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Chronic Headache after Cranio-Cervical Trauma – Hypothetical Pathomechanism Based upon Neuroanatomical Considerations

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Abstract

Background: Chronic headache after whiplash injury is common, but the underlying mechanisms have not yet been elucidated. On the basis of human neuroanatomy, we hypothesize that rear-end collision can cause leakage of the cerebrospinal fluid (CSF) into the epidural space most frequently at the lumbosacral level, inducing chronic headache.

Methods: We considered that the following phenomena would be evident in patients with chronic headache after rear-end collision: (1) orthostatic headache with early onset and long duration, (2) low intracranial pressure (ICP ≤ 60 mm H_2O), (3) CSF leakage mainly in the lumbosacral region on radioisotope-myelocisternography, and (4) diffuse pachymeningeal enhancement (DPE) on gadolinium enhanced magnetic resonant image (Gd-MRI). The clinical signs and symptoms, ICP and neuroimaging findings were analyzed retrospectively in 20 patients who complained of chronic headache after rear-end collisions.

Results: *Headaches were orthostatic and started on the* day of the accident in 14 patients. The headaches lasted more than 3 months in all patients. Mean ICP was 120 ± 30 cm H_2O. Only one patient showed low ICP. RI-myelocisternography revealed signs of CSF leakage at the lumbosacral level in 10 patients. Gd-MRI showed no abnormalities known to be characteristic of spontaneous intracranial hypotension (SIH). Chronic headache disappeared or was diminished in all patients by epidural blood patching in the lumbosacral region.

Conclusion: This clinical study partly supports the validity of our verifiable hypothetical mechanism. The ICP is not low and DPE is not observed on Gd-MRI. Therefore, CSF leakage into the epidural space may not occur, but spinal CSF absorption may be over-activated. This condition may represent a new clinical entity.

Key words: whiplash injury, chronic headache, intracranial hypotension, epidural blood patching, rear-end collision

* The first two authors contributed equally to this paper.

Abbreviations

CNS:	central nervous system
CSF:	cerebrospinal fluid
DPE:	diffuse pachymeningeal enhancement
EBP:	epidural blood patching
Gd:	gadolinium
Gd-MRI:	gadolinium enhanced magnetic resonant image
ICHD-II:	International Classification of Headache Disorders, 2nd Edition
ICP:	intracranial pressure
MRI:	magnetic resonant image
RI:	radioisotope
SAS:	spinal subarachnoid space
SIH:	spontaneous intracranial hypotension

Introduction

Rear-end collision is the most common form of motor vehicle accident in Japan [1] and causes whiplash injury. Chronic headache attributed to this minor injury is listed as a type of secondary headache in the International Classification of Headache Disorders 2nd Edition (ICHD-II) [4]. However, the pathomechanisms and treatment strategies have not yet been established [4, 14]. Whiplash injury can cause a broad spectrum of symptoms other than headache, e.g. lower back pain, paresthesia, temporomandibular joint pain, and memory and concentration difficulties [24].

Spontaneous intracranial hypotension (SIH) is caused by spontaneous leakage of spinal cerebrospinal fluid (CSF) into the epidural space and causes orthostatic headaches [17]. Many other symptoms such as photophobia, back pain, and cognitive impairment have also been noted [17]. SIH often shows characteristic features on magnetic resonant image (MRI), such as diffuse pachymeningeal enhancement (DPE) on gadolinium-enhanced MRI (Gd-MRI), subdural fluid collection, and descent of the brain [7,8]. By means of radioisotope (RI)-myelocisternography, radioactivity rarely reaches the convexities of the brain and leakage of CSF at various spinal levels can be demonstrated [9].

A recent study demonstrates that intracranial hy-

potension caused by CSF leakage from the spine can be associated with whiplash injury [10]. Shinonaga and Suzuki indicate that intracranial hypotension may be one of the causes of post-traumatic syndrome [20]. In both studies, spinal CSF leakages were observed most frequently at the lumbosacral level [10, 20]. However, patients with whiplash injuries and true SIH were treated as a single group. Furthermore, the pathomechanisms involved in the development of CSF leakage after whiplash injury were not rationally investigated.

In this study, we propose a hypothetical mechanism based upon neuroanatomical and physiological considerations. The purpose of this retrospective clinical study is to verify our hypothesis that rear-end collision can cause CSF leakage most frequently at the lumbosacral level, which in turn induces chronic orthostatic headache like that observed in SIH [6, 17].

Hypothesis of Pathomechanism and Patients

Our hypothetical mechanism of whiplash injury based upon neuroanatomical and physiological considerations such as:

1. In the posterior fossa, there is a large CSF pool in the cisterna magna, which directly communicates with the spinal subarachnoid space (SAS) (Fig. 1).
2. The covering of the arachnoid membrane forms a sharp subarachnoid angle upon merging with the pia mater [15].
3. Myelographic investigations have demonstrated that the protrusions of the CSF pouches covering the spinal nerve roots leaving the spinal cord are almost perpendicular at the cervical and thoracic levels but leave obliquely at the lumbosacral levels [19].
4. The specific gravity of the central nervous system (CNS) is greater than that of the CSF [2].
5. Epidural pressure is negative or very low [21, 23].
6. Humans maintain an upright position (to stand or to sit) except when asleep.

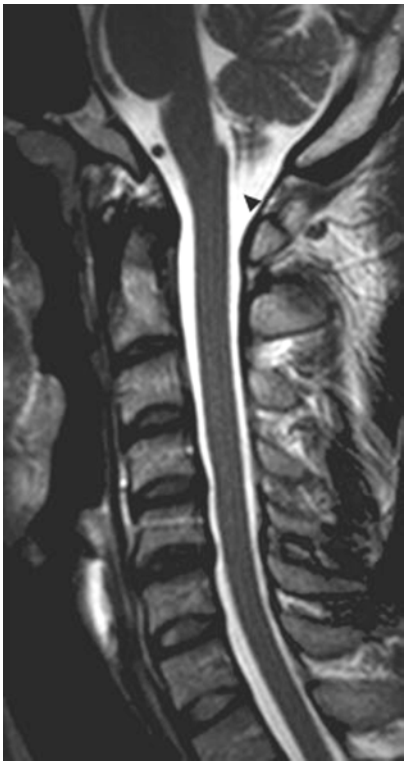

Fig. 1. Cisterna magna and spinal subarachnoid space. Sagittal section of T2-weighted brain MRI shows the large pool of CSF in the cisterna magna (arrow head) that connects directly to the spinal subarachnoid space.

Figure 2A demonstrates a simplified model of the arachnoid membrane containing CSF. In this model, CNS is omitted to allow consideration of CSF movement in the event of whiplash injury.

It is well know that whiplash injury can cause frontal and temporal lobe contusion [16]. On whiplash injury, the cerebrum moves rapidly to and fro, and the frontal and temporal lobes strike the skull at high speed, causing cerebral contusion. However, movement of the cerebellum in whiplash injury has not yet been well considered. When the head hits a seat headrest as a result of a rear-end collision, the cerebellum moves backward with rapid acceleration as a result of inertia and compresses the CSF in the cisterna magna. The arachnoid membrane containing spinal CSF is elastic. Therefore, CSF must be pushed out- and downward

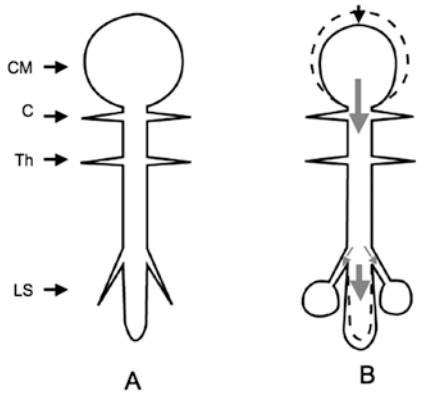

Fig. 2. Simplified model of the arachnoid membrane containing CSF (A) and CSF movement upon rear-end collision (B).
(A) Simplified model:
The central nervous system is neglected. Large circle at the top represents the cisterna magna. The spinal subarachnoid space is demonstrated as a straight pipe. Subarachnoid spaces covering the spinal nerve roots exiting the spinal cord are represented only in 3 (C : cervical, Th: thoracic, LS: lumbosacral). Only the exit of the lumbosacral spinal root is oblique to the spinal cord.
(B) CSF movement on rear-end collision:
On whiplash injury by rear-end collision, the cerebellum moves backward with rapid acceleration due to inertia and compresses the CSF in the cisterna magna (perpendicular black arrow). The arachnoid membrane containing the spinal CSF is elastic. Therefore, the CSF space in the LS region is expanded. Thick gray arrows represent flow of CSF. Because there is no perpendicular component of the flow velocity to the downward CSF flow, the cervical and thoracic arachnoid angles do not receive force. The load resulting from high-speed CSF flow stresses only the subarachnoid angle at the LS level (oblique thin arrows). The circles at LS level indicate the force.

into the spinal canal by this motion of the cerebellum (Fig. 2B). Since no perpendicular component of the flow velocity is present, the cervical and thoracic arachnoid angles are not damaged. Figure 2B also demonstrates that the load resulting from high-speed CSF flow stresses only the subarachnoid angle at the lumbosacral level. This CSF movement may damage the reflected portion of the arachnoid membrane covering the spinal nerve roots at the lumbosacral level [15].

Once the arachnoid membrane is damaged, the dura mater may also be injured, causing CSF leakage into the epidural space, resulting in low ICP. The damaged membranes may not be easily repaired, since humans are usually upright and the hydrostatic pressure constantly stresses the damaged portion.

If this hypothesis is valid, the following phenomena would be observed in patients with chronic headache after rear-end collision; (1) orthostatic headache with an early onset and long duration [4], (2) low ICP ($\leq$ 60 mm H_2O) [17], (3) CSF leakage mainly at the lumbosacral level on cisternography [10, 20], and (4) DPE on Gd-MRI [7, 8].

Patients

A retrospective analysis of prospective gathered data including all diagnostic procedures performed routinely for diagnosis of patients with orthostatic headache. An informed consent to use these clinical data was obtained from all patients.

Within one year, 49 consecutive patients complaining of various symptoms including chronic headache, back neck pain, vertigo, easy fatigability, and loss of concentration after traffic accidents were admitted to the Department of Neurosurgery. The types of accidents are shown in Figure 3. All of the patients were suspected to have traumatic intracranial hypotension. Gd-MRI was performed as soon as possible (patients with a history of asthma did not received Gd-enhancement). Axial sections of the brain were routinely taken with coronal and sagittal sections (T2-weighted / T1-weighted imaging). Clinical reports on the neuroimaging data were prepared by experienced neuroradiologists. The patients also underwent spinal tap with ICP measurement and a small amount of CSF sampled followed by RI-myelocisternography (Indium(^{111}In) DTPA Injectable, Nihon Mediphysics, Tokyo, 37 MBq, 1 ml intrathecal injection).

Twenty-three patients suffered from whiplash injuries caused by rear-end motor vehicle collisions. Among them, 20 patients were not hospitalized on the day or shortly after the accidents because they had neither objective neurological deficits nor serious radiological abnormalities attributable to the accidents. These 20 consecutive patients participated in this study with positional headache.

In accordance with the previous studies [10, 20], placement of an epidural blood patch (EBP) was performed as a treatment modality when the patient was strongly suspected to have orthostatic headache due to CSF leakage. Although whiplash injury can cause many signs and symptoms [4, 20, 24], we focused only on headache to evaluate the effectiveness of the treatment.

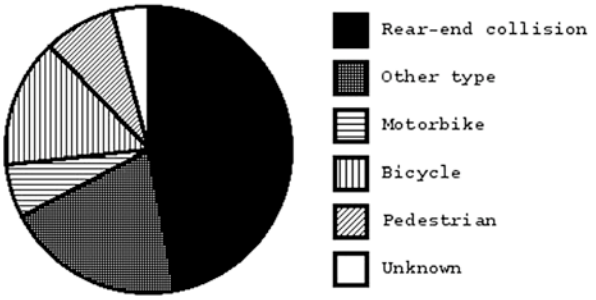

Fig. 3. Types of traffic accident. Among 49 patients with chronic headache after traffic accidents who underwent RI-myelocisternography, 23 encountered rear-end collision.

Results

20 patients (10 males and 10 females) participated in this pilot study. The mean age was 45 $\pm$3 years. Despite many associated symptoms such as memory difficulties, photophobia, and vertigo, no definite neurological deficits such as hemiparesis or anisocoria were observed. (Table 1)

Although it was unclear from the clinical records whether the headaches fulfilled the criteria for orthostatic headache associated with low ICP [4], an upright position worsened the headache, whereas recumbency relieved it in all patients. Low atmospheric pressure (characterized by weather such as rain and typhoons) worsened the headache in 17 cases. Seventeen patients noticed that taking a bath relieved the headache. Intracranial pressures in lateral recumbency were measured in 17 cases. Mean ICP was 120 $\pm$ 30 mm H_2O (Fig. 4: mean $\pm$ SD, n = 17, ranging from 0 to 260 mm H_2O). The appearance of the CSF was watery clear in all cases. Cerebrospinal fluid cell counts, protein levels, and specific gravities were all normal except in 4 patients, whose CSF protein levels were slightly higher than normal (data not shown). RI-myelocisternography showed signs of epidural CSF leakage from the

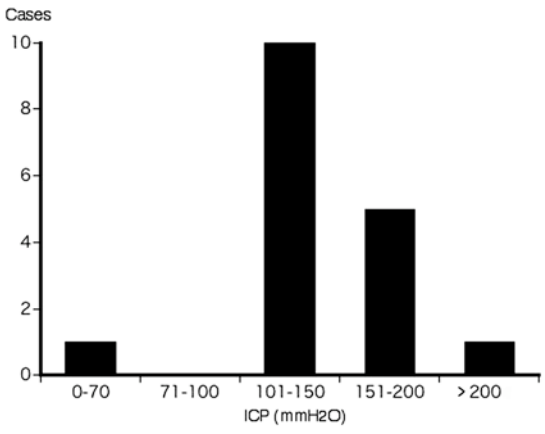

Fig. 4. Case distribution of ICP levels. Intracranial pressures were measured in 17 patients. Among them, only one had low ICP (0 mm H_2O). The other 16 cases showed normal or even high ICP levels.

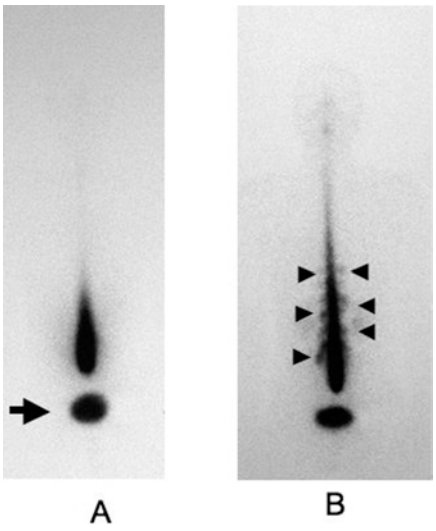

Fig. 5. Typical CSF leakage on RI-cisternography
(A) Anterior view, 2 hours after intrathecal radioisotope (RI, Indium(^{111}In) DTPA Injectable, Nihon Mediphysics, Tokyo, 37 MBq, 1 ml) intrathecal injection. Bladder was filled (black arrow, early bladder filling).
(B) Posterior view, 4 hours after intrathecal RI injection. Christmas tree-like image (arrow heads), believed to a sign of CSF leakage, is shown mostly in the LS level and slightly in the Th level.

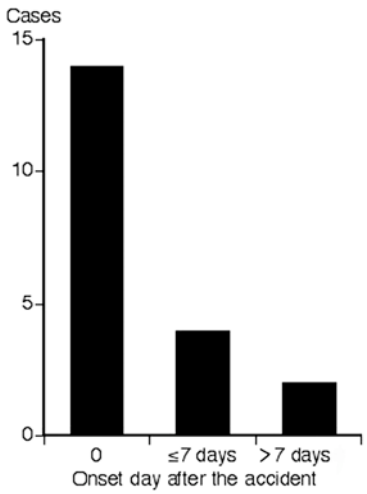

Fig. 7. Onset
Onset of the symptoms occurred on the day of the accident in 14 cases. Only one patient complained of headache beyond 7 days after the accident.

lumbosacral or lower thoracic levels in 10 patients (50%). A typical finding is demonstrated in Figure 5. No direct signs of CSF leakage at the cervical or higher thoracic regions were observed in any patients. Indirect signs of CSF leakage into the epidural space (early bladder filling; detection of radioactivity in the bladder as early as 2 hours after intrathecal injection of ^{111}In) were observed in 18 patients (90%). Two patients showed no signs of CSF leakage. Seventeen patients underwent Gd-MRI, and neuroradiologists reported no definite abnormalities associated with SIH. In only one patient, a neuroradiologist observed slight dural enhancement on Gd-MRI, compatible with SIH. Chronic subdural hygroma or haematoma, which is frequently observed in cases of SIH [22], was not observed in any of the present patients. Figure 6 shows one typical patient (55-year-old male) who complained of chronic orthostatic headache after rear-end collision. Sagittal and coronal Gd-MRI images demonstrated an enlarged fronto-parietal high-convexity subarachnoid space without descent of the tonsil. Although the degrees of extension and depth of the enlargement of medial high-convexity subarachnoid space differed, this finding was observed in 13 patients (65%). Figure 7 clearly demonstrates that the symptoms appeared most frequently on the day of the acci-

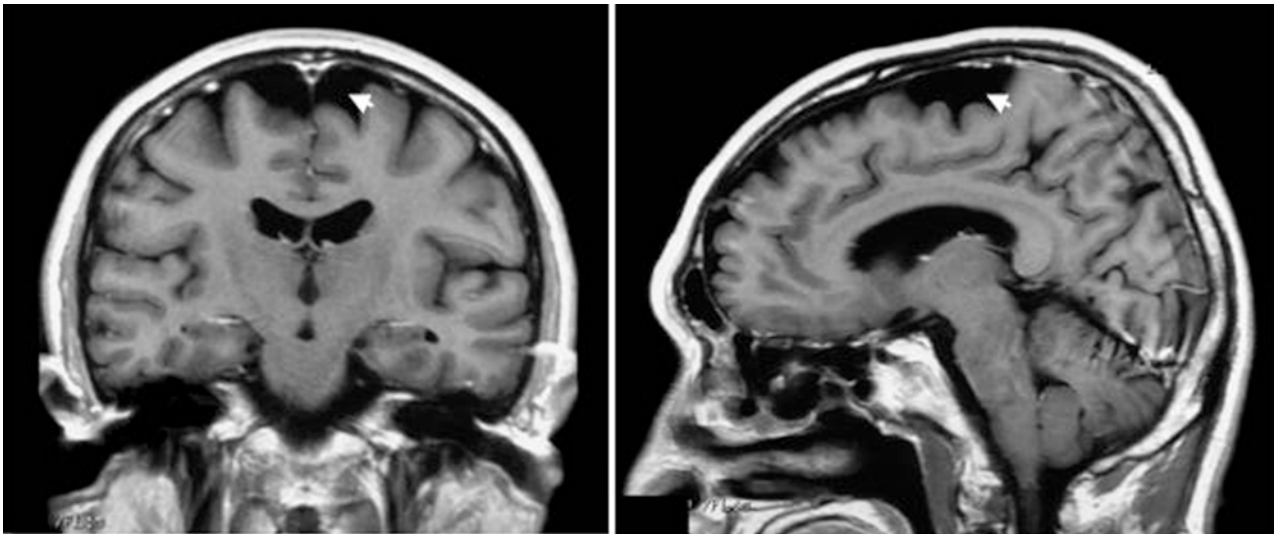

Fig. 6. Typical Gd-MRI
(A) Coronal section: no signs of DPE, with an enlarged subarachnoid space (white arrow) in the medial high-convexity region on both sides.
(B) Sagittal section: no signs of venous enlargement. The fronto-parietal subarachnoid space is enlarged (white arrow).

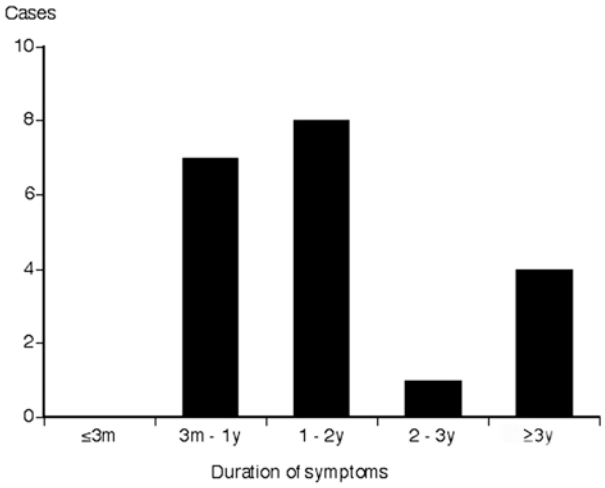

Fig. 8. Duration of symptoms. All patients complained of headache over 3 months.

dent. Eighteen of the 20 patients became aware of their symptoms within 7 days. Figure 8 shows that all of the patients complained of headache over a period of 3 months. Bed-rest and intravenous fluid administration temporarily relieved the symptoms in all cases. All the patients received EBP placement at the lumbosacral level without serious complications. Although the chronic headaches were resolved or diminished in all patients by EBP, complete remission of the symptoms was not achieved in any patient.

Discussion

As we expected, the character of the headache after whiplash injury caused by rear-end motor vehicle collision is positional, the onset of the symptoms is quite early, and the headache lasts for a long time. RI-myelocisternography demonstrated direct signs of CSF leakage at the lower lumbosacral or lower thoracic levels in 50% of the patients. Direct signs of CSF leakage at the cervical or higher thoracic level were not observed in any of the cases. However, contrary to expectation, the ICP was not low except in one patient. Furthermore, Gd-MRI did not show typical DPE

Therefore, the results of this retrospective clinical study partly support our hypothetical mechanism to explain the chronic headache that occurs after rear-end collision. It must be considered why the ICP was normal and no typical DPE was observed in all of the patients. Since DPE is considered to be characteristic of SIH [7, 8, 17] in the context of the headache associated with low intracranial pressure and one of our patients with very low ICP showed slight DPE compatible with SIH, the only discrepancy between the findings expected from our hypothetical mechanism and the observed phenomena was intracranial pressure. Since the spinal epidural pressure is negative or very low [21, 23], leakage of CSF into the spinal epidural space causes intracranial hypotension. When this occurs spontaneously, it is called SIH [17]. Taking these previous studies and the present clinical results into consideration, it is suggested that CSF leakage into the epidural space may not take place in patients with chronic headache after rear-end collision.

Mokri has broadened the clinical and imaging spectrum of the syndrome [6]. He has proposed the term CSF hypovolemia, which includes four modes depending on the symptoms, ICP, and the findings of Gd-MRI [6]. Type I shows orthostatic headache, low ICP, and DPE. Type II shows orthostatic headache, low ICP, but not DPE. Type III shows orthostatic headache, normal ICP, and DPE. Type IV shows low ICP, DPE, but not orthostatic headache.

Our patients had positional headache but the ICP was normal and Gd-MRI did not show DPE. As shown in Figure 6, at least intracranial CSF was ample or excessive. Therefore, "CSF hypovolemia" may not be the proper term to describe our cases. Although headache is one of the most common symptoms, this type of positional headache after rear-end collision has not yet been described.

Based upon previous studies, we have hypothesized that damage to the dura mater results in low ICP. However, 16 of the present patients showed normal or high ICP and only one had an ICP of 0 mm H_2O, in whom Gd-MRI demonstrated slight DPE. We suspect that dural damage had occurred only in this case, and that the dura mater was intact in all the others. Mokri also described orthostatic headache without low ICP.

Schievink has stated that SIH is caused by spontaneous leakage of spinal CSF into the epidural space, and results in orthostatic headache [17]. Many other symptoms such as photophobia, back pain, and cognitive impairment are reportedly associated with SIH [17]. Our patients also showed a range of symptoms (Table 1). These symptoms are also known to occur in hyperextension-hyperflexion injury (whiplash injury) resulting from motor vehicle accidents [24]. The findings of RI-myelocisternography and the effectiveness of EBP placement at the lumbosacral level suggest that CSF leakage at this level takes place in these patients. However, CSF may not leak into the epidural space.

Table 1. List of symptoms.

Symptoms	No. of patients
Headache and/or back neck pain	20
Shoulder stiffness and/or shoulder pain	4
Backache	6
Lumbago	1
Numbness in extremities	3
Vertigo and/or tinnitus	3
Eye symptoms (pain, diplopia, photophobia)	7
Memory and/or concentration difficulties	8

Edsbagge et al. have demonstrated the spinal CSF absorption in healthy individuals [3]. They estimated that 38 ± 20% (mean ± SD) of the CSF absorption in resting healthy individuals and 76 ± 25% in active individuals was from spinal subarachnoid space. We speculate that over-activated CSF absorption from

SAS induced by the whiplash injury may be the cause of positional headache after rear-end collision.

Taken together, these findings suggest that chronic headache after rear-end collision may constitute a new clinical entity.

We propose a new verifiable hypothetical mechanism for chronic headache after rear-end collision partly supported by this retrospective clinical study. Previous investigations of whiplash injury have been carried out in the context of cerebral contusion or mechanical cervical damage [5, 11, 16, 18, 24]. This study spotlights a new aspect of whiplash injury caused by rear-end collision indicating that the head and/or neck injuries may cause abnormalities of CSF circulation by alterations of fluid dynamics that can result in long lasting neurological symptoms without visible damage of the CNS. The results of this clinical study are sufficiently convincing to prompt further experimental and clinical studies. To confirm our simulation quantitatively, a realistic plastic model [13] or mathematical simulation [12] is indispensable.

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