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Publication date
1999

Published in
Neurology

[Link to publication](#)

Citation for published version (APA):

Molenaar, D. S. M., Vermeulen, M., de Visser, M., & de Haan, R. J. (1999). Impact of neurologic signs and symptoms on functional status in peripheral neuropathies. *Neurology*, 52, 151-156.

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NEUROLOGY

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Neurology 1999;52;151-

This information is current as of November 15, 2006

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://www.neurology.org/cgi/content/full/52/1/151>

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Impact of neurologic signs and symptoms on functional status in peripheral neuropathies

D.S.M. Molenaar, MD; M. Vermeulen, MD, PhD; M. de Visser, MD, PhD; and R. de Haan, RN, PhD

Article abstract—*Objective:* To determine whether the Neurologic Disability Score (NDS), the Neuropathic Symptom Score (NSS), and the Medical Research Council (MRC) “sumscore” are reliable, and to determine whether they provide information regarding the functional status of patients with peripheral neuropathies. *Methods:* The authors analyzed homogeneity of the frequently used outcome measures in 97 patients using Cronbach’s alpha coefficient and corrected item–total correlations. Their association with functional status (sickness impact profile and modified Rankin score) was analyzed univariately with Pearson’s and Spearman’s correlation coefficients, and multivariately with linear regression analysis. *Results:* The NDS and MRC scales were homogeneous (range of Cronbach’s alpha, 0.81 to 0.97) compared with the NSS scales (range, 0.20 to 0.63). The correlation patterns between neurologic signs and symptoms and functional status ranged from 0.13 to 0.65. Multivariate linear regression analyses showed that 40% or less of patients’ functional status could be explained by the three tested outcome measures. *Conclusion:* The NDS and MRC are reliable measures, but these measures do not correlate with measures of functional status.

NEUROLOGY 1999;52:151–156

In a previous study¹ we showed that in studies in patients with peripheral neuropathies the choice of a primary outcome measure was not based on the type of the clinical trial being performed. We argued that the aim of phase II studies is to investigate whether a treatment has any effect on the disease process. To prevent overlooking small changes, outcome measures that are closely related to this disease process, such as nerve conduction velocity studies and measurements of neurologic signs and symptoms, should be selected. During phase III studies the primary question is whether patients benefit from treatment that had been shown previously to induce changes in the disease process. Therefore, during phase III studies the preferred primary outcome measure is not an assessment of, for instance, reflexes, but of mobility in these patients. Those who are in favor of assessment of neurologic signs and symptoms, however, argue that these measures are more objective and reliable than measurement of functional status, and therefore are the outcome measures of choice irrespective of the type of study.^{2,3} Moreover, it has been argued that there is a close relation between neurologic signs and symptoms on the one hand and functional status on the other.⁴ This was shown in patients with ALS. In these patients a standardized tool for measuring muscle strength and pulmonary function was related significantly with a measure of functional status: the sickness impact profile (SIP).⁵

Therefore, we investigated 1) whether frequently used outcome measures in patients with peripheral neuropathies are reliable and 2) whether these measures are related to the functional status of these patients by using the SIP.

Methods. *Patients.* The study group comprised 97 patients with hereditary and acquired polyneuropathies. Exclusion criteria were age younger than 16 years; poor communication because of, for example, dementia or alcoholism; other disabling diseases such as stroke, degenerative joint diseases, and respiratory tract or cardiac disorders; neuropathy caused by toxins and metabolic disorders; and paraneoplastic neuropathy. A total of 56 patients were recruited from three neurologic university outpatient clinics and two rehabilitation centers in various regions of the Netherlands. After having informed the association of individuals with neuromuscular diseases (Vereniging Spierziekten Nederland) of our research project, 41 additional patients were included. Diagnosis in these patients had been confirmed by experienced neurologists. After informed consent was obtained, all patients were examined by one of the authors (D.M.).

Measures of neurologic signs and symptoms. We selected measures of neurologic signs and symptoms only requiring bedside examination of the patient. These measures had been used in previous clinical trials on patients with peripheral neuropathies and included the Neurologic Disability Scale (NDS), the Neuropathy Symptom Score (NSS), and the Medical Research Center (MRC) “sumscore” of muscle weakness.

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Supported by the Prinses Beatrix Fonds, The Hague.

Received March 25, 1998. Accepted in final form September 19, 1998.

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The NDS is a megacomposite score of the neurologic examination scored into four subsets: cranial nerve function (six items), muscle weakness (16 items), reflexes (five items), and sensory deficit (eight items).⁶⁻⁸ Each item is scored on the patient's left and right side. Several scoring systems have been used in the literature.⁶⁻¹¹ We used the following scoring system. For muscle weakness: 0, no abnormality; 1, slight abnormality; 2, moderate abnormality; 3, severe abnormality; and 4, very severe abnormality or complete loss of function. For reflexes: 0, normal or enhanced; 1, lower than normal; and 2, absent. For cranial nerve functions and sensation assessed on the index finger and the great toe: 0, normal; 1, diminished; and 2, absent function. A normal neurologic examination amounts to a score of 0, whereas maximum neurologic impairment yields a score of 204.

The NSS consists of three subsets—motor (eight items), sensory (five items), and autonomic function (four items)—and was originally derived from the neurologic history.^{6,7} An item can be judged as 0 (absent) or 1 (present). When judging abnormality, the patient's age, weight, and sex were taken into account. If a symptom was equivocal, we scored the item as absent. Absence of neurologic signs and symptoms yields a score of 0. Maximum neurologic impairment amounts to a score of 17.

As measure of weakness we included the MRC sum-score, which is the sum of muscle weakness of shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension, and dorsal flexion. Muscle functions were tested on both sides according to the MRC: 0, no visible contraction; 1, visible contraction without movement of the limb; 2, movement of the limb but not against gravity; 3, movement against gravity over (almost) the full range; 4, movement against gravity and resistance; and 5, normal power.¹² Normal strength amounts to a score of 60, whereas total paralysis yields a score of 0.¹³

Measures of functional status. The physical dimension of the SIP as well as the modified Rankin score were selected as measures of patients' functional status.

The physical dimension of the SIP consists of three subscales that refer to (instrumental) disabilities in terms of body care and movement (23 items), walking (12 items), and mobility (10 items). Each item is scored as absent or present. A total score of 100% indicates severe disability of the patient. Validity and reliability of the SIP have been evaluated extensively.¹⁴⁻¹⁷

The modified Rankin score is a short index of global disability, which also has been evaluated in detail.¹⁸⁻²¹ It is scored as follows: 0, no symptoms; 1, minor symptoms that do not interfere with lifestyle; 2, minor handicap, symptoms that lead to some restriction in lifestyle but do not interfere with the patient's capacity to look after himself; 3, moderate handicap, symptoms that restrict lifestyle significantly and prevent totally independent existence; 4, moderately severe handicap, symptoms that restrict lifestyle significantly although not needing constant attention; and 5, severe handicap, totally dependent patient who requires constant attention day and night.

Statistical analysis. The scores of outcome measures of neurologic signs and symptoms were analyzed with descriptive statistics. We additionally judged the items that were the least relevant for patients. Arbitrarily we considered items applying to no more than 10% of all patients as

seriously skewed. Homogeneity, a special type of reliability of a scale, was analyzed with Cronbach's alpha coefficient and corrected item-total correlations.²² Cronbach's alpha coefficient is based on the weighted average correlation of items within a scale. Homogeneity, or internal consistency, is considered to be good when alpha is >0.80, and excellent when alpha is >0.90. The corrected item-total correlation reflects the correlation between the concerning scale item and the total scale score without it. Items with a corrected item-total correlation of <0.20 were considered weak items of the scale.

The relation between the neurologic impairments and measures of functional status was analyzed with Pearson's correlation coefficient and explained variability (r^2). Because the MRC items and the Rankin score are ordinal scales, association with these scales was analyzed with a nonparametric technique (Spearman's correlation coefficient). Additionally, the impact of neurologic signs and symptoms on functional status was analyzed with linear regression models (with a forward stepwise inclusion strategy), using the F-statistics with $p = 0.05$ on the criterion level for inclusion. Residual analysis was performed to search for violations of necessary assumptions in multiple regression in terms of linearity, equality of variance, normality, and influential data points (Cook's distances). The possible presence of collinear data was explored with the tolerance statistics. All analyses were performed using SPSS for Windows 6.0 (SPSS, Chicago, IL).

Results. We included 51 women and 46 men with symmetric neuropathy. There were 41 patients with a hereditary motor and sensory neuropathy (types I and II) and 56 with an acquired neuropathy. In the latter group, Guillain-Barré syndrome (GBS) was diagnosed in 29 patients, chronic inflammatory demyelinating polyneuropathy in nine, nonsystemic vasculitis in three, multifocal motor neuropathy in two, and polyneuropathy with monoclonal gammopathy of undetermined significance in two. In two patients, neuropathy was classified as chronic idiopathic axonal neuropathy,²³ and in nine patients the sensorimotor neuropathy was not classified further. The median age of the patients was 50 years (range, 16 to 82 years).

Table 1 shows the results of the descriptive statistics. As can be seen from the (standardized) mean and median sumscores on the NDS, NSS, and MRC, patients had relatively mild impairment of neurologic signs and symptoms. The only exception was the NDS subscale that focused on reflexes. The items of the scales of neurologic signs and symptoms that applied to no more than 10% of the patients are listed in the same table. In general, these items focused on cranial nerve functions and autonomic functions.

The functional health scores on both the SIP and the Rankin score also indicated that patients were mildly disabled: standardized mean of the physical dimension of the SIP, 0.24; median Rankin score, 2 (minor handicap; symptoms that lead to some restriction in lifestyle but do not interfere with the patient's capacity to look after himself).

Reliability, in terms of homogeneity, of the NDS and the MRC subscales was substantial, as shown in table 2 (range of alpha coefficients, 0.81 to 0.97). However, the internal consistency of the NSS scale was rather poor (range, 0.20 to 0.63). Because the alpha coefficient is related to the

Table 1 Descriptive statistics of the measures of neurologic signs and symptoms

Scale	No. of items within the scale	Possible scoring range	Mean	SD	Median	Standardized mean*	Skewed items applying to no more than 10% of the patients, and no. of items
NDS cranial nerve function	12	0–24	0.5	1.4	0	0.02	All cranial nerve functions, except for L facial weakness, 11
NDS weakness	32	0–128	19.6	16.5	17	0.15	Respiratory muscle weakness (L + R), 2
NDS reflexes	10	0–20	16.1	4.9	20	0.81	N/A, 0
NDS sensation	16	0–32	10.3	7.6	10	0.32	Position sense of hand (L + R), 2
NDS sumscore	70	0–204	46.4	21.6	42.5	0.23	15
NSS weakness	8	0–8	2.7	1.6	2	0.34	Weakness of tongue and swallowing difficulty, 2
NSS sensory symptoms	5	0–5	2.1	1.3	2	0.42	Sensory disturbances of the mouth, 1
NSS autonomic functions	4	0–4	0.2	0.5	0	0.05	Postural fainting, urinary incontinence, and nocturnal diarrhea, 3
NSS sumscore	17	0–17	5.0	2.4	5	0.29	6
MRC sumscore	12	0–60	53.0	5.9	54	0.12†	N/A, 0

* Standardized mean = mean/possible scoring range.

† Because lower MRC scores implicate more neurologic deficit, we calculated $1 - \text{standard mean}$ to be able to compare the standardized mean of the MRC sumscore with the other scales.

NDS = Neurologic Disability Score; NSS = Neuropathic Symptom Score; MRC = Medical Research Council; N/A = not applicable.

number of items included in the scale, we also assessed the homogeneity with help of corrected item–total correlations. Eight of 15 severely skewed NDS items also turned out to be the least homogeneous items (see table 1). The relevant items assessed cranial nerve function. Two of the six severely skewed items of the NSS that focused on autonomic functions (postural fainting and nocturnal diarrhea) were also the least homogeneous items (see table 1).

Table 3 shows the correlation coefficients between the measures of neurologic signs and symptoms and the functional measures. Pearson's correlations between the sum-scores of the NDS, the NSS, and the MRC on the one hand, and the physical dimension of the SIP on the other, ranged from $r = 0.56$ to 0.65 (r^2 , 32 to 42%). A slightly lower

correlation was seen between the sumscores of the neurologic signs and symptoms, and the functional status as assessed with the modified Rankin score (Spearman's correlation coefficient, 0.43 to 0.50).

Table 4 shows the results of the multiple linear regression analyses. Weakness as assessed with the NDS and the NSS was the most important independent explanatory factor of the patients' level of impaired functional status (R^2 range, 14 to 31%). Sensory symptoms assessed with either the NDS or the NSS also explained approximately 10% of the functional status as measured with the SIP. Reflexes and cranial nerve function measured with the NDS, and autonomic functions measured with the NSS, did not contribute to the level of disabled functional status.

Table 2 Reliability of NDS, NSS, and MRC sumscore as analyzed with Cronbach's alpha coefficients and corrected item–total correlations ($n = 97$)

Scale	No. of items within the scale	Alpha	Items with corrected item–total correlation < 0.20	No. of items
NDS cranial nerve function	12	0.81	Papilloedema (L + R), weakness of palatum (L + R), of tongue (L + R), and impairment of IV nerve (L + R)	8
NDS weakness	32	0.94	N/A	0
NDS reflexes	10	0.97	N/A	0
NDS sensation	16	0.88	N/A	0
NDS sumscore	70	0.93		
NSS weakness	8	0.62	Weakness of hands	1
NSS sensory symptoms	5	0.50	Pain	1
NSS autonomic functions	4	0.20	Postural fainting, impotence, nocturnal diarrhea	3
NSS sumscore	17	0.63		
MRC sumscore	12	0.84	N/A	0

NDS = Neurologic Disability Score; NSS = Neuropathic Symptom Score; MRC = Medical Research Council; N/A = not applicable.

Table 3 Association between neurologic signs and symptoms (NDS, NSS, MRC) and functional status (physical dimension of the SIP and the Rankin score) presented with Pearson's and Spearman's correlation coefficients

Scales of signs and symptoms	SIP physical dimension		Rankin, Spearman†
	Pearson	r^{2*}	
NDS cranial nerve function	0.31	9%	0.18
NDS weakness	0.56	31%	0.48
NDS reflexes	0.25	6%	0.22
NDS sensation	0.42	17%	0.27
NDS sumscore	0.65	42%	0.50
NSS weakness	0.46	21%	0.36
NSS sensory symptoms	0.42	17%	0.31
NSS autonomic functions	0.20	4%	0.13
NSS sumscore	0.56	32%	0.43
MRC sumscore	-0.59‡	34%	-0.47‡
Spearman†			
MRC shoulder abduction‡	-0.23		-0.33
MRC elbow flexion‡	-0.27		-0.36
MRC wrist extension‡	-0.47		-0.34
MRC hip flexion‡	-0.47		-0.35
MRC knee extension‡	-0.47		-0.37
MRC dorsal flexion‡	-0.41		-0.26

* Squared correlation coefficient indicating the percentages of the variability of the functional data explained by neurologic signs and symptoms.

† Because the Rankin score and MRC subscales are ordinal, the association with these measures was assessed using Spearman's correlation coefficient.

‡ Because lower MRC scores implicate more neurologic deficit, signs of the coefficients are opposite to those of other scales.

SIP = sickness impact profile; NDS = Neurologic Disability Score; NSS = Neuropathic Symptom Score; MRC = Medical Research Council.

The MRC sumscore could explain 27 to 34% of the functional status. Hip flexion, shoulder abduction, and foot dorsal flexion were the three most important explanatory muscle groups.

Additional linear regression analyses of three subgroups of patients with severe impairment of neurologic signs and symptoms (25th percentile of the NDS, NSS, and MRC) did not show a higher impact level of all neurologic signs and symptoms on functional status of the patients (R^2 range, 0 to 41%).

Discussion. In this study we investigated the reliability of three frequently used outcome measures in peripheral neuropathies. This was done by assessing the internal consistency (homogeneity) of the measurements in a group of patients with acquired and hereditary neuropathies. Because the different items of these measures are all directed at the severity of the disease, there ought to be a high correlation

Table 4 Multivariate linear regression models (forward selection) explaining the independent impact of neurologic signs and symptoms (NDS, NSS, MRC subscales) on functional status (SIP physical dimension and Rankin score)*

Outcome measure	SIP physical dimension, adjusted R^2	Selected outcome measure	Rankin score, adjusted R^2
NDS weakness	30%	NDS weakness	31%
NDS sensation	11%		
Total	41%		
NSS weakness	20%	NSS weakness	14%
NSS sensory symptoms	8%		
Total	28%		
MRC hip flexion	19%	MRC shoulder abduction	17%
MRC dorsal flexion	11%	MRC dorsal flexion	7%
MRC shoulder abduction	4%	MRC hip flexion	3%
Total	34%	Total	27%

* No violations of necessary assumptions in multiple regression analyses could be detected (residuals, detection of outliers, and measures of collinearity).

SIP = sickness impact profile; NDS = Neurologic Disability Score; NSS = Neuropathic Symptom Score; MRC = Medical Research Council.

tion between the items. The results show that both the NDS and the MRC sumscores are reliable in contrast to the NSS. In particular, the NSS subscale measuring autonomic functions performed rather poorly, partly due to seriously skewed score patterns. Regarding the NDS, approximately one-fifth of the items assessing several cranial nerve functions applied to no more than 10% of the patients. A number of these items also turned out to be the least homogeneous. From a psychometric as well as a clinical point of view, these weak items could be deleted without losing clinically relevant information or decreasing reliability. Other aspects of reliability of these measures have been tested before. Dyck et al.⁶⁻⁸ have tested reproducibility of the NDS in patients with diabetes and had excellent results when patients were examined by trained neurologists (intraclass correlation coefficient [ICC] > 0.90). Again, the results of the NSS were rather poor. With respect to the MRC sumscore, excellent reproducibility has been demonstrated in GBS patients (ICC = 0.98).¹³

The second question of the study was whether these scales give information on the functional status of patients with peripheral neuropathies. As in patients with ALS, this was tested with a generic and generally accepted measure of functional status—the SIP.⁵ For this study we used the physical dimension of this profile, which consists of three sub-

scales that test disabilities in terms of mobility. We also investigated whether these results could be reproduced with another functional scale that has also been used in studies in patients with chronic inflammatory demyelinating neuropathy.²⁴ The physical dimension score of the SIP and the Rankin score detected disability in our patients. Univariate and multivariate analyses revealed that the three tested scales that are mainly scoring systems of signs and symptoms of the disease explained only partly, at most 40%, of the score variation of the functional scales. Apparently the functional scales we used were sensitive enough to detect disability; therefore, the explanation of this rather poor correlation is not the absence of disability in these patients. The explanation is, however, that signs and symptoms do not always have a direct impact on functional status. It is not surprising, for instance, that reflexes have no correlation with functional status; patients may recover completely from GBS but still have areflexia.

Our results certainly cannot be generalized to all scoring systems of signs and symptoms because such a system as used in ALS had a good correlation with one of the functional status measures of our study.⁵

In view of the poor reliability of the NSS, this measure is not recommended in clinical studies. In contrast, the NDS and the MRC have been shown to be reliable and can therefore be recommended for use in clinical trials. If in clinical trials, however, functional status measurements are required, these measures are not appropriate. Instead, disability measures like the functional abilities or GBS leg index, both of which have been used in patients with GBS, may be more appropriate, but it remains to be investigated whether these indexes are reliable and valid in assessing functional status.

Whether functional status measurements should be used in phase III clinical trials is a matter of debate. Some²⁵ are of the opinion that if a treatment has a beneficial effect on, for instance, the number of lesions seen on MRI in MS patients or on a pain score in patients with migraine, there is no need for trials in which the effects of these changes on the functional status of patients is measured. Others²⁶ argue that before treatments can be accepted in clinical practice, it is insufficient only to have measured changes in signs and symptoms, nerve conduction velocities, or size of tumors, although this can be measured more objectively than is possible with measures of functional status. They consider functional measures more relevant for patients, and therefore more important than objectivity of measurements. Furthermore, they argue that in clinical trials this problem of objectivity can be solved by strict blinding of the trial. For these proponents of functional measurement,²⁷ it is relevant that the three frequently used outcome measures in peripheral neuropathy do not correlate with measures of functional status.

Acknowledgment

The authors thank E. Wieman, J.H.C. Vorsteveld, A.R. Wintzen, D. Mulder, and B.G.M. van Engelen for including patients, and we thank all patients and the Vereniging Spierziekten Nederland for their friendly cooperation.

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Visual symptoms with dural arteriovenous malformations draining into occipital veins

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Article abstract—*Objective:* To determine the cause of the visual dysfunction and effect of treatment on dural arteriovenous malformations (DAVMs) that secondarily involve the occipital lobe. *Background:* DAVMs are an infrequent cause of visual dysfunction that should be amenable to treatment if diagnosed before permanent visual field loss. *Methods:* The records of seven patients with cerebral visual disturbances associated with DAVMs were analyzed with attention to visual symptoms, visual field testing, and vascular anatomy. *Results:* Sudden visual loss occurred in five patients, two with a hemorrhage and one with a venous infarct in the occipital lobe. Fortification images occurred in three patients, two of whom had palinopsia (one with de novo formed visual hallucinations). Homonymous quadrantic or hemianoptic field defects, some fluctuating, were found in six patients. Angiography revealed each DAVM was supplied solely by dural arteries and drained into occipital pial veins due to retrograde blood flow through the sites near or in the wall or lumen of the dural venous channels that normally drain the occipital lobe. Unlike DAVMs in other locations, only two patients had occlusion of an adjacent venous sinus. These patients, particularly the two with posterior fossa DAVMs remote to the occipital lobe, clearly demonstrate the visual and neurologic dysfunction resulting from venous hypertension. In six patients, intra-arterial embolization of the arterial feeders and nidus (one patient required additional surgery) resulted in resumption of normal occipital venous emptying. No further visual episodes occurred in five of these six patients. The visual fields normalized in three patients and improved in one with venous infarct but were unchanged in both patients with a hemorrhage. *Conclusions:* DAVMs that drain into occipital veins cause field loss and other visual disturbances because of venous hypertension in the occipital lobe, which can be reversed by occluding the DAVM nidus. If a venous infarct or hemorrhage has not caused irreversible damage, visual recovery should be complete.

NEUROLOGY 1999;52:156–162

Distortion of visual perception occurs with any of the many vascular disorders that disturb the occipital lobe.¹ Although ischemia and hemorrhage from arterial disease are the most common, venous disorders can cause similar symptoms. Typically, patients experience transient or permanent visual field loss. Less often patients have episodes of distortion in the visual scene, or visual hallucinations or palinopsia. When the cause is associated with an arteriovenous (AV) shunt or malformation, a reduction of posterior cerebral arterial inflow or an arterial steal is often

assumed incorrectly to be the mechanism of the cerebral symptoms. Particularly when the AV shunt does not involve the cerebral arteries, as in the situation of dural AV malformations (DAVMs), which are supplied by the dural meningeal arteries, an arterial “steal” cannot be the cause.¹ Another mechanism, such as a disturbance in the normal cerebral venous drainage, must be considered.^{2–4} We describe seven patients with occipital lobe dysfunction as a result of secondary involvement of the occipital pial venous system because of the abnormal venous drainage from a DAVM.

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Received April 10, 1998. Accepted in final form September 19, 1998.

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Figure 1. Patient 1. (A) Axial T2-weighted MRI shows flow voids along the medial occipital surface and in the anterior occipital lobe. The brain parenchyma appears normal. (B) Sagittal T1-weighted MRI shows flow voids along the medial surface of the occipital lobe that correspond to the dilated occipital veins (arrowhead) in figure 2.

Methods. We reviewed the records of all six patients with cerebral visual dysfunction associated with a DAVM (verified angiographically) by the Institute of Neurology and Neurosurgery and New York University interventional neuroradiology services from 1982 to 1996, in addition to one patient from the Royal Perth Hospital in Perth, Australia. Each patient had complete neuro-ophthalmologic evaluation; CT, MRI, or both; and a complete cerebral angiography, including investigation of both external carotid arteries. The patients, except Patient 4 (who refused therapy), were treated via percutaneous selective arterial embolization, principally with liquid acrylic agent and polyvinyl alcohol particles when use of a liquid agent was considered unsafe.

Case histories. *Patient 1.* A 46-year-old man awoke with a severe headache and nausea that lasted for 5 hours. Approximately 12 hours later he complained of difficulty seeing written words and kaleidoscopic images in the left field of both eyes, with eyes open or closed, for 1 hour. The visual imagery recurred every few days until he was given phenytoin. Neurologic and visual field examinations were normal. No abnormalities were seen on EEG. MRI revealed a vascular malformation in the region of the occipital lobe without cerebral edema (figure 1). A DAVM with drainage into the cortical veins of the occipital lobe was evidenced on cerebral angiography (figure 2).

After embolization therapy, anticonvulsant therapy was

Figure 2. Patient 1. (A) Mid-phase lateral external carotid angiogram shows the middle meningeal artery (arrows) supplying the dural arteriovenous malformation (DAVM; asterisk), which drains into the wall of the superior sagittal sinus and then into the occipital veins (broad arrow), which are markedly dilated. Additional dural supply (not shown) arising from the occipital and meningeal branches from the vertebral arteries also supplied the DAVM. (B) The late venous phase of the external carotid artery angiogram shows reflux from the superior sagittal sinus into the cortical veins in the entire parietal occipital region. The cortical venous drainage was rerouted to the deep venous system (curved arrow). (C) The venous phase of the internal carotid artery angiogram shows a lack of filling of the parietal occipital cortical veins (arrowheads). (D) After acrylic embolization of the DAVM, the venous phase of the internal carotid artery angiogram shows filling of the cortical parietal occipital veins (arrowheads) in the normal sequence. Note the radiopaque acrylic cast that has been partially subtracted.

Figure 3. Patient 2. Threshold perimetry demonstrates a left inferior homonymous partial quadrantanopia, slightly worse in the left eye (B) than in the right eye (A).

withdrawn and there were no visual difficulties for 6 months. The patient then experienced two episodes of flashes, and he was unsure whether they involved the left field or the left eye. Reinvestigation demonstrated a recurrence of the DAVM draining into the occipital lobe. At that time, depression of the left homonymous inferior field was found on perimetry but the remainder of the neurologic examination was normal. Additional embolization and surgical resection resulted in no additional visual episodes and resolution of the visual field defect (using threshold perimetry) during the subsequent 5-year follow-up.

Patient 2. A 51-year-old man complained of episodic loss of the left lower visual field for 6 months. Five months after the symptoms began he complained of flashing and

pulsation in an area of persistent scotoma in the left lower field followed by loss of the entire left field. After carbamazepine was begun, the visual disturbances were less intense and occurred only after exercising. Once the patient had pulsation in the left field followed by a generalized motor seizure after exercise. After one visual episode he experienced palinopsia and visual imagery, as if he was viewing a "rolling" television screen. He had seen a real cat and the image persisted in the left lower field for 30 minutes. His neurologic examination was normal except for a left inferior wedge-shaped visual field defect (figure 3). MRI showed a vascular malformation in the region of the anterior medial occipital lobe without edema. Cerebral angiography demonstrated a DAVM, with reflux into the ce-

Figure 4. Patient 2. (A) Superselective catheterization of the parietal branch of the middle meningeal artery (arrow), lateral view mid-arterial phase, shows shunting (asterisk) into the cortical occipital veins (broad arrow) via the wall of the venous sinus. Note the adjacent venous sinus lumen does not opacify from this circulation. (B) Superselective injection occipital artery angiogram shows the transmastoid branch (arrow) supplying the shunt (asterisk) on the dural surface, which drains into the same dilated cortical veins.

Figure 5. Patient 3. (A) The lateral view left common carotid arteriogram demonstrates an extensive dural arteriovenous malformation (DAVM; asterisk) that is supplied by the posterior branches of the middle meningeal artery (curved arrow) and the occipital artery (straight arrow) arising from the external carotid artery. There was no direct blood supply to the DAVM from the cerebral arteries. The DAVM is located along the wall of the occluded sigmoid sinus. There is reflux that

resulted in drainage to the supratentorial cerebral veins of the occipital lobe (broad arrow). (B) The lateral view external carotid artery angiogram demonstrates the posterior branches of the middle meningeal artery (curved arrows) supplying the DAVM (asterisk). The occipital artery (straight arrow) supplies the AV shunt via the stylomastoid and mastoid branches (small arrows). After embolic treatment of the middle meningeal, ascending pharyngeal, and occipital blood supplies to the DAVM, the lateral view common carotid artery angiogram did not opacify the DAVM (not shown).

rebral veins of the occipital lobe (figure 4). After embolization therapy, the vascular malformation was obliterated. The patient was withdrawn from carbamazepine without further visual episodes. Four months after embolization, the visual field defect resolved. Repeat visual field and MRI examinations remained normal during the next 4 years.

Patient 3. A 43-year-old woman had a 1-month history of three recurrent 2-hour episodes of headache and a “flamelike” right visual field disturbance, followed by difficulty understanding spoken words. Her neurologic and visual examinations were normal. EEG revealed slow wave activity over the left parietal and occipital lobes. The visual, but not the speech, disturbance recurred despite anticonvulsant therapy. Cerebral angiography revealed a DAVM with reflux into the veins of the left occipital lobe (figure 5). After embolic closure of the vascular shunt, no additional visual or neurologic disturbances occurred, even after withdrawal from anticonvulsant therapy.

Patient 4. A 57-year-old man with a 20-year history of recurrent headaches, predominantly behind the right eye, had episodic left visual disturbances for 1 year. He described flashes of lights composed of numerous colors covering the entire left field and lasting 10 minutes to 2 hours. At times he would see objects within his field as

either very large or small, or distorted into unreal shapes. He had a 1-hour episode while watching television: the head of one actor was projected onto the head of the other actors in the same scene. The next day he perceived that all the people he saw had exceptionally broad noses. The next day he noted that every face had a “cabbage patch” appearance. He did not look at himself in a mirror on either day and no other body parts of the people he saw appeared abnormal. Several days later, after dealing with a merchant of Chinese origin, all the people he saw, including his daughter, appeared to have Chinese facial features. His neurologic examination was normal except for a dense right superior quadrantanopsia. MRI showed abnormal vascular channels in the medial occipital sulci without any parenchymal changes. Cerebral angiography demonstrated a DAVM, near the torcula, that drained along the tentorium and into the right occipital and parietal lobes. There was no evidence of venous sinus thrombosis. The patient refused therapy of his vascular malformation.

Patient 5. A 62-year-old diabetic man developed severe headache and a left homonymous visual field defect. His neurologic examination was normal except for a dense left homonymous field defect that was worse inferiorly. A right occipital hematoma was found on CT. A DAVM was demonstrated on angiography. The middle meningeal artery

Figure 6. Patient 6. (A) Lateral common carotid artery angiogram shows the enlarged middle meningeal artery (arrow) supplying an arteriovenous (AV) shunt (asterisk). The dural AV malformation (DAVM) drains into the cerebral veins, which have an aneurysmal dilatation (curved arrow) in the occipital lobe (seen on CT and MRI performed before the angiogram, not shown), which drained into the transverse sinus. (B) The anteroposterior view of the common carotid artery angiogram shows that the middle meningeal artery supplies the DAVM (asterisk) at the inferior lateral wall of

the superior sagittal sinus. The shunt drains into the dilated pial venous drainage (arrow) from the expected entrance of the cerebral vein to the sinus.

Table 1 Pretreatment visual symptoms and findings

Patient no.	Age, y	Sex	Imagery positive/negative	Palinopsia	Formed hallucination	Visual field defect
1	46	M	Y/N	N	N	Y
2	51	M	Y/Y	Y	N	Y
3	43	F	Y/Y	N	N	N
4	57	M	Y/N	Y	Y	Y
5	62	M	N/Y*	N	N	Y*
6	45	M	N/Y*	N	N	Y*
7	78	F	Y/N†	N	N	Y†

* Related to occipital hemorrhage.

† Related to venous infarct.

supplied an area of AV shunting in the wall but not in the lumen of the superior sagittal sinus. There was reflux into dilated cortical veins that drained into the patent superior sagittal sinus and into the deep venous system. Embolization therapy obliterated the DAVM but the visual fields never improved.

Patient 6. A 45-year-old man developed a right occipital headache and loss of his entire right visual field. His neurologic examination was normal except for a complete left homonymous hemianopia. MRI and CT demonstrated a right occipital hemorrhage with an aneurysmally dilated vessel. A DAVM was found on angiography (figure 6). The shunt drained into cortical veins that were dilated aneurysmally, and drained into the transverse sinus. Embolization therapy obliterated the DAVM but the visual field defect recovered only partially.

Patient 7. A 78-year-old woman had symptoms of intermittent "swishing" in the right ear beginning in 1988, followed 3 years later by the onset of episodic left visual field disturbances. These attacks consisted of black, unformed marks moving in the left field, followed by moving circles in the same area. Carbamazepine therapy was instituted, but the events still occurred. Her neurologic examination was normal except for a left homonymous quadrant field defect that encroached on the central fixation point. MRI showed signs of a vascular malformation with gliosis or edema in the right occipital lobe. Cerebral angiography demonstrated a DAVM. The middle meningeal artery supplied the DAVM in the wall of the sigmoid sinus, which then drained into the partially thrombosed

sigmoid and transverse sinuses. There was secondary reflux anteriorly into the vein of Labbe and via the transverse sinus into the occipital pole veins, bypassing the torcular region. The entire DAVM was obliterated with intra-arterial embolization therapy. The peripheral visual field defect remained but the central superior 10 deg normalized. Despite DAVM closure, episodes of left upper quadrant flickering lights recurred, but were controlled with carbamazepine.

Comment. Positive, unformed visual imagery occurred in the five patients without a hemorrhage (table 1). Two of these patients also experienced palinopsia, and one also had de novo formed hallucinations. Visual field defects were documented in six of the seven patients. No patient had signs of anterior visual pathway dysfunction or papilledema.

The adjacent or involved dural venous sinus was thrombosed in only two patients (table 2). No patients had narrowing of cerebral veins. The DAVM drained into the sinus wall in four patients, and drained directly into the sinus in two of these patients. In three patients the DAVM appeared not to involve the sinus lumen or wall.

After treatment, the six patients were followed 3 to 10 years (mean, 5.8 years). None experienced new or worse visual field loss or an intracranial hemorrhage. The positive, unformed visual imagery; palinopsia; and formed hallucinations resolved in all but one patient (Patient 7). The visual fields normalized in four and improved in two patients (Patients 6 and 7) after treatment. MRI performed in all six patients did not reveal recurrence of the DAVM.

Table 2 Radiologic findings

Patient no.	Cerebral angiography				MRI/CT			
	Dural venous sinus occlusion	Narrow cerebral vein	Direct drain to dural sinus	Arterialized pial veins	Dilated cortical vessels	Blood	Venous infarct	White matter gliosis/edema
1	N	N	N	Y	Y	N	N	N
2	N	N	N	Y	Y	N	N	N
3	Y	N	Y	Y	Y	N	N	N
4	N	N	N	Y	Y	N	N	N
5	N	N	N	Y	Y	Y	N	Y
6	N	N	N	Y	Y	Y	N	Y
7	Y	N	Y	Y	Y	N	Y	Y

Discussion. When a DAVM drains directly or indirectly into pial veins, it can cause neurologic dysfunction similar to the disorders caused by a pial AV malformation. If an individual without papilledema with a DAVM in the region of the transverse or posterior sagittal sinus dural venous sinuses has a visual disturbance, it is highly suggestive of abnormal venous drainage of the occipital lobe. The dural AV shunt can affect the pial venous system adversely via reflux through the normal-occurring cerebral vein to dural venous sinus connections because of restriction of outflow, either mechanical or functional, in the sinus, or by abnormal flow into veins in the dura near the major venous sinuses.²⁻⁴ The affected pial veins normally drain directly or indirectly into the transverse sinus. The occipital vein, which drains the lateral occipital lobe, empties directly, and the posterior calcarine vein, which drains the medial posterior occipital lobe, and the occipital basal vein, which drains the inferior and inferomedial aspects of the occipital lobe, empty indirectly via the lateral tentorial sinus into the transverse sinus.⁵ The normal flow of the occipital lobe veins is blocked or slowed by thrombus (in two of our patients)⁶ or increased pressure in the dural sinuses because of the arterialized venous output from the DAVM (in all seven of our patients).^{3,7} As shown in an experimental model,⁸ our Patients 1, 2, 4, 5, and 6 clearly support reports by others⁹ that suggest that DAVMs can develop without dural venous thrombosis or outflow restriction. However, it is possible that a transient sinus occlusion could contribute to the development of the DAVM and the direction of the abnormal venous drainage.

The DAVM often involves the dural sinus wall,¹⁰ which in normal subjects may¹¹ or may not⁹ contain microscopic AV anastomoses, with drainage into the dural venous sinus dural lakes.¹² In patients with DAVMs, but not in normal subjects, dural arteries communicate directly with dural veins via “crack-like” vessels near the dural venous sinuses.⁹ Three of our patients (Patients 2, 4, and 6) likely had this type of histopathology without direct involvement of the dural venous sinus channel because each DAVM appeared to drain into the dural sinus wall, bypassing the sinus lumen, with abnormal flow into the cerebral veins. Also, this was probably the circumstance in the two patients with dural AV shunts said to be located in the leptomeninges.² This is not unlike DAVMs located along the tentorium or the floor of the anterior cranial fossa, which do not have a direct relation with a venous sinus.¹³ All of our patients had retrograde drainage into the cortical veins from the dural venous sinus, or direct drainage with or without venous ectasia.¹⁴ None of our patients had a direct single-hole fistula from a dural artery to a cerebral vein.

Because the occipital arterial blood supply remains unaffected, there is no arterial “steal,” and the occipital dysfunction results from one or more pathologic mechanisms in the occipital pial venous circula-

tion. Our two patients with posterior fossa DAVM and abnormal reflux into the supratentorial venous circulation to the occipital lobe prove this concept definitively. When venous hypertension causes reversal or slows or compromises the normal occipital venous blood outflow severely,⁴ this results in microscopic subclinical hemorrhages and edema^{7,15} in the occipital lobe. Congestion of occipital veins also disrupts local cerebral metabolism and can cause local tissue necrosis.¹⁶

Thrombosis in the secondarily affected pial veins not infrequently causes a venous infarct or hemorrhage in the occipital lobe, accounting for the homonymous visual field loss (Patients 5 through 7). The field loss in Patients 1, 2, and 4 could have developed from edema and a local metabolic disturbance. Another possible cause could be that following local seizure activity, postictal neuronal “fatigue” or local tissue hypoxia/acidosis results, or a loss of excitation results in an increase of “surround inhibition” in the functional cortical architecture. Although a local mass effect from aneurysmal venous dilatation could cause a visual field defect, none of the patients in our series demonstrated this. Fortunately, following DAVM closure, the field defect resolved in patients without an infarct or bleed and improved in our one patient with an infarct. However, the vision did not change in the two patients with a hemorrhage. Therapy that closes the dural AV shunt results in normalization of abnormal occipital cortical venous flow (in patent vessels), and in the majority of patients the visual loss improves or resolves.

Positive visual imagery developed in all of our patients with unruptured DAVMs. These included lines and unformed bright and colored flashes in the field opposite the affected occipital lobe. Palinopsia occurred in two patients (Patients 2 and 4), one of whom had prolonged, exaggerated symptoms as well as de novo hallucinations. Because of frequency reduction of these episodes by anticonvulsant therapy (Patients 1 and 2, but not Patients 3 and 7), seizure activity was diagnosed as the cause. In Patient 3, a possible migrainelike disturbance was suspected. These positive, spontaneous visual images could also have developed because of release from local inhibitory visual input¹⁷ or a loss of normally occurring cortical inhibition. Although both formed and unformed hallucinations have been described in patients with occipital pial AVM,¹⁸ in a recent review¹⁹ of 70 occipital pial AVMs, none had palinopsia or visual hallucinations except for unformed, positive visual imagery similar to migraine. This suggests that DAVMs may have a different mechanism of cortical dysfunction. Palinopsia has been reported with astrocytoma²⁰ and infarcts in occipital lobe,¹⁸ but not in patients with pial AVM.¹⁹ In these patients and our patients, hallucinations and palinopsia were associated with concomitant homonymous visual field loss. The visual fields were normal in only one of our four patients who experienced positive visual phenomena. Similar symptoms of palinopsia and visual

hallucinations have been described previously in three patients with DAVM, all with homonymous visual field defects—two prior to therapy,^{6,21} and one after surgical resection.²² In our patients the local venous hypertension probably caused the positive visual imagery because in three of the four patients, restitution of normal occipital pial venous flow resulted in cessation of the episodes.

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Impact of neurologic signs and symptoms on functional status in peripheral neuropathies

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Neurology 1999;52;151-

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