Sistema Socio Sanitario

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ASST Mantova

Le patologie della mielina Diagnosi differenziale delle malattie del sistema nervoso periferico. Il ruolo della neurofisiologia

Dr.Paolo Buzzi UOC Neurologia

ASST Mantova

Cremona , 9 Giugno 2017

Lo studio elettrodiagnostico

- Complementare ad un adeguato inquadramento anamnestico , clinico (valutazione attenta dei segni e sintomi), laboratoristico ed eventualmente genetico.
- Conferma o meno le alterazioni evidenziate dall'esame clinico
- Può svelare alterazioni in distretti neuro-muscolari clinicamente non coinvolti.
- Valuta la gravità,la prognosi e la risposta alle terapie.
- Ma solo raramente indirizza verso una specifica etiologia.

Potenzialità dell'EDX

- Tipo di fibre coinvolte :motorie, grandi fibre sensitive, piccole fibre , autonomiche.
- Distribuzione delle alterazioni: distale simmetrica , poliradicoloneuropatia, mononeurite multipla , prevalente arti superiori o inferiori
- Processo patologico: perdita assonale, demielinizzazione, forme miste .
- Livello del danno nervoso: lieve , medio, grave .
- Monitoraggio evolutivo.

I criteri EDX della demielinizzazione

- Rallentamento della velocità di conduzione.
- Aumento delle latenze distali.
- Alterazione delle risposte tardive F ed H.
- Presenza di blocchi di conduzione.
- Aumentata dispersione temporale del potenziale d’azione motorio composto.

La velocità di conduzione

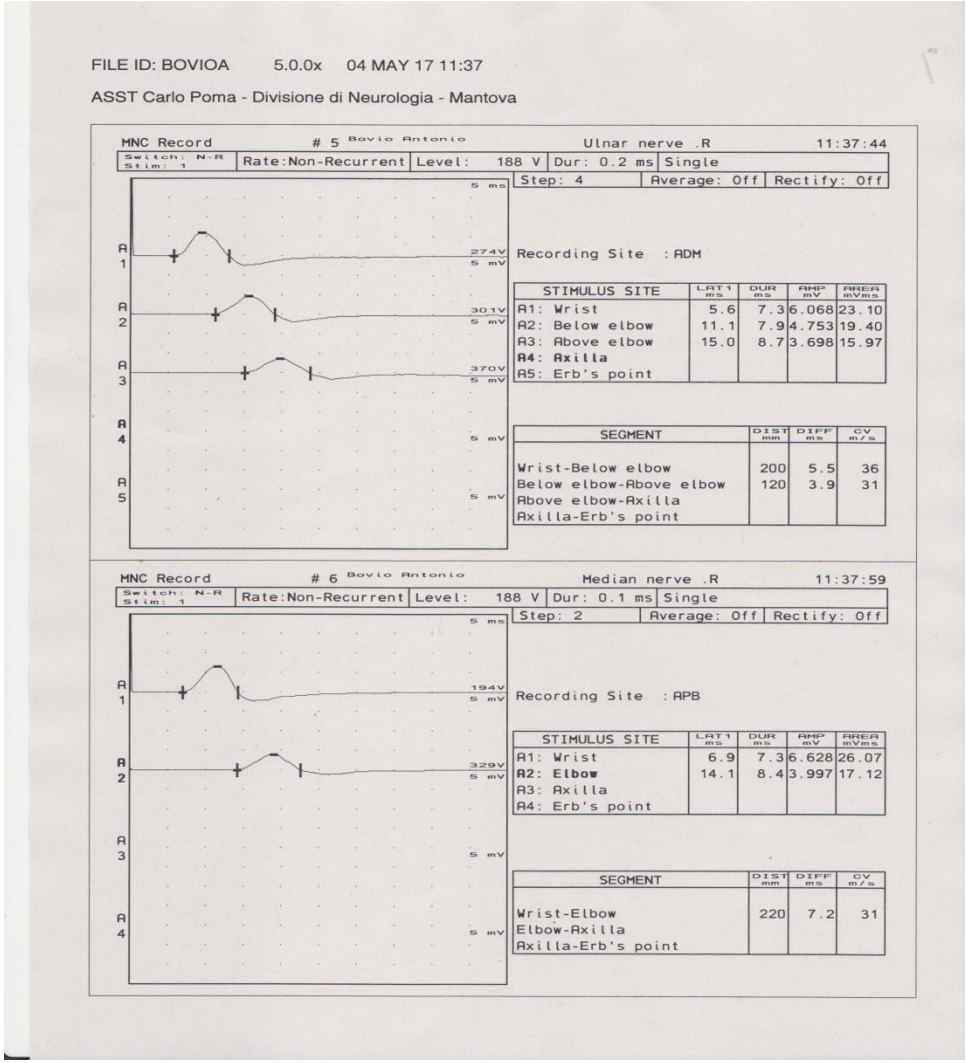
-Legata all'integrità della guaina mielinica ma anche degli assoni di grosso calibro .

-Stretta correlazione tra riduzione della conduzione ed ampiezza del potenziale motorio composto nella definizione di demielinizzazione.

-La riduzione della VC deve essere maggiore del 80% o 70% del LLV a seconda dell'ampiezza del Cmap.

-La massima riduzione delle VC si vede nelle forme genetiche (CMT1) .

--Non correla strettamente con la riduzione della forza muscolare.



Il blocco di conduzione

L'impossibilità del potenziale d'azione a propagarsi lungo un assone integro dovuta al danno mielinico.

Il potenziale composto distale deve essere di ampiezza nella norma.

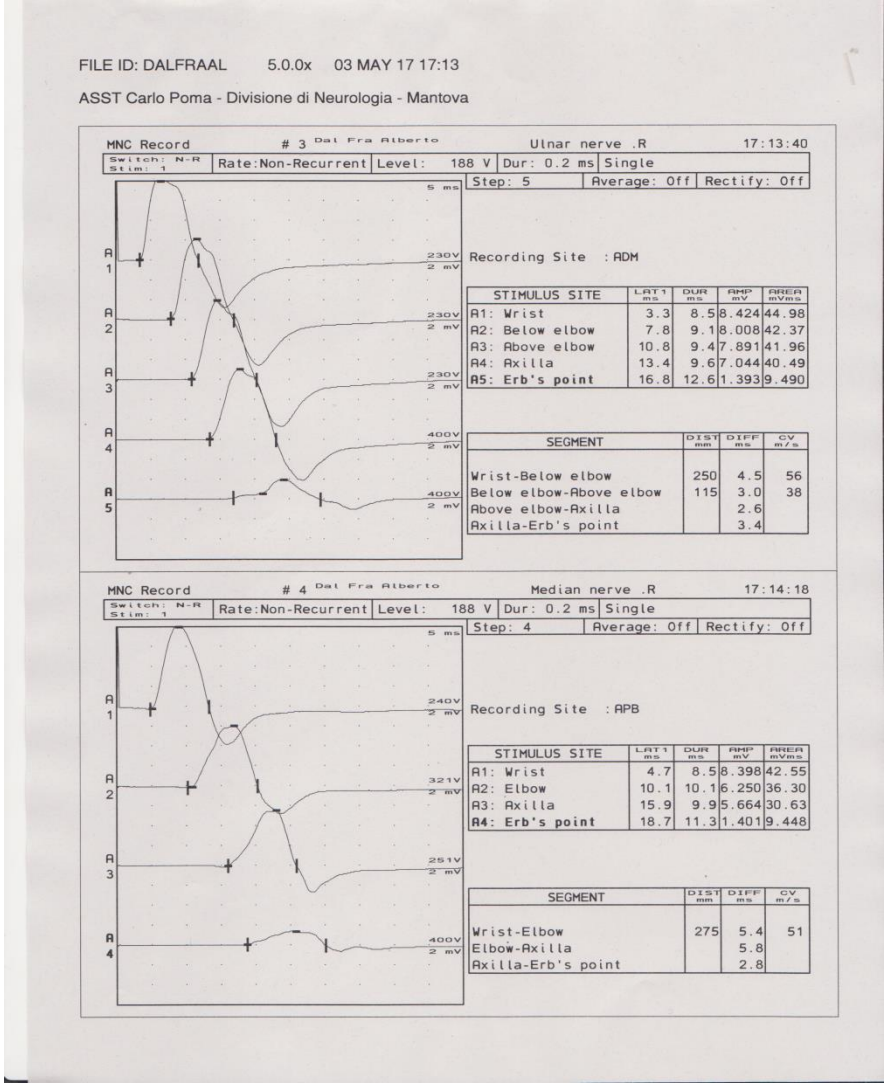
Vari criteri utilizzati per la definizione di blocco (caduta di ampiezza e di area del potenziale per stimolazione prossimale dal 50 % al 70% rispetto distale)

Assenza di rilevante dispersione temporale del potenziale (deve essere inferiore al 30%.).

Eliminazione di problemi tecnici

Utilità delle tecniche di inching.

Correla strettamente con deficit motorio.



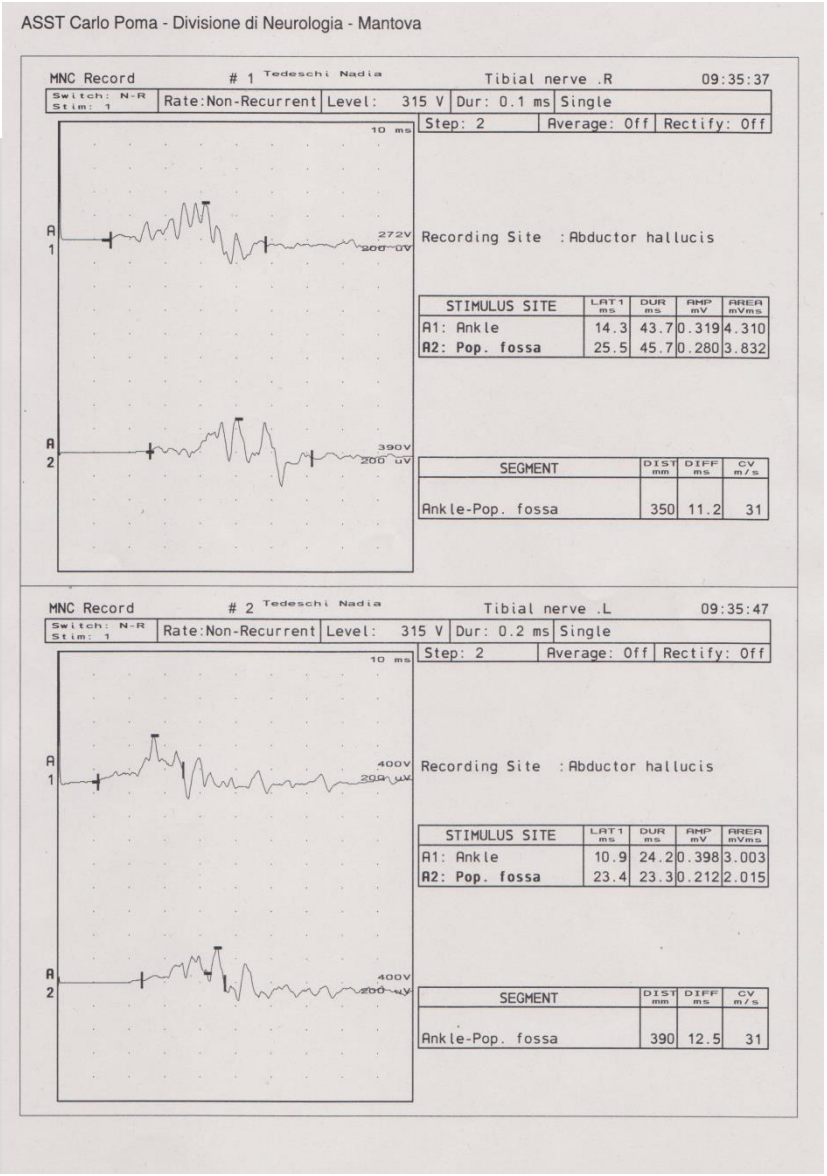
La dispersione temporale

Desincronizzazione del potenziale d'azione lungo le fibre demielinizzate che presentano conduzione alterata.

Prolunga la durata del Cmap (> del 30%) e ne altera la morfologia (onde irregolari);

Confronto tra durata del Cmap prossimale rispetto al distale.

Può essere l'esito del blocco di conduzione.



Alterazioni dell'onda F

Utile per valutare la conduzione nei tratti prossimali.

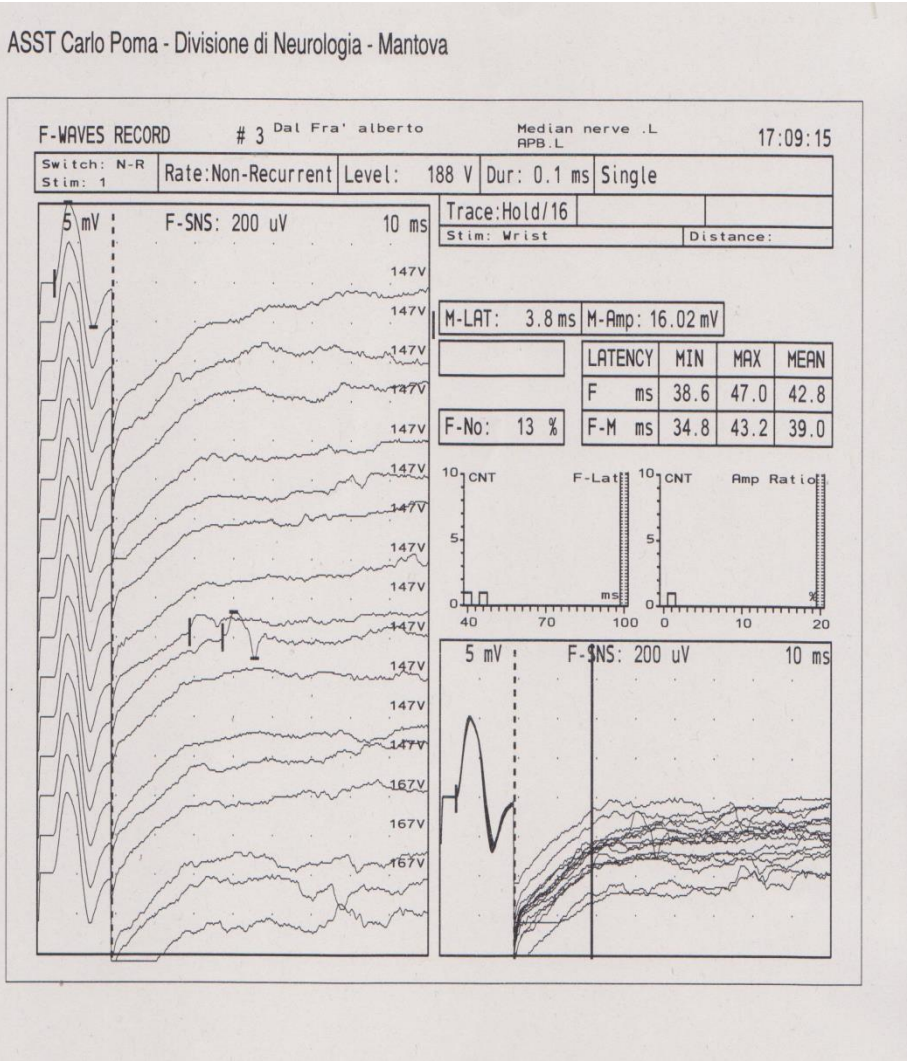
Aumento di **latenza** >120%-150%

Persistenza : < 50% arti superiori,< 80% n.Tibiale posteriore, <10% n. Peroneo.

Crono-dispersione (differenza di latenza tra l'onda F più lunga e più breve).

…purchè l'ampiezza del Cmap sia nella norma o solo moderatamente ridotta.

Alterata anche in altre situazioni (plessopatie, radicolopatie etc.)



La sindrome di Guillain-Barrè.

Key points

- Guillain–Barré syndrome (GBS) is a heterogeneous disease characterized by rapidly progressive, symmetrical limb weakness with hyporeflexia or areflexia; sensory disturbances and cranial nerve deficits occur in some patients
- The clinical diagnosis of GBS can be supported by additional investigations (such as cerebrospinal fluid examination and nerve conduction studies), which are especially useful in patients with atypical features or diagnostic doubt
- Molecular mimicry, antiganglioside antibodies and, likely, complement activation are involved in the pathogenesis of GBS; a potential role for genetic susceptibility requires further investigation
- Intravenous immunoglobulin and plasma exchange are proven effective treatments, but improved therapies are needed as ~25% of patients require artificial ventilation and 20% are unable to walk after 6 months
- Pain is an important symptom that may be present before onset of weakness, and can impede correct diagnosis, especially in children; other residual features (sensory disturbances and fatigue) may persist for years
- Prognostic models can predict patient outcomes at 4 weeks, 3 months and 6 months, as well as the probability of respiratory insufficiency, even early in the course of the disease

Guillain-Barrè syndrome : pathogenesis,diagnosis, treatment and prognosis
Van Den Berg et al, Nat.Rev.Neurol. 10, 469-482,2014

La diagnosi neurofisiologica della s. di Guillain-Barrè.

- La diagnosi è clinica , gli esami neurofisiologici, biologici (esame liquorale e esami immunologici) sono di supporto.
- La EDX permette di distinguere tra le varie forme di G.B , non distinguibili clinicamente (AIDP, AMAN, AMSAN).
- Può essere negativa nelle fasi precoci.
- Raccomandati controlli seriati.
- Non vi sono criteri EDX di diagnosi accettati a livello internazionale .
- I criteri proposti si differenziano per sensibilità e specificità

Table 1 Criteria for AIDP. Must have one of the following in two nerves in all the criteria sets.

	Ho et al., 1995	Hadden et al., 1998	Dutch GBS Study Group., 1995	Rajabally et al., 2015
MCV	< 90% LLN < 85% If d-amp < 50%	< 90% LLN < 85% If d-amp <50% LNN	< 70% LLN	< 70% LLN
DL	> 110% ULN > 120% If d-amp < LLN	> 110% ULN > 120% If d-amp < LLN	> 150% ULN	> 150% ULN
TD	Unequivocal	Not considered	D-P duration ratio > 150% ULN Distal duration > 300% ULN	Not considered
CB	Not considered	< 0.5 prox-dist amp ratio and d-amp > 20% LLN	Amp decrease > ULN > 16% ulnar > 11% median > 41% peroneal	< 0.7 prox-dist amp ratio in two nerves with an additional parameters[a]
F-wave L	> 120% ULN	> 120% ULN	> 150% ULN	> 120% ULN or > 150% ULN if distal CMAP < 50% LLN Absence in two nerves with distal CMAP ≥ 20% LLN with an additional parameter in one other nerve[a]

MCV: motor conduction velocity; DL: distal latency; TD: temporal dispersion; CB: conduction block; L: latency; LLN: lower limit of normal; d-amp: distal CMAP amplitude; amp: CMAP amplitude; dur: CMAP duration; prox: proximal; dist: distal; ULN: upper limit of normal; DP duration: disto-proximal duration.

[a] These electrodiagnostic are enough alone to reach the diagnosis.

Criteri diagnostici di AIDP

1. Normal
   (All the following in all nerves tested)
   - DML ≤100% ULN
   - F-wave present with latency ≤100% ULN
   - MCV ≥100% LLN
   - Distal CMAP ≥100% LLN
   - Proximal CMAP ≥100% LLN
   - Proximal CMAP/distal CMAP ratio >0.5
2. Primary demyelinating
   (At least one of the following in each of at least two nerves, or at least two of the following in one nerve if all others inexcitable and distal CMAP ≥10% LLN)
   - MCV <90% LLN (85% if Distal CMAP <50% LLN)
   - DML >110% ULN (120% if Distal CMAP <100% LLN)
   - Proximal CMAP/distal CMAP ratio <0.5 and distal CMAP ≥20% LLN
   - F-response latency >120% ULN
3. Primary axonal
   - None of the above features of demyelination in any nerve (except one demyelinating feature allowed in one nerve if distal CMAP <10% LLN) and
   - Distal CMAP <80% LLN in at least two nerves
4. Inexcitable
   - Distal CMAP absent in all nerves (or present in only one nerve with distal CMAP <10% LLN)
5. Equivocal
   - Does not exactly fit criteria for any other group

CMAP, compound muscle action potentials; DML, distal motor latency; LLN, lower limit of normal; MCV, motor conduction velocity; ULN, upper limit of normal.

Criteri di diagnosi di GB proposti da Hadden et al. 1998

Criteri di Van den Bergh et al. modificati da Rajabally et al. nel 2015 per la diagnosi di AIDP e AMAN.

Electrophysiological diagnosis of Guillain-Barrè syndrome subtype .
Rajabally et. Al , J Neurol Neurosurg Psy, 2015

Box 2 Proposed modified set of electrodiagnostic criteria for Guillain–Barré syndrome (based on Van den Bergh and Piéret,[7] for demyelinating cut-offs and incorporating use of new knowledge on axonal GBS to define primary axonal forms[1 2])

1. Normal
   (All the following in all nerves tested)
   - DML ≤100% ULN
   - F-wave present with latency ≤100% ULN
   - MCV ≥100% LLN
   - Distal CMAP ≥100% LLN
   - Proximal CMAP/distal CMAP ratio >0.7 (excluding the tibial nerve)
2. Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)
   - At least one of the following in at least two nerves:
     - MCV <70% LLN
     - DML >150% ULN
     - F-response latency >120% ULN, or >150% ULN (if distal CMAP <50% of LLN)
   - OR
     - F-wave absence in two nerves with distal CMAP ≥20% LLN, with an additional parameter, in one other nerve
   - OR
     - Proximal CMAP/distal CMAP ratio <0.7 (excluding the tibial nerve), in two nerves with an additional parameter, in one other nerve
3. Axonal GBS including inexcitable forms
   - *Axonal GBS*:

   None of the above features of demyelination in any nerve (except one demyelinating feature allowed in one nerve if distal CMAP <10% LLN), and at least one of the following:
     - Distal CMAP <80% LLN in two nerves
     - F-wave absence in two nerves with distal CMAP ≥20% LLN, in absence of any demyelinating feature in any nerve
     - Proximal CMAP/distal CMAP ratio <0.7, in two nerves (excluding the tibial nerve)
     - F-wave absence in one nerve with distal CMAP ≥20% LLN OR proximal CMAP/distal CMAP ratio <0.7 (excluding the tibial nerve), in one nerve; with IN ADDITION, distal CMAP <80% LLN in one other nerve
   - Inexcitable:

   If distal CMAP absent in all nerves (or present in only one nerve with distal CMAP <10% LLN)
4. Equivocal
   - Abnormal range findings however not fitting criteria for any other group

I vari autori concordano su quali siano i criteri neurofisiologici indicativi di demielinizzazione, ma non c'è accordo su quante alterazioni debbano essere presenti, quali siano i livelli di "cut-off" e sul numero di nervi che debbono essere coinvolti; ciò produce una diversa sensibilità e specificità dei criteri proposti.
Nessun criterio proposto ha una sensibilità del 100% e una soddisfacente specificità nei primi giorni di malattia.

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Early electrodiagnostic abnormalities in acute inflammatory demyelinating polyneuropathy: A retrospective study of 58 patients

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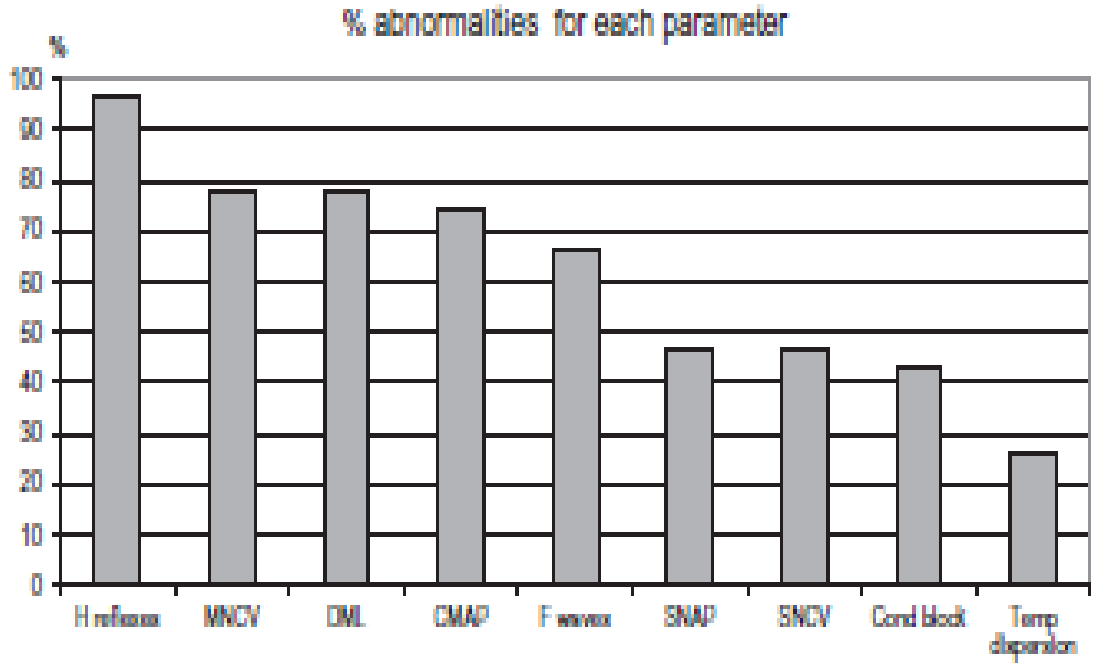
Département de Neurologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, France



Alterazioni riscontrate entro 7 gg dall'esordio

Proposed criteria for the EDX diagnosis of early AIDP.

Must have one of the 6 following features:

1) DML >125% of ULN in one nerve (150% if CMAP amplitude <80% of the lower limit of the normal).
2) MNCV <80% of LLN in one nerve (70% if CMAP amplitude is <80% of LLN).
3) Absent F waves in one nerve or minimum latency >120% of ULN.
4) Conduction block in one nerve defined by a decrease of 30% or more between the distal and proximal stimulus without increase in more than 15% of the CMAP duration*.
5) Temporal dispersion in one nerve defined by an increase of 30% or more between the distal and proximal stimulus.
6) Sural sparing pattern (an abnormal sensitive nerve in the upper limbs associated with normal sural nerve when sensitive symptoms are present in lower limbs).

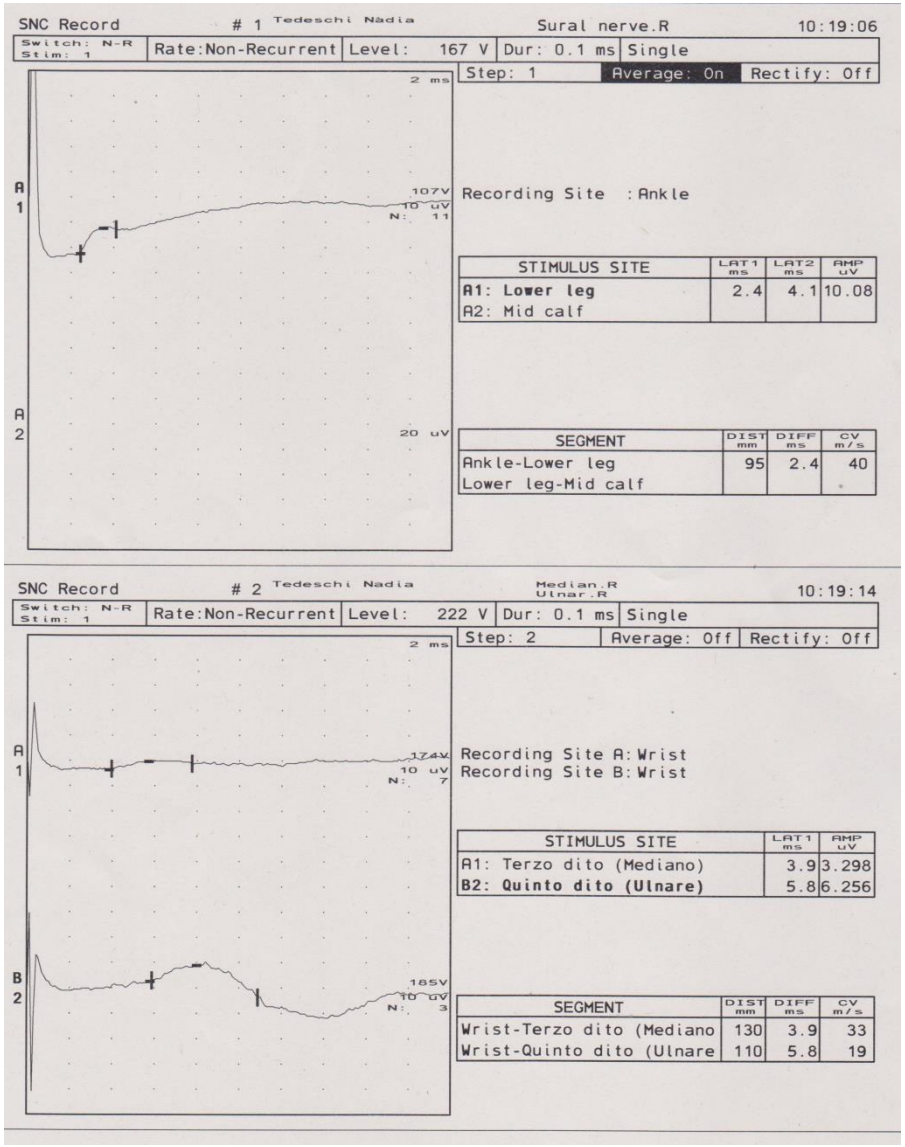
Must have a supplemental abnormality in another nerve
Including abnormal H reflexes, F waves, DML, MNCV, SNCV, CMAP or SNAP in any nerve

Suggeriscono che una sola alterazione in un nervo di quelle riportate,
piu' un'altra in un secondo nervo sarebbero diagnostiche in fase iniziale.
(specificità 64%).

J.B. Chanson et al, Clinical Neurophysiology, 2014

Sural sparing pattern

Conservazione del potenziale sensitivo del nervo Surale associata ad alterazione dei SAP dei nervi sensitivi degli arti superiori in presenza di sintomi sensitivi agli arti inferiori.



Published in final edited form as:
Muscle Nerve. 2014 November ; 50(5): 780–784. doi:10.1002/mus.24226.

Sural sparing pattern discriminates Guillain-Barré syndrome from its mimics

Angelika Derksen, MD[1], Christian Ritter, MD[2,3], Parveen Athar, MD[4], Bernd C. Kieseier, MD[1], Pedro Mancias, MD[4], Hans-Peter Hartung, MD[1], Kazim A. Sheikh, MD[4], and Helmar C. Lehmann, MD[2]

" the Sural sparing pattern is a common abnormality that occurs early in 39-67% of GBS; compared to patients with non GBS diagnosis, the sural sparing pattern has modest sensitivity (35%) but high specificity (93%);… the occurance of this pattern Is highly suggestive of AIDP in the initial electrophysiological examination on patients"

Incidenza della AIDP e AMAN

- 90% in Europa e Nord America;
- 63% in Israele
- 46% in Pakistan
- 36% in Giappone
- 24% in Cina

- 4% Europa e Nord America
- 7% in Inghilterra
- 22% in Israele
- 31% in Pakistan
- 38% in Giappone
- 65% Cina

Legata a diversa suscettibilità genetica , ai precedenti infettivi, ma anche ai differenti criteri neurofisiologici utilizzati.
Controlli EDX seriati spostano la diagnosi da AIDP ad AMAN

Contents lists available at SciVerse ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Electrodiagnostic criteria for Guillain–Barrè syndrome: A critical revision and the need for an update

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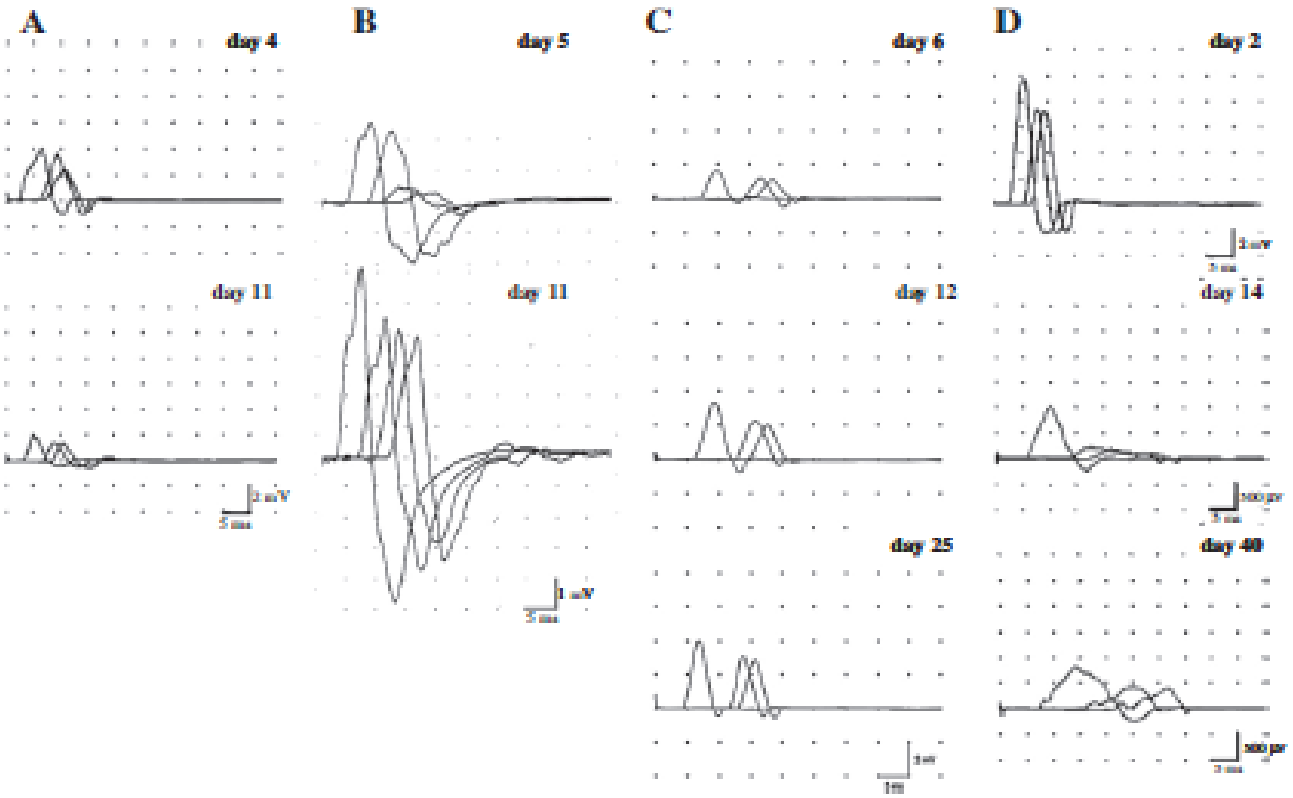
[b] Department of Neurology, Graduate School of Medicine, Chiba University, Chiba, Japan

See Editorial, pages 1483–1484

Il **blocco di conduzione reversibile** (RCF): nei tratti intermedi e distali del nervo; caduta di ampiezza del Cmap prossimale, aumento latenza distale e riduzione di ampiezza del Cmap. Si risolve spontaneamente in 30-40 gg., senza comparsa di dispersione temporale del Cmap tipico delle lesioni demielinizzanti.
Pazienti con antecedente infezione da CJ e presenza di ac anti GM1, anti GD1A e B.
Sono forme di AMAN "benigne "
Possono essere inizialmente erroneamente diagnosticate come AIDP, necessario controllo EDX.



A: AMAN
B: AMAN con RCF tratto intermedio
C. AMAN con RCF tratto distale
D: AIDP.

Contents lists available at SciVerse ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Short communication

Reversible conduction failure is distinct from neurophysiological patterns of recovery in mild demyelinating Guillain–Barré syndrome

Norito Kokubun [a,*], Nortina Shahrizaila [b], Koichi Hirata [a], Nobuhiro Yuki [c]

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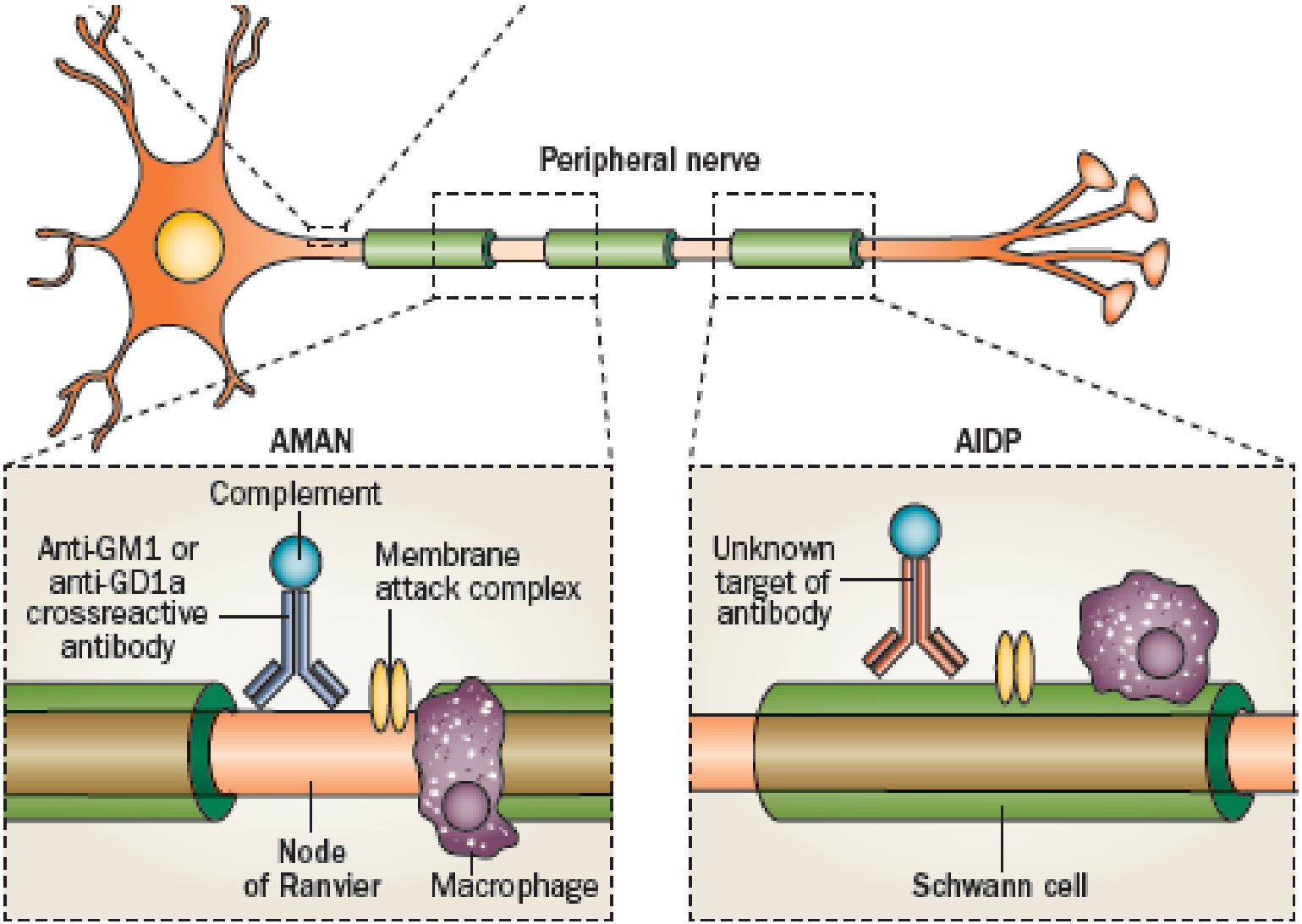
[b] Division of Neurology, Department of Medicine, University of Malaya, Kuala Lumpur, Malaysia
[c] Department of Medicine, National University of Singapore, Yong Loo Lin School of Medicine, Singapore, Singapore

Gli ac anti GM1 e anti Gd1A disgregano con l'intervento del complemento il nodo di Ranvier, che appare allungato, distaccano i loop di mielina terminale al paranodo, e provocano il blocco dei canali del Na , con blocco di conduzione della fibra (**AMAN con RCF).**

Se il danno procede si ha ingresso di Sali di Ca nella fibra, alterazione delle proteine del citoscheletro, degenerazione Walleriana **(AMAN con degenerazione assonale).**



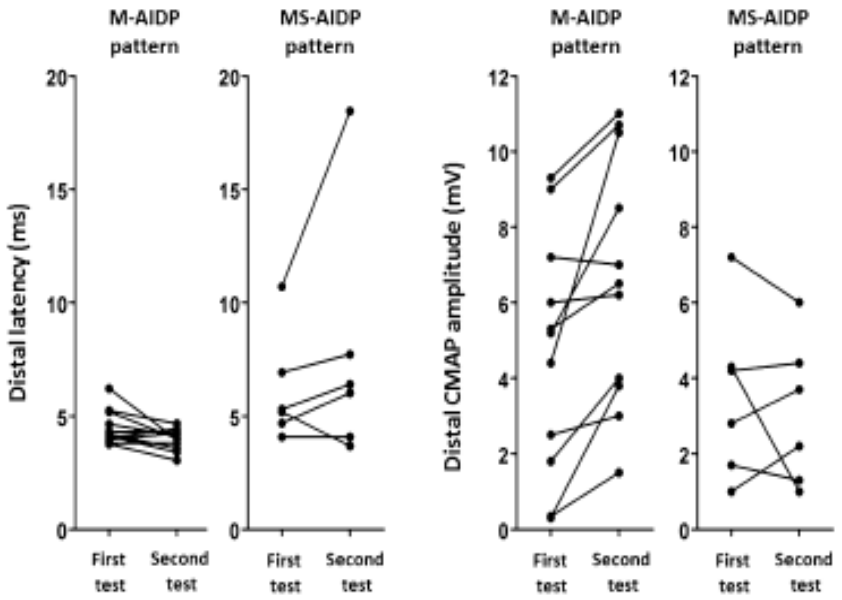
Possibili siti di aggressione immunologica nella AMAN e AIDP

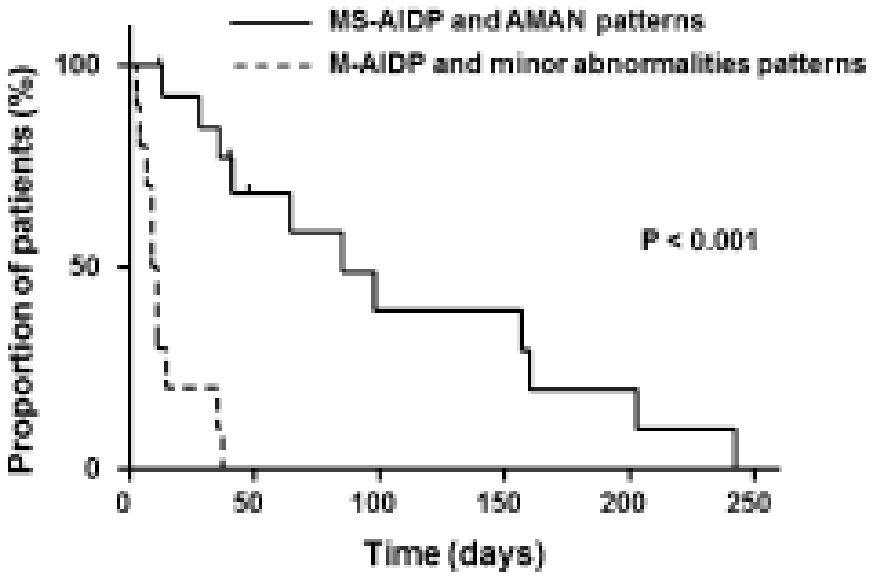
J Neurol (2014) 261:1986–1993
DOI 10.1007/s00415-014-7452-2

ORIGINAL COMMUNICATION

An electrophysiological classification associated with Guillain–Barré syndrome outcomes

Takafumi Hosokawa · Hideto Nakajima · Kiichi Unoda · Kazushi Yamane · Yoshimitsu Doi · Shimon Ishida · Fumiharu Kimura · Toshiaki Hanafusa





Evoluzione parametri EDX Proporzione paz.in grado di deambulare.

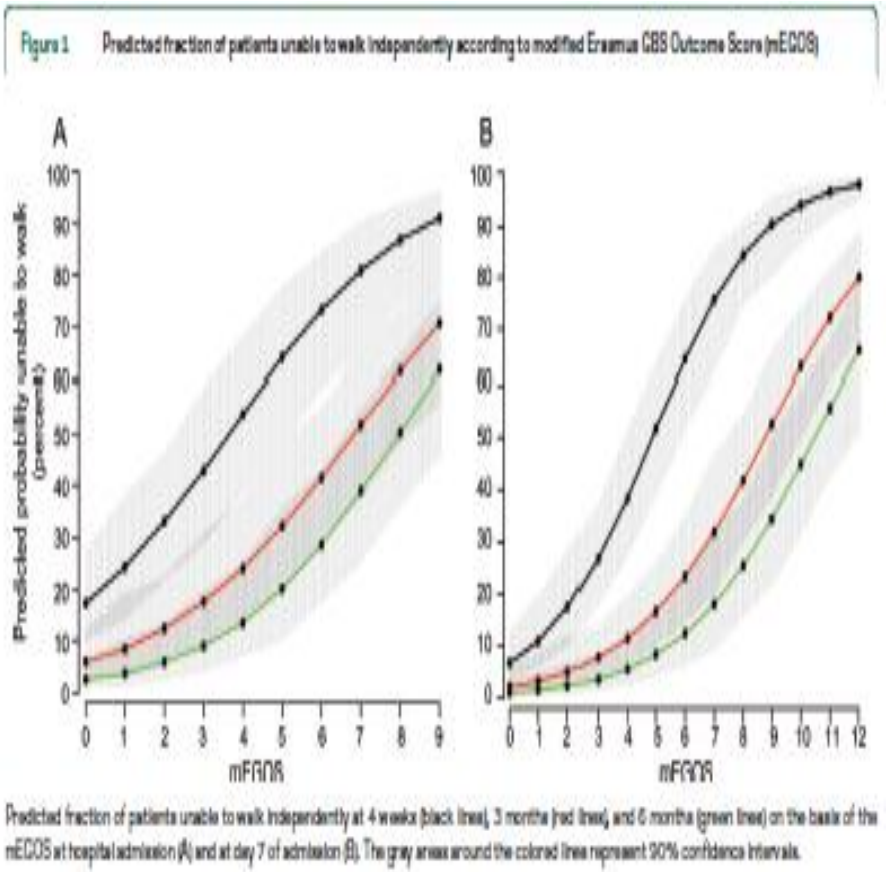
Il parametro EDX che correla con il recupero è l'ampiezza del Cmap, ma va integrato dai dati clinici.

Modified Erasmus GBS score

Prognostic factors	Score	Prognostic factors	Score
Age at onset, y		Age at onset, y	
≤40	0	≤40	0
41-60	1	41-60	1
>60	2	>60	2
Preceding diarrhea[a]		Preceding diarrhea[a]	
Absent	0	Absent	0
Present	1	Present	1
MRC sumscore (at hospital admission)		MRC sumscore (at day 7 of admission)	
51-60	0	51-60	0
41-50	2	41-50	3
31-40	4	31-40	6
0-30	6	0-30	9
mEGOS	**0-9**	**mEGOS**	**0-12**

Abbreviations: mEGOS = modified Erasmus GBS Outcome Score; MRC = Medical Research Council.

[a] Diarrhea in the 4 weeks preceding the onset of weakness.



Waalgard et al. Early recognition of poor prognosis in GBS Neurology, 76 (11)968-975 2011.

European Journal of Neurology 2012, **19:** 15–20 doi:10.1111/j.1468-1331.2011.03445.x

REVIEW ARTICLE

Miller Fisher syndrome: brief overview and update with a focus on electrophysiological findings

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SENSORY NERVES ARE FREQUENTLY INVOLVED IN THE SPECTRUM OF FISHER SYNDROME

NORTINA SHAHRIZAILA, DM, FRCP,[1] KHEAN J. GOH, FRCP,[1] NORITO KOKUBUN, MD, PhD,[2] AI H. TAN, MRCP,[1] CHENG Y. TAN, MMed,[1] and NOBUHIRO YUKI, MD, PhD[3]

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Accepted 16 July 2013

Muscle and nerve , 49; 559-63, 2014

- Riduzione di ampiezza dei potenziali sensitivi.
- Variabili alterazioni delle onde F
- Nella norma le fibre motorie
- Elevata frequenza di alterazioni del riflesso H.

Criteri diagnostici clinici della CIDP

Table 4 Clinical diagnostic criteria

(1) Inclusion criteria
- (a) Typical CIDP
  - Chronically progressive, stepwise, or recurrent symmetric proximal and distal weakness and sensory dysfunction of all extremities, developing over at least 2 months; cranial nerves may be affected; and
  - Absent or reduced tendon reflexes in all extremities
- (b) Atypical CIDP (still considered CIDP but with different features)
  - One of the following, but otherwise as in (a) (tendon reflexes may be normal in unaffected limbs):
  - Predominantly distal (distal acquired demyelinating symmetric, DADS) or
  - Asymmetric [multifocal acquired demyelinating sensory and motor neuropathy (MADSAM), Lewis–Sumner syndrome] or
  - Focal (e.g., involvement of the brachial or lumbosacral plexus or of one or more peripheral nerves in one upper or lower limb)
  - Pure motor or
  - Pure sensory (including chronic immune sensory polyradiculopathy affecting the central process of the primary sensory neuron)

(2) Exclusion criteria
- Borrelia burgdorferi infection (Lyme disease), diphtheria, drug or toxin exposure probably to have caused the neuropathy
- Hereditary demyelinating neuropathy
- Prominent sphincter disturbance
- Diagnosis of multifocal motor neuropathy
- IgM monoclonal gammopathy with high titre antibodies to myelin-associated glycoprotein
- Other causes for a demyelinating neuropathy including POEMS syndrome, osteosclerotic myeloma, diabetic and non-diabetic lumbosacral radiculoplexus neuropathy. PNS lymphoma and amyloidosis may occasionally have demyelinating features

EFNS Task Force, Eur.J. of Neurol. 2010:17,356-357

CIDP e patologie associate

-**Paraproteinemie**: MGUS, POEMS, Mieloma multiplo, Amiloidosi, m. di Waldestrom;
-Infezioni croniche: HIV, Lyme disease, Epatite C, Epstein-Barr;
-**Malattie del connettivo:** Les, Sjogren, Artrite reumatoide, Sarcoidosi ;
**-Malattie sistemiche : ** Diabete mellito, Tireotossicosi, Insufficienza renale cronica ;
-Neoplasie : carcinoma epatico, melanoma, carcinoma pancreatico, ADK colon.

Box 5
AAN ad hoc subcommittee electrodiagnostic research criteria for CIDP

3 of 4 criteria must be fulfilled in 2 or more nerves:

1. Reduction in conduction velocity in 2 or motor nerves:
   a. <80% of lower limit of normal (LLN) if amplitude >80% of LLN
   b. <70% of LLN if amplitude is <80% of LLN
2. Partial conduction block in 1 or more motor nerves defined as <15% change in duration between proximal and distal sites and >20% drop in negative peak (–p) and/or peak-to-peak (p–p) area or peak-to-peak (p–p) amplitude between proximal and distal sites.
3. Prolonged distal motor latencies in 2 or more nerves:
   a. >125% of upper limit or normal (ULN) if amplitude is >80% of LLN
   b. >150% of ULN if amplitude is <80% of LLN
4. Absent F-waves or prolonged minimum F-wave latencies in 2 or more motor nerves:
   a. >120% of ULN if amplitude >80% of LLN
   b. >150% of ULN if amplitude <80% of LLN

Data from Cornblath DR, Asbury AK, Albers JW, et al. Report from an Ad Hoc Subcommittee of the American Academy of Neurology AIDS Task Force. Research criteria for the diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP). Neurology 1991;41:617–8.

Table 1 Electrodiagnostic criteria

(1) Definite: at least one of the following

(a) Motor distal latency prolongation ≥50% above ULN in two nerves (excluding median neuropathy at the wrist from carpal tunnel syndrome), or

(b) Reduction of motor conduction velocity ≥30% below LLN in two nerves, or

(c) Prolongation of F-wave latency ≥30% above ULN in two nerves (≥50% if amplitude of distal negative peak CMAP <80% of LLN values), or

(d) Absence of F-waves in two nerves if these nerves have distal negative peak CMAP amplitudes ≥20% of LLN + ≥1 other demyelinating parameter[a] in ≥1 other nerve, or

(e) Partial motor conduction block: ≥30% amplitude reduction of the proximal negative peak CMAP relative to distal, if distal negative peak CMAP ≥ 20% of LLN, in two nerves, or in one nerve + ≥1 other demyelinating parameter[a] in ≥1 other nerve, or

(f) Abnormal temporal dispersion (> 30% duration increase between the proximal and distal negative peak CMAP) in ≥2 nerves, or

(g) Distal CMAP duration (interval between onset of the first negative peak and return to baseline of the last negative peak) increase in ≥1 nerve (median ≥ 6.6 ms, ulnar ≥ 6.7 ms, peroneal ≥ 7.6 ms, tibial ≥ 8.8 ms)[b] + ≥1 other demyelinating parameter[a] in ≥1 other nerve

(2) Probable

≥30% amplitude reduction of the proximal negative peak CMAP relative to distal, excluding the posterior tibial nerve, if distal negative peak CMAP ≥ 20% of LLN, in two nerves, or in one nerve + ≥1 other demyelinating parameter[a] in ≥1 other nerve

(3) Possible

As in (1) but in only one nerve

Criteri EDX della EFNS Task Force ; 2010.

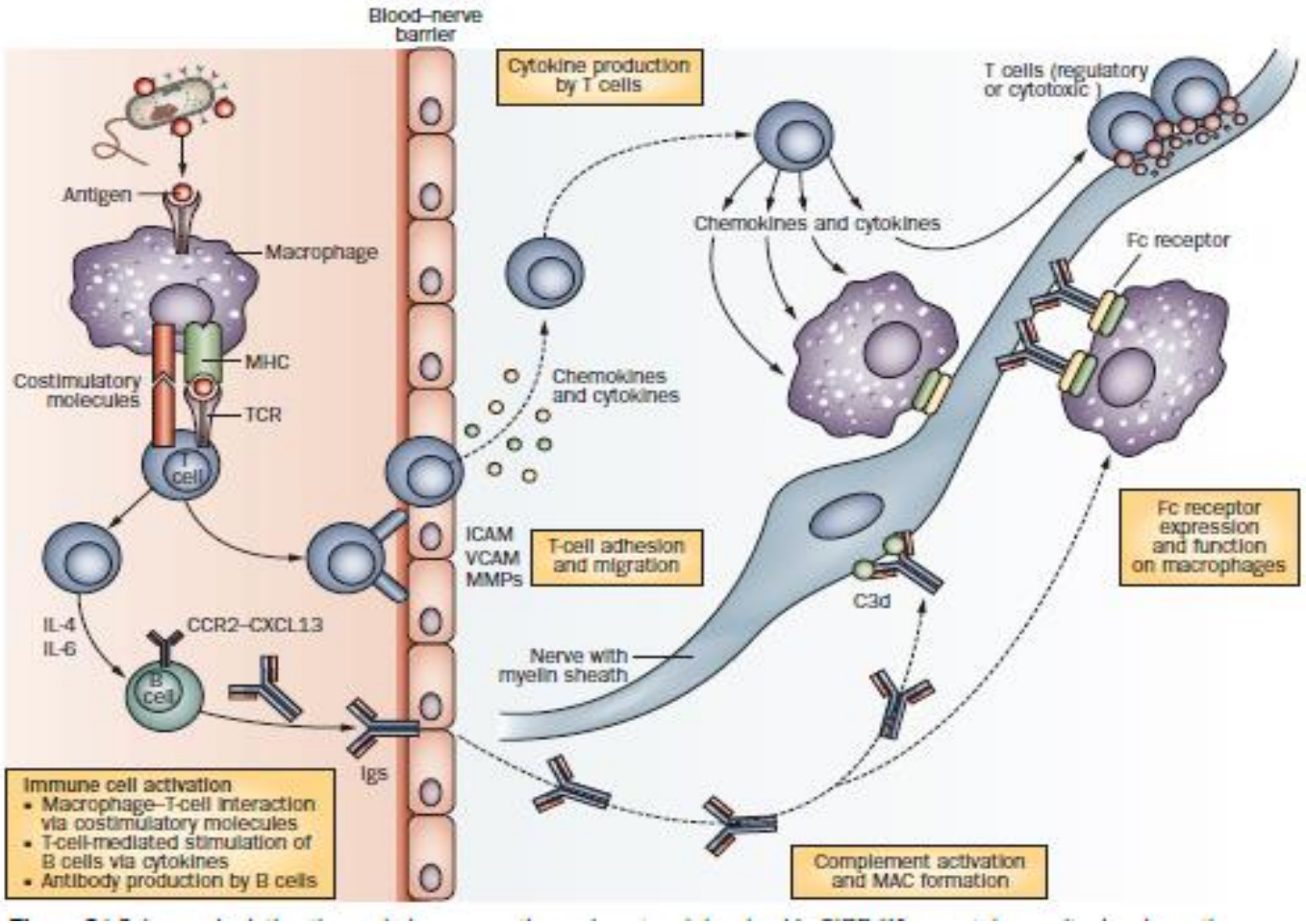
European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society – First Revision

Joint Task Force of the EFNS and the PNS†

Journal of the peripheral Nervous system , 15.1-9; 2010

Table 5. Supportive criteria.

1. Elevated CSF protein with leukocyte count <10/mm^3 (level A recommendation)
2. MRI showing gadolinium enhancement and/or hypertrophy of the cauda equina, lumbosacral or cervical nerve roots, or the brachial or lumbosacral plexuses (level C recommendation)
3. Abnormal sensory electrophysiology in at least one nerve (Good Practice Points):
   a. Normal sural with abnormal median (excluding median neuropathy at the wrist from carpal tunnel syndrome) or radial sensory nerve action potential (SNAP) amplitudes; or
   b. Conduction velocity <80% of lower limit of normal (<70% if SNAP amplitude <80% of lower limit of normal); or
   c. Delayed somatosensory evoked potentials without central nervous system disease
4. Objective clinical improvement following immunomodulatory treatment (level A recommendation)
5. Nerve biopsy showing unequivocal evidence of demyelination and/or remyelination by electron microscopy or teased fibre analysis (Good Practice Points)



Schema della possibile immunopatogenesi della CIDP

"Advances in the diagnosis , pathogenesis and treatment of CIDP "
M.Dalakas et al, Nat.Rev.Neurol.2011

RESEARCH PAPER

Paranodal dissection in chronic inflammatory demyelinating polyneuropathy with anti-neurofascin-155 and anti-contactin-1 antibodies

Haruki Koike,[1] Masato Kadoya,[2] Ken-ichi Kaida,[2] Shohei Ikeda,[1] Yuichi Kawagashira,[1] Masahiro Iijima,[1] Daisuke Kato,[3] Hidenori Ogata,[4] Ryo Yamasaki,[4] Noriyuki Matsukawa,[3] Jun-ichi Kira,[4] Masahisa Katsuno,[1] Gen Sobue[1,5]

J Neurol Neurosurg Psy,2017 ,0,1-9

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Neuromuscular Disorders 27 (2017) 290–293

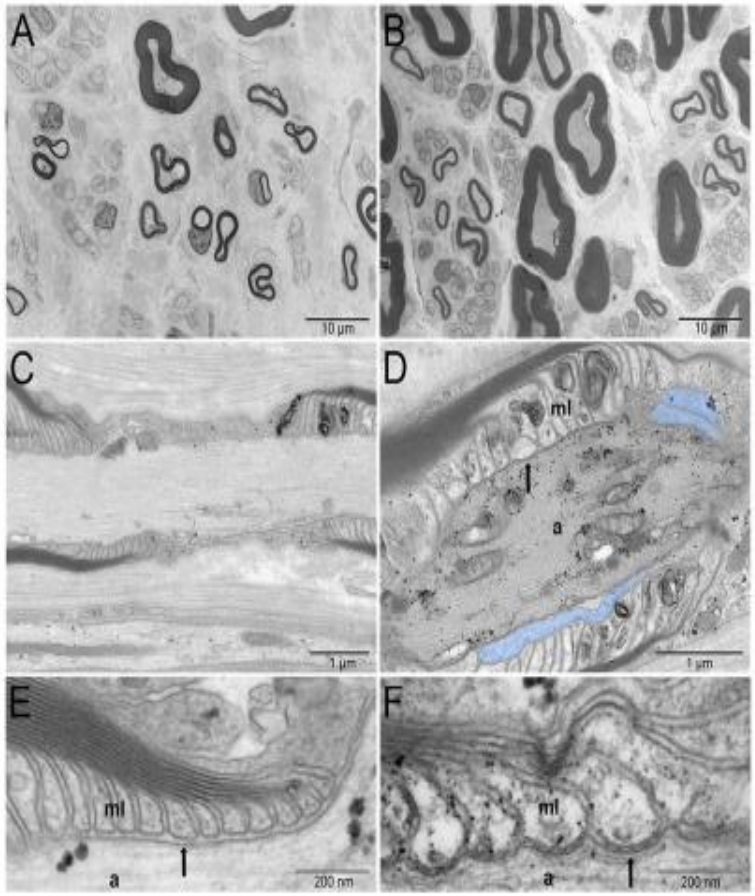
NMD

www.elsevier.com/locate/nmd

Short communication

Paranodal lesions in chronic inflammatory demyelinating polyneuropathy associated with anti-Neurofascin 155 antibodies

Jean-Michel Vallat [a,*], Nobuhiro Yuki [b], Kenji Sekiguchi [c], Norito Kokubun [d], Nobuyuki Oka [e], Stéphane Mathis [f], Laurent Magy [a], Diane L. Sherman [g], Peter J. Brophy [g], Jérôme J. Devaux [h]



Molecole coinvolte nella stretta connessione tra assolemma e le lamelle di mielina non compatta a livello del paranodo.

Gli anticorpi producono slargamento dei nodi di Ranvier, distacco dei loop di mielina dall'assone , e aumento dello spazio periassonale, perdita delle bande trasverse.

J Diabetes Complications. 2016 Sep-Oct;30(7):1401-7. doi: 10.1016/j.jdiacomp.2016.05.007. Epub 2016 May 10.

The dilemma of diabetes in chronic inflammatory demyelinating polyneuropathy.

Bril V[1], Blanchette CM[2], Noone JM[2], Runken MC[3], Gelinas D[3], Russell JW[4].

Acta Neurol Scand. 2015 Oct;132(4):278-83. doi: 10.1111/ane.12394. Epub 2015 Mar 25.

Diagnostic criteria of chronic inflammatory demyelinating polyneuropathy in diabetes mellitus.

Lotan I[1], Hellman MA[1], Steiner I[1].

- Maggiore incidenza della CIDP nei diabetici.
- Diabete di tipo due, ben compensato , > 50 anni .
- Peggioramento rapido.
- Alterazioni di tipo demielinizzante nella neuropatia diabetica
- Liquor alterato nei diabetici.
-50% buona risposta alle IG vena .
- Assenza di criteri diagnostici validati per la diagnosi differenziale

Journal of the Peripheral Nervous System 15:295–301 (2010)

EFNS/PNS MMN GUIDELINE

European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of multifocal motor neuropathy. Report of a Joint Task Force of the European Federation of Neurological Societies and the Peripheral Nerve Society – first revision

Joint Task Force of the EFNS and the PNS†

Table 1. Clinical criteria for multifocal motor neuropathy.

Core criteria (both must be present)

1. Slowly progressive or stepwise progressive, focal, asymmetric* limb weakness, that is, motor involvement in the motor nerve distribution of at least two nerves, for more than 1 month.† If symptoms and signs are present only in the distribution of one nerve only a possible diagnosis can be made (Table 4)
2. No objective sensory abnormalities except for minor vibration sense abnormalities in the lower limbs‡

Supportive clinical criteria

3. Predominant upper limb involvement§
4. Decreased or absent tendon reflexes in the affected limb¶‖
5. Absence of cranial nerve involvement**
6. Cramps and fasciculations in the affected limb
7. Response in terms of disability or muscle strength to immunomodulatory treatment

Exclusion criteria

8. Upper motor neuron signs
9. Marked bulbar involvement
10. Sensory impairment more marked than minor vibration loss in the lower limbs
11. Diffuse symmetric weakness during the initial weeks

-EDX : blocchi di conduzione
-Ac anti GM 1 elevati (35%-70%)
-Lieve aumento proteine liquorali
-Incremento di intensità di segnale RMN in T2 del plesso brachiale.
-Miglioramento con IV IG.
-Possibile comparsa nel tempo di alterazioni sensitive

SENSORY LOSS IN MULTIFOCAL MOTOR NEUROPATHY: A CLINICAL AND ELECTROPHYSIOLOGICAL STUDY

VIRGINIE LAMBRECQ, MD,[1] ELSA KRIM, MD,[2] MARIE ROUANET-LARRIVIÈRE, MD,[3] and ALAIN LAGUENY, MD[1]

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[2] Neurology Department, CH Pau, France
[3] Neurophysiology Department, CHU Bordeaux, Hôpital Pellegrin, France

LEWIS–SUMNER SYNDROME AND MULTIFOCAL MOTOR NEUROPATHY

ANNIE VERSCHUEREN, MD,[1] JEAN PHILIPPE AZULAY, MD, PhD,[1] SHAHRAM ATTARIAN, MD,[1] JOSÉ BOUCRAUT, MD, PhD,[2] JEAN FRANÇOIS PELLISSIER, MD,[3] and JEAN POUGET, MD[1]

[1] Department of Neurology and Neuromuscular Diseases, Timone Hospital, Boulevard Jean Moulin, 13005 Marseille, France
[2] Immunology Laboratory, Faculty of Medicine, University of Aix-Marseille II, Marseille, France
[3] Department of Pathology, Timone Hospital, Marseille, France

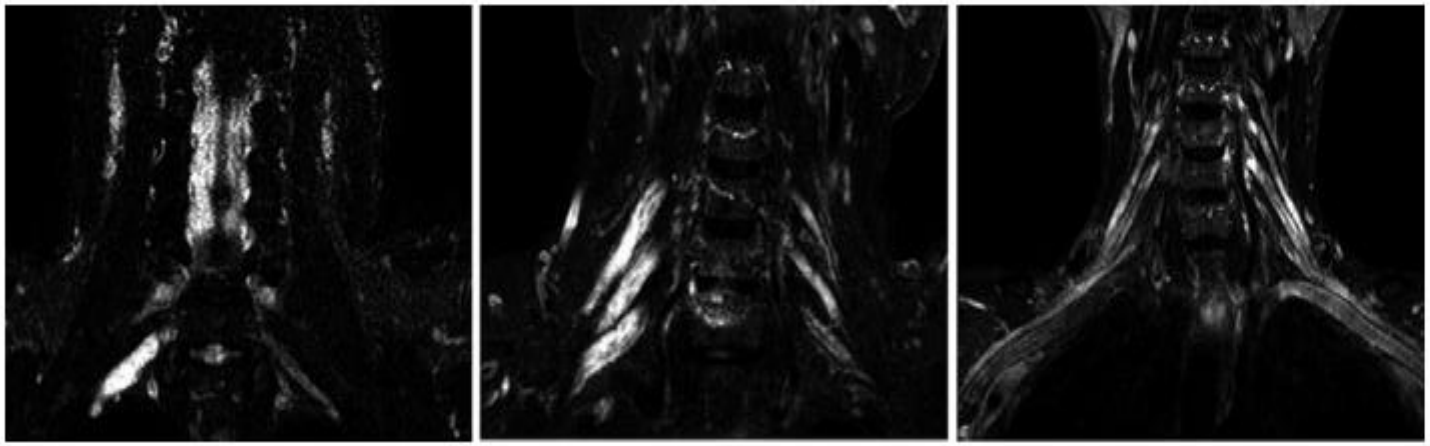
Muscle and nerve 31;88.94; 2005

Fattori	MMN	Lewis-Sumner
Sesso	Maschi >femmine (2:1)	Maschi-femmine :1:1
Sintomi sensitivi	no	sì
VCS	Normale	Alterata
Anti GM1 Ab	35%-80%	no
Biopsia	normale	Demielinizzazione 90%
Risposta steroide	no	buona

Brain Behav. 2017 Apr 4;7(5):e00632. doi: 10.1002/brb3.632. eCollection 2017 May.

Brachial plexus magnetic resonance imaging differentiates between inflammatory neuropathies and does not predict disease course.

Jongbloed BA[1], Bos JW[1], Rutgers D[2], van der Pol WL[1], van den Berg LH[1].



Hypertrophy and nerve thickening on bilateral coronal T2 STIR MR imaging of the brachial plexus in inflammatory neuropathies. Left: unilateral hypertrophy and thickening of cervical nerve roots in an multifocal motor neuropathy (MMN) patient. Middle: Bilateral and asymmetrical abnormalities in an Lewis-Sumner syndrome (LSS) patient. Right: Bilateral and symmetrical abnormalities in a chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) patient

Electrodiagnostic features of hereditary neuropathy with liability to pressure palsies

P.-B. Andersson, MBChB, PhD; Eric Yuen, MD; Karen Parko, MD; and Yuen T. So, MD, PhD

Neurology, 2000, 54; 40-44.

Table *Electrophysiologic characteristics by percent of nerves abnormal*

Feature	SNCV % < LLN (n)	SNCV − ES % < LLN (n)	MNCV % < LLN (n)	DML % > ULN (n)	DML − ES % > ULN (n)	F WAVE % > ULN (n)
HNPP	93 (29)	90 (20)	31 (32)	78 (32)	67 (21)	90 (21)
CIDP	28 (61)	27 (40)	69 (103)	50 (107)	47 (75)	92 (61)
DM	33 (67)	10 (40)	40 (163)	25 (169)	13 (124)	96 (115)

The frequency of abnormal responses by electrodiagnostic parameter for HNPP, CIDP, and DM is expressed as a percentage of the total nerve responses obtained. Data are shown both with and without (−ES) the median nerve entrapment site.

SNCV = sensory nerve conduction velocity; MNCV = motor nerve conduction velocities; DML = distal motor latencies; HNPP = hereditary neuropathy with liability to pressure palsy; CIDP = chronic inflammatory demyelinating polyneuropathy; DM = diabetic polyneuropathy.

Blocchi di conduzione nei siti di entrapment
Rallentamento diffuso della conduzione sensitiva
Lieve rallentamento della conduzione motoria
Marcato aumento della DML dei nervi Mediano e Peroneo (<TLI)
Aumento della latenza delle onde F.

ORPHANET JOURNAL OF RARE DISEASES

REVIEW Open Access

PMP22 related neuropathies: Charcot-Marie-Tooth disease type 1A and Hereditary Neuropathy with liability to Pressure Palsies

Barbara W van Paassen[1*], Anneke J van der Kooi[2], Karin Y van Spaendonck-Zwarts[1], Camiel Verhamme[2], Frank Baas[3] and Marianne de Visser[2]

Table 1 Key features of CMT1A and HNPP

	CMT1A	HNPP
	Duplication of PMP22	**Deletion of PMP22**
Clinical features	Age of onset mainly in first two decades	Painless attacks of numbness, muscular weakness, and atrophy, recurrent and focal
	Presenting symptom is difficulty walking or running	Preceded by minor compression on nerve
	Distal symmetrical muscle weakness and wasting, legs > arms	Age at onset mostly in the second or third decade
	Pes cavus very frequent	Pes cavus found in 4-47% of patients
	Sensory symptoms (stocking-glove distribution) usually less prominent, legs > arms	Full recovery in 50% of episodes, usually in days to weeks
	Pain more common than previously recognized	Sequelae rarely severe
	Reflexes absent or depressed	Large intrafamilial clinical variability
	Large clinical variability between patients, even within family	
Electrophysiological features	Homogeneous and diffuse MCV and SCV slowing	Increase in distal motor latencies, especially of median and peroneal nerve
	CMAP amplitudes reduced, especially distally in the legs	Focal motor slowing at entrapment sites
	SNAP amplitudes frequently reduced to absent	MCV normal to slightly reduced in other segments
		SCV decreased and SNAP amplitudes often reduced
Neuropathological features	Abnormal myelination over the whole nerve length	Segmental de-and remyelination
	Onion bulbs	Tomacula pathologic hallmark, but not pathognomonic
	Decreased density of myelinated nerve fibres	Variable large-fibre loss

Conclusioni

- Lo studio EDX è componente fondamentale della valutazione di una neuropatia periferica.
- I pattern neurofisiologici (MNCS,SNCS, needle EMG) permettono di riconoscere il tipo di neuropatia e restringere le ipotesi diagnostiche.
- Nuove tecniche (RMN , ultrasonografia del SNP) sono complementari all'EDX e possono incrementare le potenzialità diagnostiche.

Grazie per l’attenzione