mg 3 times per day) and placebo for the primary endpoint (treatment failure), but did identify significant differences in the time to treatment failure, the number of paroxysms, average daily pain score, and assessments of overall function and quality of life. The drug was well tolerated, with headache and dizziness being the most frequent adverse events.[10] Despite the negative result for the primary endpoint, the trial clearly suggests that Nav1.7 antagonists may be clinically relevant in neuropathic pain, justifying continued clinical research. For this reason, new clinical trials are currently being performed to analyse the use of vixotrigine to treat both TN and other models of neuropathic pain (eg, small-fibre neuropathy, erythromelalgia, and lumbosacral radiculopathy).[9]

In conclusion, the identification of Nav subtypes associated with specific pain conditions, and their potential role as therapeutic targets, offers a glimpse of the potential for truly individualised treatment and a much-needed transformation of the care provided to these patients. The available evidence suggests that Nav blockers are underused. However, current research has identified this as a promising area for additional clinical trials to better guide clinical practice.

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Midbrain Virchow-Robin spaces and Parkinsonism: A case report and literature review*

Espacios de Virchow-Robin mesencefálicos y parkinsonismo: caso clínico y revisión de la literatura

Dear Editor:

The pathogenic association between Virchow-Robin spaces (VRS) and parkinsonism is unclear.[1—11] We present a patient with midbrain VRS and a parkinsonian syndrome, and discuss the pathophysiology of this association.

The patient was a 57-year-old man who consulted due to tremor in the right hand, slowness in everyday activities, and more monotonous tone of voice. He had presented tuberculous meningitis at the age of 8 years. Physical examination identified divergent strabismus of the right eye with limitation of adduction, peripheral facial palsy with synkinesis of the orbicularis oris muscle, and hypoacusia; all symptoms were considered to be secondary to previous tuberculous meningitis. He presented mildly inexpressive facies, moderate resting tremor in the right upper limb, mild stiffness and bradykinesia of both right limbs, reduced right arm swing when walking, and normal postural reflexes. A brain MRI study (Fig. 1A and B) detected cystic lesions in the cerebellum, hippocampus, caudal part of the striatum, and bilateral midbrain; the lesions behaved as cerebrospinal fluid on all sequences, and corresponded to perivascular spaces or VRS. Images also showed encephalomalacia of the right temporal lobe and cystic lesions in the fourth ventricle, which were judged to be sequelae of meningitis. A SPECT study with ioflupane (I-123) (DaTSCAN) showed reduced tracer uptake

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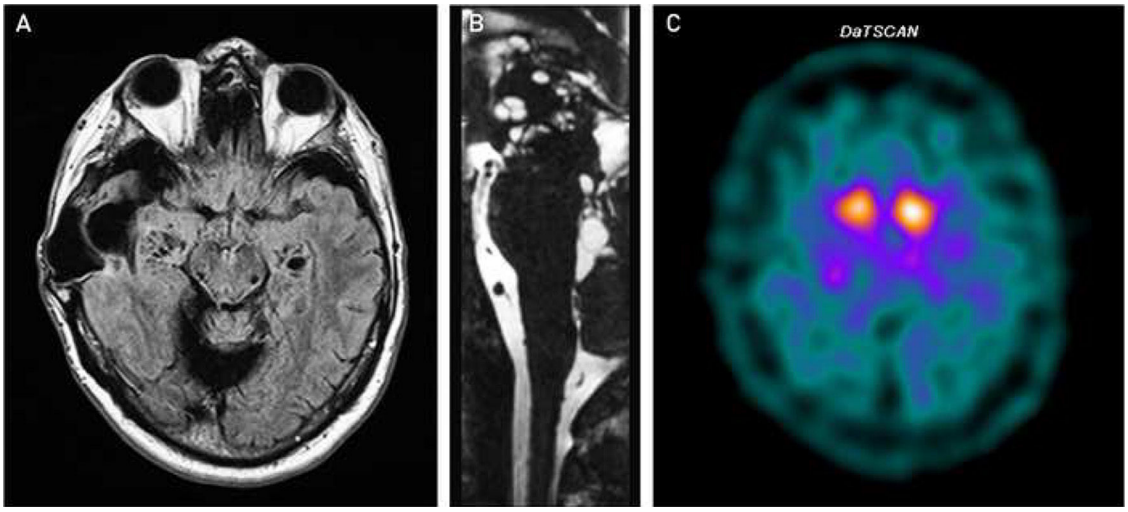

Figure 1 A) Axial FLAIR MRI sequence, showing extensive right temporal encephalomalacia associated with a craniectomy performed due to tuberculous meningitis during childhood, as well as perivascular spaces in the hippocampus, caudal part of the striatum, and bilateral midbrain. B) Sagittal 3D T2-weighted (CISS) MRI sequence, showing cystic lesions in the fourth ventricle and perivascular spaces in the midbrain. C) SPECT study with ioflupane (I-123) (DaTSCAN), showing reduced tracer uptake in the putamen bilaterally.

Table 1 Cases of Virchow-Robin spaces associated with parkinsonian syndromes.

	No. patients; mean age of onset (range); sex	VRS location	DaTSCAN/^{1}8F-FP-CIT PET	Levodopa response
Laitinen et al.,[1] 2000	40; 62.9 (47—80); 28M/12W	Bilateral striatum	NP	Good
Krause et al.,[2] 2005	1; 63; W	Left midbrain	Left DA deficit	Good
Kim et al.,[3] 2007	1; 67; M	Hemispheric white matter bilaterally	NP	Poor
Mehta et al.,[4] 2013	1; 44; W	Bilateral striatum and white matter, right midbrain	Bilateral DA deficit	Poor
Omidi et al.,[5] 2014	1; 52; W	Periventricular and juxtacortical, bilateral	NP	Not reported
Mestre et al.,[6] 2014	3; 51 (41—61); 2M/1W	Unilateral putamen	Unilateral DA deficit	None
Lee et al.,[7] 2015	1; 64; M	Right hemisphere white matter	Normal	Not reported
Lee et al.,[8] 2015	11; 72 (65—80); 5M/6W	Striatum (putamen and/or caudate)	Bilateral DA deficit (9)/normal (2)	Not reported
López Fernández et al.,[9] 2016	1; 55; M	Bilateral striatum	Bilateral DA deficit	Not administered
Ferrer et al.,[10] 2017	1; 80; M	Bilateral midbrain and right thalamus	NP	Not reported
Conforti et al.,[11] 2018	1; 69; W	Left striatum	NP	Good
Our patient	1; 55; M	Caudal striatum and bilateral midbrain	Bilateral DA deficit	Poor

DA: dopaminergic; M: men; NP: not performed; VRS: Virchow-Robin spaces; W: women.

in the putamen bilaterally (Fig. 1C). We started treatment with levodopa at 400 mg/24 hours, which achieved a limited improvement; the following year, we added pramipexol up to 1.57 mg, which achieved no clinically relevant changes. Two years after the initial consultation, the patient presented disabling postural tremor, which appeared when extending the limbs without latency; and irregular intention tremor, of high amplitude and low frequency, when picking up objects. He did not present dysmetria, and physical examination showed right-sided laterocollis. Five years after symptom onset, he began to present instability with falls and ataxic gait, and scored 2/4 in the retropulsion test; laterocollis had also worsened. Cervical dystonia improved with administration of botulinum toxin. Seven years after the initial consultation, the patient reported freezing of gait when beginning to walk and when turning, and scored 4/4 on the retropulsion test. Treatment was started with safinamide, but no improvements were observed. Throughout the progression of his disease, the patient never reported motor fluctuations or dyskinesia, and limb tremor and bradykinesia remained stable. Therefore, our patient presented a parkinsonian syndrome with several atypical characteristics:

scarce response to dopaminergic treatment, early onset of highly disabling postural and intention tremor, and progressive laterocollis due to cervical dystonia. Five years after onset, he also began presenting instability, falls, ataxic gait, and freezing of gait.

While it is not possible to unequivocally rule out a degenerative cause, we believe that some of these manifestations may have been influenced by the presence of the midbrain VRS. Through compressive or ischaemic mechanisms, these spaces can damage such structures as the dentatorubrothalamic tract; this may explain the patient's tremor, which resembled rubral tremor due to the large amplitude and low frequency.[12] The cervical dystonia, presenting as laterocollis, may also be explained by structural damage to the midbrain,[13] as this is not a common form of presentation of cervical dystonia in atypical parkinsonism.

Perivascular spaces or VRS are interstitial fluid — filled spaces that surround blood vessels along their course through the brain parenchyma; they are continuous with the subpial space and do not directly connect with the subarachnoid space. It has been suggested in recent years that they may play a role in the lymphatic drainage of the brain.[14] The precise reason that they appear is unknown. One hypothesis suggests that they originate from altered arterial wall permeability due to vasculitis; this may be related to the history of tuberculous meningitis in our patient. VRS are generally not considered to be pathological, although cases have been reported of an association with parkinsonian syndromes; a pathogenic role is probable when they are located in the midbrain or striatum (Table 1). Some patients present clinical manifestations of atypical parkinsonism, as is the case with our patient.[8,9]

In conclusion, while VRS are a common finding in neuroimaging studies, we believe that they may play a pathogenic role when they are large and numerous, and when they involve structures related to the patient's symptoms.

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