Intracranial Hypertension Is Painless!

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Abstract *Introduction:* Headache is usually considered a key symptom of intracranial hypertension (ICHT). However, there are no published experimental data to support the concept that increased intracranial pressure (ICP) is painful in humans. *Materials and Methods:* This prospective study was performed in 16 patients with suspected normal-pressure hydrocephalus, necessitating a lumbar infusion test with measurement of cerebrospinal fluid (CSF) hydrodynamics. During the test, ICP was increased from baseline to a plateau. Headache was scored on a visual analog scale (VAS) (0 = no pain, 10 = very severe pain) at baseline ICP and when ICP plateaued. *Results:* At baseline, mean ICP was 11 ± 3.6 mmHg and VAS was 0. At plateau, mean ICP was 28 ± 9.5 mmHg and VAS was 0. There was a significant increase in ICP (p <0.001), but no increase in headache intensity (VAS). An acute (20-min) moderate increase in ICP was not accompanied by a headache. *Discussion:* We demonstrate that an acute, isolated increase in CSF pressure does not produce a headache. To occur, a headache needs activation of the pain-sensitive structures (dura and venous sinuses) or central activation of the cerebral nociceptive structures. This peripheral or central activation does not occur with an isolated increase in CSF pressure.

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Introduction

Headache (pain anywhere in the region of the head) is a symptom of a number of different conditions; however, intracranial diseases can produce pain by only a limited number of mechanisms. Headache is usually considered a key symptom in the clinical presentation of increased intracranial pressure (ICP). There is no clear definition of intracranial hypertension, but 25 mmHg is an accepted upper threshold [1]. Intracranial hypertension is deemed to cause headache in acute or chronic situations associated with increased ICP, such as brain tumor, intracranial bleed or idiopathic intracranial hypertension (*pseudotumor cerebrii*). However, voluntarily increased ICP does not always cause a headache (e.g., Valsalva maneuver).

The following intracranial structures are pain-sensitive: meningeal arteries, proximal portions of the cerebral arteries, dura (skull base), and venous sinuses. Nociception is conducted by cranial nerves (CNs) V, VII, IX, X and the C1, C2 and C3 nerves, mainly to the trigeminocervical nucleus within the brainstem (Fig. 1) [2].

If there is a causality between intracranial hypertension and headache, then increased ICP should activate pain-sensitive structures within the brain. However, there are no published experimental data to support the concept that intracranial hypertension per se, that is, increased ICP, is painful in humans. We wanted to measure how painful a controlled acute moderate ICP increase might be.

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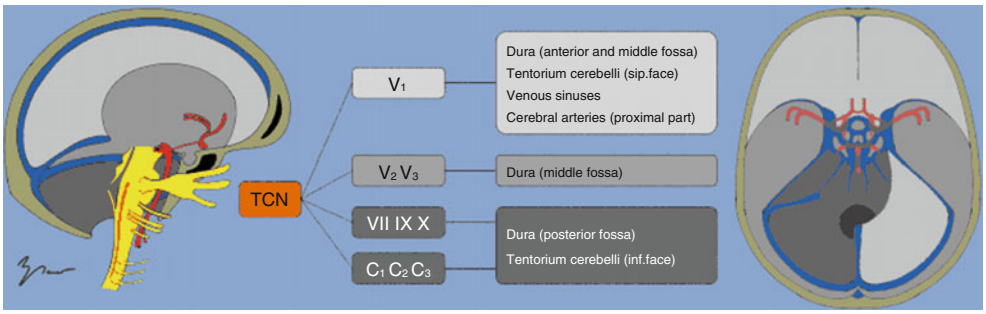

Fig. 1 Anatomy of intracranial pain sensitive structures. *Sagittal view*: neurological structures implied in intracranial pain integration (*TCN*: trigeminocervical nucleus/cranial nerves V, VII, IX, X/cervical nerves C1, C2, C3). *Superior view* of skull base: dural and vascular pain-sensitive territories (Illustration: R. Manet)

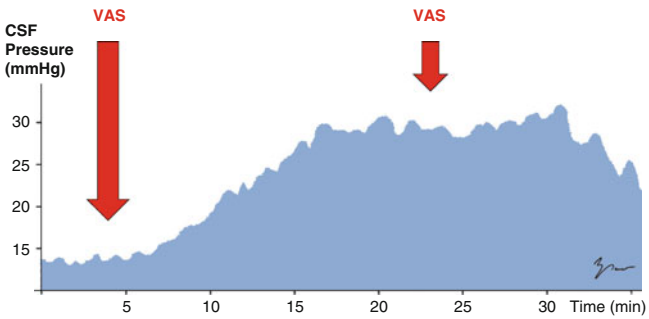

Fig. 2 Schematic representation of an infusion test. During the infusion study, intracranial pressure (ICP) increased from baseline to a plateau. *Red arrows* indicate visual analog scale (VAS) evaluations (illustration: R. Manet)

Materials and Methods

Sixteen patients (9 female, 7 male, mean age 69), with suspected normal-pressure hydrocephalus, were prospectively included. CSF infusion tests were performed via lumbar single needle puncture. CSF pressure is a surrogate marker of ICP [3]. During the infusion test, saline was injected into the subarachnoid space. ICP increased from baseline to a plateau (Fig. 2). A visual analogue scale (VAS) was used to measure headache (0 = no pain, 10 = very severe pain) at baseline ICP and when ICP plateaued (Fig. 2).

Results

Table 1 displays the results. During the timeframe of an infusion test (20 min), ICP increased significantly to a level of intracranial hypertension, but did not yield a headache in any of the patients.

Table 1 Comparison of intracranial pressure (ICP) and visual analog scale (VAS) score at baseline and plateau

	Baseline		Plateau	
	ICP (mmHg)	VAS	ICP (mmHg)	VAS
Mean (SD, minimum, maximum)	11 (3.6; 7; 22)	0	28 (9.5; 17;49)	0

Discussion

In our study, we demonstrate that intracranial hypertension is painless. Indeed, an acute moderate rise in CSF pressure did not produce a headache. Hence, increased ICP does not result in the activation of intracranial pain-sensitive structures. Intracranial nociceptors are deemed to be multimodal, highly sensitive to mechanical stimuli, with a probable enhancement of their sensitization by chemical irritants [4]. Traction on the intracranial basal dura or distortion of the intracranial vessels would be the main mechanical nociceptive stimulation able to promote headache. Intracranial expansive processes that distort the dura or the intracranial vasculature (in particular at the skull base) induce headache by the same stretching stress, even in the absence of raised ICP.

In contrast, "low pressure headache" can result from any situation of CSF low pressure (following drainage or leakage). In these cases, headache is presumed to result from the traction on the venous sinuses when the brain sinks toward the tentorium, as it loses CSF flotation. This is thought to be the mechanism of headache following lumbar puncture, which is relieved when the patient lies down.

In our study, we analyzed intracranial hypertension for roughly half an hour. We cannot say what would happen under such conditions for a longer time period. Chronic raised ICP in relation to idiopathic intracranial hypertension can elicit a headache. Moreover, some authors have

described headache triggered by the head-down tilt test, presumably due to an increase in the intracranial CSF volume [5]. It is important to emphasize that these two situations correspond not only to raised ICP, but also to raised venous pressure. It has also been shown that disturbance in CSF flow may produce headache in Chiari malformation [6].

Overall, we infer, from our observation, that the CSF component of ICP does not elicit a headache per se, but probably because of pressure gradients, resulting in structural changes and displacement of the structure of the encephalon, causing stretching stress over the dura and venous sinuses of the skull base.

Conflict of Interest None.

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