

CONSENSUS STATEMENT

Consensus document on neurosonological techniques in headaches

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KEYWORDS

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Abstract

Introduction: Neurosonology is a medical discipline that utilizes ultrasound techniques to study the nervous system, with its applications progressively increasing. The indications and methodology for applying these techniques in patients with headaches are not well defined, thus there is a need for a consensus guideline, based on expert opinion, to standardize their application in clinical practice.

Development: Experts in headaches and neurosonology, appointed by the headache study group of the Spanish Society of Neurology and the Spanish Society of Neurosonology, identified primary and secondary headaches where neurosonology has the greatest clinical application. A qualitative systematic review of the literature was conducted, based on available scientific evidence.

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Conclusions: Cervical color duplex is considered a screening technique in patients with a high clinical suspicion of arterial dissection and may also be indicated for follow-up. Transcranial Doppler is a useful technique for evaluating the presence of vasospasm based on changes in mean flow velocity, and resistance and pulsatility indexes. Identification of the halo sign is highly specific for temporal arteritis. Measurement of the optic nerve sheath allows evaluation of the presence of intracranial hypertension. Finally, neurosonology may assist in occipital infiltration procedures or lumbar puncture and enables identification of changes in structures involved in the pathophysiology of migraine such as the periaqueductal gray matter and the raphe nuclei. © 2024 Sociedad Española de Neurología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

PALABRAS CLAVE

Neurosonología;
Cefalea;
Diagnóstico

Documento de consenso sobre técnicas neurosonológicas en cefaleas

Resumen

Introducción: La neurosonología es una disciplina médica que utiliza las técnicas de ultrasonografía para estudiar el sistema nervioso, y sus aplicaciones van progresivamente en aumento. Las indicaciones y la metodología de aplicación de estas técnicas en pacientes con cefalea no están bien definidas por lo que existe la necesidad de una guía de consenso, basada en la opinión de expertos, que permita estandarizar su aplicación en la práctica clínica.

Desarrollo: Expertos en cefaleas y neurosonología, designados por el grupo de estudio de cefaleas de la Sociedad Española de Neurología y la Sociedad Española de Neurosonología, identificaron las cefaleas primarias y secundarias en las que neurosonología tiene mayor aplicación clínica. Se realizó una revisión sistemática cualitativa de la bibliografía, en base a la evidencia científica disponible

Conclusiones: El dúplex color cervical se considera una técnica de screening en pacientes con alta sospecha clínica de disección arterial y podría estar indicada también para el seguimiento. El Doppler transcraneal es una técnica útil para evaluar la presencia de vasoespasm basándose en los cambios la velocidad media de flujo, e índices de resistencia y pulsatilidad. La identificación del “signo del halo” es altamente específico de arteritis temporal. La medición de la vaina del nervio óptico permite evaluar la presencia de hipertensión intracraneal. Finalmente, la neurosonología puede ser de ayuda en procedimientos de infiltración occipital o para la realización de una punción lumbar y permite identificar cambios en las estructuras involucradas en la fisiopatología de la migraña como la sustancia gris periacueductal y los núcleos del rafe.

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Introduction

Neurosonology is a medical discipline that uses ultrasound-based techniques to study the nervous system. Currently, the indications and application of these techniques in patients with headache are not clearly defined, highlighting the need for a consensus guide based on experts' opinions to standardise their use in clinical practice.

The Spanish Society of Neurology's Headache Study Group and the Spanish Society of Neurosonology created a panel of experts, who reached a consensus on the primary and secondary headaches in which neurosonology techniques have a more prominent role.

A qualitative systematic literature review of the available evidence was conducted on such databases as PubMed and Cochrane Library to identify articles published from January 1990 to January 2024, as well as clinical practice guidelines and consensus statements, incorporating the authors' experience.

Spontaneous cervical artery dissection

Cervical artery dissection, defined by the presence of haematoma in the wall of the carotid or vertebral artery, represents one of the leading causes of stroke in young adults.^{1,2} The most frequent initial manifestations are headache and neck pain.^{1,2} Diagnosis of extracranial artery dissection requires imaging evidence of at least one of the following specific findings³: intramural haematoma, dissecting aneurysm, long stenosis or occlusion with a characteristic flame-shaped or tapering appearance, intimal flap, double lumen, or occlusion located > 2 cm above the carotid bifurcation revealing a dissecting aneurysm.

MRI and CT are the techniques of choice for confirming the presence of arterial dissection, while digital subtraction angiography is reserved for young adults with high clinical suspicion and negative findings on non-invasive imaging.^{1,4}

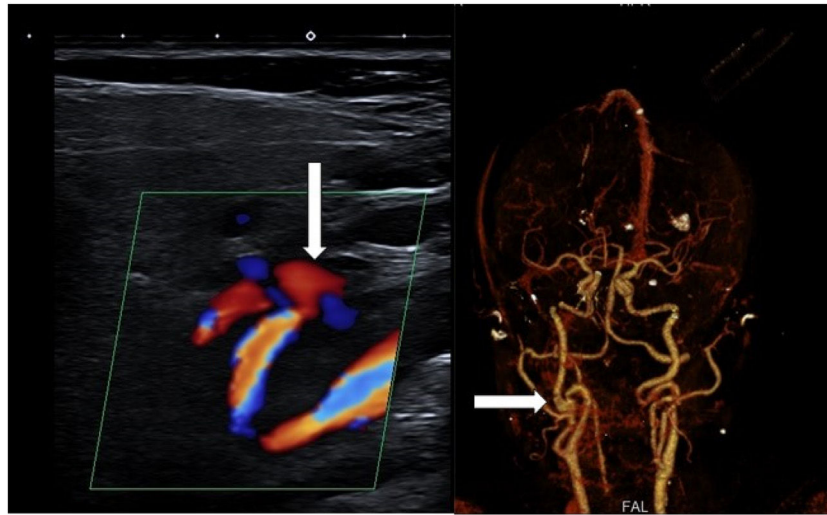


Figure 1 Duplex ultrasound and CT angiography reconstruction showing a dissecting aneurysm in a patient with history of right internal carotid artery dissection.

According to several studies, the sensitivity of neurosonology techniques (colour duplex ultrasound) for detecting severe dissection when performed by experts in the field is higher than 90%, compared to MRI or CT.^{5,6} However, ultrasound assessment of the supra-aortic trunks has important limitations^{1,2} in the assessment of certain artery segments (eg, supramandibular segment of the carotid artery and V2 segment of the vertebral artery), short dissections, dissections with minimal stenosis, and dissections manifesting exclusively with local symptoms, such as Horner syndrome.⁷ Therefore, confirmation by MRI or CT is essential when extracranial artery dissection is suspected based on neurosonology findings.^{1,8,9}

Stenosis and occlusion are the most frequently reported findings in cervical artery dissection.⁵ However, these are nonspecific, with the characteristic flame-shaped morphology only occasionally being observed.⁹ Unlike typical stenoses, arterial dissection often presents with intrastenotic peak systolic velocities that are not markedly elevated, with a post-stenotic flow pattern characterised by very high resistance and slow diastolic flow.⁹

On many occasions, ultrasound does not reveal specific signs of arterial dissection. Specifically, the detection of a double lumen or an eccentric hypoechoic area suggestive of mural thrombus is observed in fewer than 25% of patients,⁵ while the intimal flap is detected even less frequently.^{5,7} However, dissecting aneurysms may be visualised when present (Fig. 1).

In the light of the above, cervical colour duplex ultrasound is currently considered a screening tool for patients with strongly suspected arterial dissection, and may also be useful in follow-up.^{1,8,9}

Intracranial artery vasospasm. Subarachnoid haemorrhage. Reversible cerebral vasoconstriction syndrome

Thunderclap headache is the most frequent manifestation of subarachnoid haemorrhage (SAH). Vasospasm is one of the

most frequent complications of SAH, occurring in 30%-70% of patients, and can be assessed with transcranial Doppler ultrasound (TDU). In one-third of cases, vasospasm may result in delayed ischaemia or represent an angiographic finding with no clinical correlation.¹⁰ It involves pathological narrowing of the cerebral arteries, and typically presents 3 to 7 days after SAH. TDU may be useful due to its non-invasive nature.¹¹ Mean flow velocity (mV), the most relevant measure in the evaluation of vasospasm, is typically elevated in these patients. The resistivity and pulsatility indexes, which reflect changes in vascular resistance, must also be analysed, as they are also usually elevated.¹²

To mitigate such confounding factors as age or conditions affecting cerebral blood flow, corrected indexes are used, such as the Lindegaard index, which is defined as the ratio of mV in the middle cerebral artery to mV in the extracranial internal carotid artery.¹³ Table 1 presents standardised mV, Lindegaard index, and Sloan ratio values for the diagnosis of vasospasm in the different arteries of the circle of Willis.¹⁴

Reversible cerebral vasoconstriction syndrome (RCVS) is a clinical-radiological syndrome probably resulting from endothelial dysfunction and abnormal vascular tone regulation. It is characterised by diffuse, multifocal, segmental arterial vasoconstriction that typically resolves within 3 months. RCVS may be accompanied by SAH and/or ischaemic foci.¹⁵ It can be idiopathic or secondary, with common triggers including early postpartum state, pre-eclampsia, and the use of certain medications, mainly serotonergic, sympathomimetic, or immunomodulatory agents. The clinical hallmark of the condition is recurrent thunderclap headache,¹⁶ which may be associated with focal neurological symptoms and/or epileptic seizures.¹⁷

Currently, angiography remains the gold standard for diagnosing RCVS.¹⁸ TDU has nearly 90% sensitivity as compared to arteriography.^{19,20} The main finding is increased flow velocity in at least one of the major cerebral arteries (mean of 120 cm/s), with maximum values between the third and fourth weeks after symptom onset.

The parameters used to establish the severity of vasoconstriction are typically the same as those applied in vasospasm following SAH.

Table 1 Standard flow velocity values and corrected indexes for the diagnosis of vasospasm in the different arteries of the circle of Willis.

Artery	PSV (cm/s)	mV (cm/s)	LI/SR
MCA	108	35–90	< 3
Mild vasospasm	200–250	120–150	3–4
Moderate vasospasm	250–300	150–200	4–6
Severe vasospasm	> 300	> 200	> 6
ACA			
Mild-to-moderate vasospasm	> 120	> 80	> 4
Severe vasospasm	> 155		
ICA			
Mild-to-moderate vasospasm	> 120	> 130	
Severe vasospasm	> 155		
PCA			
Mild-to-moderate vasospasm	> 100	> 110	
Severe vasospasm	> 120		

ACA: anterior cerebral artery; ICA: internal carotid artery; LI: Lindegaard index; MCA: middle cerebral artery; mV: mean flow velocity; PCA: posterior cerebral artery; PSV: peak systolic velocity; SR: Sloan ratio (used in ACA).

Posterior reversible encephalopathy syndrome (PRES) is a clinical-radiological syndrome that overlaps with RCVS. Diagnosis is based on a combination of characteristic clinical features, the presence of risk factors, and typical brain MRI findings. PRES may be caused by multiple factors, including cytotoxic and immunosuppressive agents, autoimmune disorders, and such other systemic processes as hypertensive crisis, sepsis, transplantation, eclampsia, or kidney failure.

PRES may present vasoconstriction signs similar to those observed in RCVS, making TDU a useful tool in these cases.²¹ Some authors also support the use of transorbital ultrasound for non-invasive detection of signs of increased intracranial pressure.²²

Giant-cell arteritis

Giant-cell arteritis is a form of vasculitis that affects cerebral blood vessels, the temporal artery, and extracranial arteries (the aorta and its branches),^{23,24} and is more common in individuals older than 50 years.²⁵ It has an incidence of 10 cases per 100 000 person-years and a prevalence of 50 cases per 100 000 population.

Advanced age is the main risk factor, due to the involvement of degenerative processes, oxidative stress, mutations, and mitochondrial dysfunction.^{26,27} Furthermore, it has been suggested that certain infectious agents may trigger the activation of vascular dendritic cells.²⁸

The most common initial manifestation is new-onset, persistent headache, occurring in up to 60% of cases.²⁹ Although pain is primarily located in the temporal region, as a result of temporal artery inflammation, it can also be frontal, occipital, or generalised.³⁰ Giant-cell arteritis can also be associated with jaw claudication and anterior ischaemic optic neuropathy, among other conditions.^{31–33} The examination may reveal tenderness, induration, and absence of pulse of the temporal artery and/or other cranial arteries.³¹ While these findings are characteristic of giant-cell arteritis, their absence does not rule

out the diagnosis. Furthermore, some older adults may present prominent temporal arteries without pathological significance.³⁴

Although temporal artery biopsy has traditionally been the gold standard, its sensitivity may be influenced by such factors as the surgeon's experience, patient phenotype, and the length and quality of the sample.³⁵ The skip lesions caused by giant-cell arteritis results in false-negative biopsy results in approximately 50% of cases.³⁶ Blood tests usually reveal an erythrocyte sedimentation rate > 50 mm/h and C-reactive protein levels > 20 mg/L. Other findings include anaemia, leukocytosis, and thrombocytosis. High-resolution contrast-enhanced MR angiography enables visualisation of temporal artery inflammation and mural oedema.³⁷ However, the need for contrast administration and the associated costs constitute limitations to its generalised use.

To avoid the limitations of biopsy studies, colour duplex ultrasound of the head, neck, and upper limbs has become a highly valuable diagnostic tool. With a spatial resolution of 0.1 mm, it enables visualisation of the temporal artery and other small cranial vessels, such as the facial, occipital, and vertebral arteries. Sensitivity ranges from 55% to 100%, with specificity ranging from 78% to 100%.³¹ The study should ideally be performed before treatment onset or within the first week, as glucocorticoid therapy decreases the sensitivity of the technique. The axillary and subclavian arteries should also be assessed, since vasculitic changes in larger arteries may be overlooked when only cerebral arteries are examined.³⁸ The typical finding is the "halo sign" (Fig. 2), which is defined as a hypoechoic ring measuring 0.3 to 2.0 mm around the vascular lumen, indicating presence of mural oedema.³⁹ Bilateral halo sign in the temporal arteries is a highly specific finding of temporal arteritis.⁴⁰ The compression sign is also highly specific, and refers to the persistence of the halo sign after compression of the vascular lumen with the ultrasound probe.⁴¹ Furthermore, colour duplex ultrasound can also detect stenosis (with markedly increased flow velocity) and occlusion, but its specificity is considerably lower.

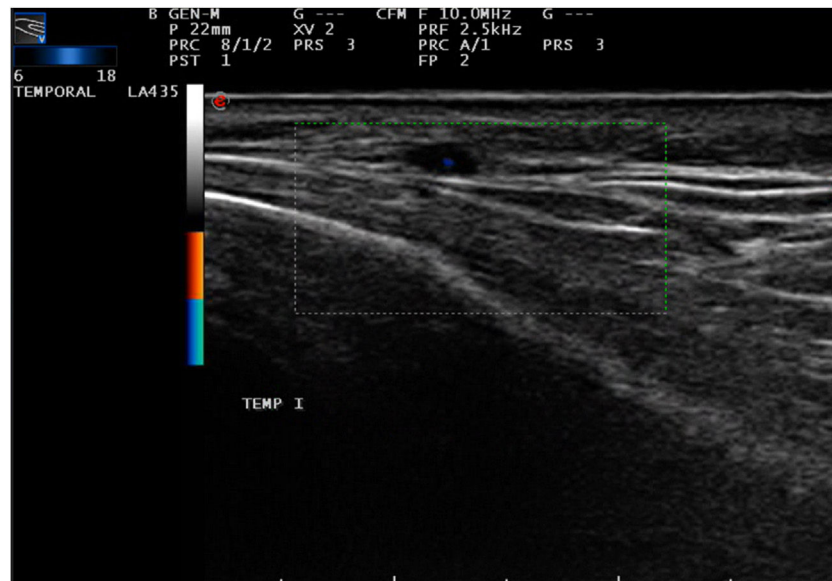


Figure 2 Colour-coded Doppler ultrasound of the temporal artery showing a hypoechoic ring around the vascular lumen; this indicates pathological wall thickening, a typical finding of giant-cell arteritis.

Doppler ultrasound has the limitation of being operator-dependent. Furthermore, it is highly influenced by such factors as variability in ultrasound equipment, probe settings, ultrasound technique, and the clinical context. Standardisation of these parameters facilitates the widespread adoption of the technique in the diagnosis of temporal arteritis.

At a minimum, the study should include assessment of the temporal arteries, although it should examine as many potentially affected arteries as possible (supra-aortic trunks; occipital, mandibular, orbital, and axillary arteries; circle of Willis), particularly when symptoms suggest involvement of these territories. The cervical, extracranial, orbital, and axillary arteries are assessed with a linear probe (3–12 MHz). High frequencies (≥ 15 MHz) are preferred for the assessment of the temporal artery, although frequencies 3–12 MHz are adequate. A low-frequency (1–4 MHz) sector probe should be used for the assessment of the intracranial arteries of the circle of Willis and the aortic arch.

Optic nerve assessment in intracranial hypertension and hypotension

Idiopathic intracranial hypertension (IIH) may cause daily headaches of variable characteristics, and worsens with coughing, exertion, or in decubitus positions.^{42,43} It is associated with transient visual obscurations, diplopia, loss of visual acuity, and pulsatile tinnitus. Papilloedema is also frequent. The cause of IIH remains unknown, although it has been suggested that it may be due to alterations in CSF absorption or uni- or bilateral transverse sinus stenosis.⁴⁴ Obesity and hormonal and metabolic alterations also play a crucial role.

The disorder can be diagnosed based on brain MRI and lumbar puncture (LP) results. These techniques are highly accurate and sensitive, but also have important limitations;

MRI is costly and time-consuming, whereas LP may cause important secondary effects.⁴⁵ Colour duplex ultrasound is a simple, quick-to-administer, affordable, and non-invasive technique that can be performed at the bedside and has little intra- or interobserver variability. All these characteristics make it the ideal technique for use at neurological consultations.

The optic nerve is a long tubular structure measuring approximately 5 cm long, surrounded by 3 meningeal layers and a narrow subarachnoid space. Several studies have demonstrated the usefulness of optic nerve sheath diameter (ONSD) measurement for detecting IIH, with increased values being observed in patients as compared to healthy individuals (Fig. 3).^{46–49} Some patients also present optic nerve head protrusion secondary to papilloedema.⁴⁶ The technique is therefore useful for both diagnosis and follow-up, with values normalising once appropriate treatment is administered.^{46,48,50} Several studies have shown a strong correlation between this technique and brain MRI, with ultrasound providing a more affordable and accessible option for general neurologists.^{45,49,50}

Headache attributed to spontaneous intracranial hypotension is caused by CSF leakage, frequently at the spinal level. It is more frequent among middle-aged women, and is associated with connective tissue disorders or degenerative disc disease. In cases secondary to mild trauma, underlying nerve root sheath defects are often present, including meningeal diverticula, rupture due to disc herniation or osteophytes, or CSF-venous fistulae. Headache is orthostatic (although it may disappear in chronic cases), bilateral, occipital, and of variable intensity, and may worsen with Valsalva manoeuvres or coughing. It is associated with neck rigidity, nausea, vomiting, tinnitus, hearing loss, instability, or vertigo. Brain MRI is highly useful for diagnosis.

Ultrasound reveals a significant reduction in ONSD when the patient moves from a supine position to standing, as

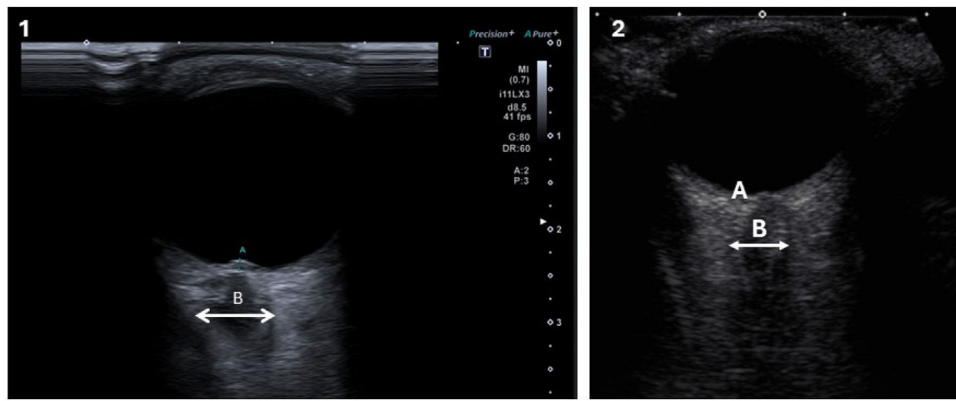


Figure 3 B-mode orbital ultrasound. 1: papilloedema is visible, with protrusion in the globe (A), the optic nerve (B), and the optic nerve sheath (arrow). 2: normal orbital ultrasound, showing the optic disc (A), optic nerve (B), and optic nerve sheath (arrow). Image courtesy of Dr Rodríguez Pardo de Donlebún.

compared to healthy controls and patients with intracranial hypotension without headache.⁵¹ A reduction in ONSD has also been observed at diagnosis, with values returning to normal after several months of treatment with caffeine and epidural blood patches.⁵²

Anaesthetic block of the greater occipital nerve^{42,53–57}

The greater occipital nerve (GON) is the sensory branch of the posterior division of the C2 spinal nerve. Together with the lesser occipital nerve, the GON conveys tactile and nociceptive sensory input from the occipital region to the vertex.

Randomised clinical trials have demonstrated the benefits of anaesthetic block of the GON for migraine, cluster headache, cervicogenic headache, and occipital neuralgia. Contraindications include allergy to local anaesthetic drugs and cranial bone defects. The most frequent adverse effect is vasovagal reaction.

GON ultrasound helps to precisely locate the nerve for infiltration of the intermediate segments, which seems to be more effective.

The GON may be located with a high-frequency (10–12 MHz) linear probe placed at the cervical level, with the medial border of the probe placed on the C2 spinous process and the lateral border towards the C1 transverse process. Thus, the probe rests obliquely over the location of the obliquus capitis inferior muscle. At this point is located the semispinalis capitis muscle, which runs superficial to the obliquus capitis inferior muscle. The transverse section of the GON is located between both muscles. Colour duplex ultrasound does not enable visualisation of the occipital artery (as it is at a more cephalic location), but it does show the vertebral artery if we follow the trajectory of the obliquus capitis inferior muscle laterally. Therefore, this artery is not directly related to the GON, but it should be located with a view to preventing accidental puncture during infiltration.

Any local anaesthetic may be used, injected with a 2–5 mL syringe and a 25 G needle measuring 4–5 cm. To improve

Table 2 Conditions most frequently hindering lumbar puncture based on anatomical landmarks.

Obesity (BMI > 35)
Subcutaneous lesions upon examination/palpation (increased risk of bleeding)
Spinal deformities
History of spinal surgery (scoliosis, hyperlordosis, hyperkyphosis)
History of spinal trauma
Risk of bleeding
Poor patient cooperation

BMI: body mass index.

needle visualisation, the infiltration should be performed following the in-plane approach once the nerve and the vertebral artery have been identified, advancing the needle from the lateral to the medial edge of the probe. A volume of 2–5 mL of local anaesthetic solution is usually infiltrated.

Lumbar puncture^{58–61}

The use of ultrasound guidance for LP was first described in 1971 by the Russian physicians Bogin and Stulin. Ultrasound guidance is recommended whenever this equipment is available. When ultrasound is not accessible, the procedure may be scheduled when the presence of obstacles to the trajectory of the needle is suspected or in patients with increased risk of bleeding (Table 2). This technique is also recommended in patients likely to display poor cooperation (with high levels of anxiety, in children, etc). Ultrasound-guided LP is also recommended for physicians lacking experience with the procedure, although ultrasound itself also requires a certain level of expertise. Finally, ultrasound guidance should be considered after several failed attempts at conventional LP.

The 3 most frequent indications for ultrasound-guided LP are scoliosis in young patients, osteoarthritis in older adults, and obesity.

Other applications include subcutaneous lesions detectable upon examination or palpation (lipomas,

sebaceous cysts, etc), abnormal curvature of the spine (scoliosis, hyperlordosis, hyperkyphosis, etc), congenital or acquired spinal deformities (osteoarthritis, rheumatic diseases, etc), and history of vertebral disc surgery or severe spinal trauma in the area of the puncture. Ultrasound-guided LP may also be indicated to minimise the risk of bleeding in patients with subcutaneous vascular malformations at the puncture site, as well as in patients undergoing myelography or receiving intrathecal drug injections and those with history of complications in previous LP or spinal anaesthesia procedures (intracranial hypotension syndrome, paraspinal haematoma, acute radiculopathy, meningitis, abscesses, etc).

Future applications

In the acute phase of venous sinus thrombosis, dural sinus occlusion may be diagnosed with transcranial colour-coded duplex sonography following the application of a contrast agent, which reveals a filling defect. Collateral venous flow may be evaluated either with TDU or with transcranial colour-coded duplex sonography. Duplex sonography is particularly useful when venous sinus thrombosis extends to the jugular veins. Although ultrasound is not sufficiently sensitive to rule out cerebral venous thrombosis, it may complement other imaging techniques.^{62,63} Contrast-enhanced transcranial ultrasonography is likely to be a valuable tool for the diagnosis of venous sinus thrombosis when other imaging techniques are unavailable or when only bedside clinical assessment is feasible.⁶⁴

Several studies have explored the usefulness of transcranial ultrasound for the study of deep cerebral structures, such as the periaqueductal grey matter, which plays a central role in migraine. This region modulates nociception, enables the inhibition of painful stimuli, and connects with other brain structures, ascending spinal fibres, and the raphe nuclei. A case-control study found that patients with chronic migraine presented structural alterations in the periaqueductal grey matter (larger area and lower intensity of echogenicity, greater heterogeneity) as compared to patients with episodic migraine and controls.⁶⁵

Hypoechoogenicity of the raphe nuclei is more prevalent among patients with unipolar depression than in controls.⁶⁶ The comorbidity between migraine and depression is bidirectional, which suggests a common pathogenic mechanism involving serotonergic dysfunction.^{67–69} To date, 5 studies and one meta-analysis have explored the association between migraine and raphe nucleus hypoechoogenicity. Three of the 5 studies, as well as the meta-analysis, reported a higher prevalence of raphe nucleus hypoechoogenicity in patients with migraine than in controls.^{70–72} In patients with migraine, the presence of raphe nucleus hypoechoogenicity has been associated with higher scores on depression scales,^{71,73} greater attack frequency,⁷⁴ and greater analgesic use.⁷⁰

The technique is performed with a 2-MHz ultrasound probe with a penetration depth of 14 cm and a dynamic range of 45–55 dB. The examination is performed through the transtemporal bone window to assess the mesencephalic and thalamic planes. On ultrasound, the periaqueductal grey

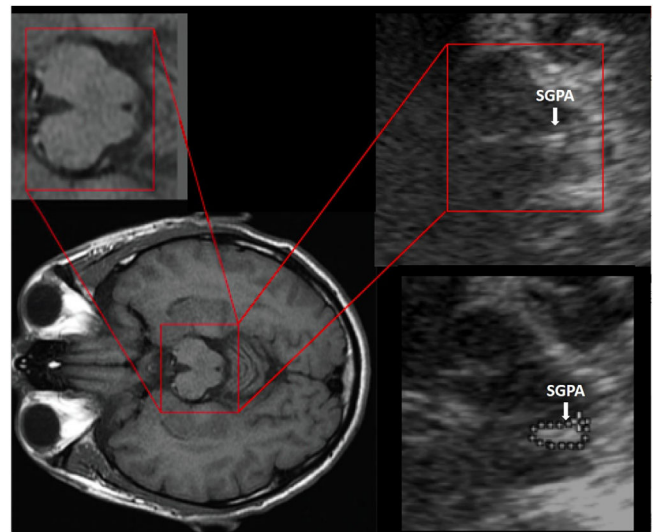


Figure 4 Axial sequences of the midbrain obtained by magnetic resonance imaging (A) and transcranial ultrasound (B), showing the periaqueductal grey matter.

matter is identified as a structure surrounding the aqueduct of Sylvius, showing greater echogenicity than the CSF signal observed in the aqueduct and the surrounding tissue (Fig. 4). Hypoechoogenicity of the raphe nuclei is defined as interruption or absence of echogenicity in these midline structures of the midbrain.⁶⁶

Declaration of competing interest

None.

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