, Pareja JA (2009) Generalized mechanical pain sensitivity over nerve tissues in patients with strictly unilateral migraine. Clin J Pain 25:401–406
14. Cianchetti C, Hmaidan Y (2007) Saline pomphus around scalp arteries can block migraine pain. J Neurol 254:1746–1747
15. Cianchetti C (2010) Capsaicin jelly against migraine pain. Int J Clin Pract 64:457–459
16. Hmaidan Y, Cianchetti C (2006) Effectiveness of prolonged compression of scalp arteries on migraine attacks. J Neurol 253:811–812
17. Cianchetti C, Cianchetti ME, Pisano T, Hmaidan Y (2009) Treatment of migraine attack by compression of temporal superficial arteries using a device. Med Sci Monit 15:185–188
18. Cianchetti C, Serci MC, Pisano T, Ledda MG (2010) Compression of superficial temporal arteries by a handmade device: a simple way to block or attenuate migraine attacks in children and adolescents. J Child Neurol 25:67–70
19. Shevel E (2007) Vascular surgery for chronic migraine. Therapy 4:451–456
20. Pearce JMS (2008) Greater occipital nerve block: a diagnostic test? Adv Clin Neurosci Rehab 8:15–17
21. Bovim G, Sand T (1992) Cervicogenic headache, migraine without aura and tension-type headache: diagnostic blockade of greater occipital and supra-orbital nerves. Pain 51:43–48