



Deposited via The University of Sheffield.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/id/eprint/218250/>

Version: Published Version

---

**Article:**

Arends, S., Drenthen, J., de Koning, L. et al. (2024) Electrodiagnostic subtyping in Guillain–Barré syndrome patients in the international Guillain–Barré outcome study. *European Journal of Neurology*, 31 (9). e16335. ISSN: 1351-5101

<https://doi.org/10.1111/ene.16335>

---

**Reuse**

This article is distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) licence. This licence only allows you to download this work and share it with others as long as you credit the authors, but you can't change the article in any way or use it commercially. More information and the full terms of the licence here: <https://creativecommons.org/licenses/>

**Takedown**

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing [eprints@whiterose.ac.uk](mailto:eprints@whiterose.ac.uk) including the URL of the record and the reason for the withdrawal request.

## ORIGINAL ARTICLE

# Electrodiagnostic subtyping in Guillain–Barré syndrome patients in the International Guillain–Barré Outcome Study

Samuel Arends<sup>1,2</sup>  | Judith Drenthen<sup>1</sup>  | Laura de Koning<sup>1</sup> | Peter van den Bergh<sup>3</sup>  | Robert D. M. Hadden<sup>4</sup>  | Satoshi Kuwabara<sup>5</sup> | Ricardo C. Reisin<sup>6</sup>  | Nortina Shahrizaila<sup>7</sup> | Senda Ajroud-Driss<sup>8</sup> | Giovanni Antonini<sup>9</sup> | Shahram Attarian<sup>10</sup> | Claudia Balducci<sup>11</sup> | Tulio Bertorini<sup>12</sup> | Thomas H. Brannagan<sup>13</sup> | Guido Cavaletti<sup>11</sup> | Chi-Chao Chao<sup>14</sup> | Govind Chavada<sup>15</sup> | Klaus-Ulrich Dillmann<sup>16</sup> | Mazen M. Dimachkie<sup>17</sup>  | Giuliana Galassi<sup>18</sup> | Gerardo Gutiérrez-Gutiérrez<sup>19</sup> | Thomas Harbo<sup>20</sup> | Badrul Islam<sup>21</sup> | Zhahirul Islam<sup>22</sup>  | Hans Katzberg<sup>23</sup> | Susumu Kusunoki<sup>24</sup> | Fiore Manganelli<sup>25</sup>  | James A. L. Miller<sup>26</sup> | Julio Pardo<sup>27</sup> | Yann Pereon<sup>28</sup> | Yusuf A. Rajabally<sup>29</sup>  | Soren Sindrup<sup>30</sup> | Mark Stettner<sup>31</sup> | Antonino Uncini<sup>32</sup>  | Camiel Verhamme<sup>33</sup> | Michal Vytopil<sup>34</sup> | Waqar Waheed<sup>35</sup>  | Bart C. Jacobs<sup>1,36</sup> | David R. Cornblath<sup>37</sup> | The IGOS Consortium

## Correspondence

Samuel Arends, Department of Neurology,  
Erasmus University Medical Center,  
Rotterdam, The Netherlands.  
Email: [s.arends@erasmusmc.nl](mailto:s.arends@erasmusmc.nl)

## Abstract

**Background and purpose:** Various electrodiagnostic criteria have been developed in Guillain–Barré syndrome (GBS). Their performance in a broad representation of GBS patients has not been evaluated. Motor conduction data from the International GBS Outcome Study (IGOS) cohort were used to compare two widely used criterion sets and relate these to diagnostic amyotrophic lateral sclerosis criteria.

**Methods:** From the first 1500 patients in IGOS, nerve conduction studies from 1137 (75.8%) were available for the current study. These patients were classified according to nerve conduction studies criteria proposed by Hadden and Rajabally.

**Results:** Of the 1137 studies, 68.3% ( $N=777$ ) were classified identically according to criteria by Hadden and Rajabally: 111 (9.8%) axonal, 366 (32.2%) demyelinating, 195 (17.2%) equivocal, 35 (3.1%) inexcitable and 70 (6.2%) normal. Thus, 360 studies (31.7%) were classified differently. The areas of differences were as follows: 155 studies (13.6%) classified as demyelinating by Hadden and axonal by Rajabally; 122 studies (10.7%) classified as demyelinating by Hadden and equivocal by Rajabally; and 75 studies (6.6%) classified as equivocal by Hadden and axonal by Rajabally. Due to more strictly defined cutoffs fewer patients fulfilled demyelinating criteria by Rajabally than by Hadden, making more

The IGOS Consortium Members are presented in the Appendix A.

For affiliations refer to page 9.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2024 The Authors. *European Journal of Neurology* published by John Wiley & Sons Ltd on behalf of European Academy of Neurology.

patients eligible for axonal or equivocal classification by Rajabally. In 234 (68.6%) axonal studies by Rajabally the revised El Escorial (amyotrophic lateral sclerosis) criteria were fulfilled; in axonal cases by Hadden this was 1.8%.

**Conclusions and discussion:** This study shows that electrodiagnosis in GBS is dependent on the criterion set utilized, both of which are based on expert opinion. Reappraisal of electrodiagnostic subtyping in GBS is warranted.

#### KEYWORDS

amyotrophic lateral sclerosis, electrodiagnosis, Guillain–Barré syndrome, nerve conduction studies, polyneuropathy

## INTRODUCTION

Electrodiagnostic (EDx) studies and, in particular, nerve conduction studies (NCS) are used to support the diagnosis and subtyping of the Guillain–Barré syndrome (GBS), an immune-mediated polyradiculoneuropathy. According to the Brighton Collaboration criteria, NCS findings consistent with GBS are necessary to meet level 1 of diagnostic certainty [1]. GBS is divided into acute inflammatory demyelinating polyradiculoneuropathy (AIDP) and acute motor or motor-sensory axonal neuropathy based on electrodiagnostic and pathological hallmarks. In histopathological studies, AIDP demonstrated demyelination and inflammatory infiltrates in spinal roots and peripheral nerves, with or without signs of axonal degeneration [2]. Axonal GBS was characterized by axonal degeneration of motor or motor-sensory fibers without demyelination. Axonal GBS is often associated with ganglioside antibodies and preceding bacterial infections, especially *Campylobacter jejuni*. Preceding viral infections such as cytomegalovirus and Zika virus were more frequently described in AIDP [3].

After the first description of NCS criteria by Asbury et al. in 1978, various other criterion sets were proposed [4–11]. Those proposed by Hadden et al. and Rajabally et al. are amongst the ones frequently used in GBS research [9, 10]. Using these criteria, each NCS variable and then the whole study can be classified into the following categories: axonal, demyelinating, equivocal, inexcitable, normal. Both criterion sets focus on subtyping into axonal and demyelinating subtypes, with a tendency of studies to be more frequently classified as axonal by Rajabally criteria and as demyelinating by Hadden criteria [10]. Moreover, a substantial percentage of studies do not meet either the axonal or demyelinating criteria. According to the previous work by Hadden et al. [9] and Rajabally et al. [10], NCS were classified equivocal in 22.8% and 7.7% and normal in 2.4% and 1.1% respectively. Despite differences in criteria, the contributions of each specific criterion within these sets on subtyping have never been investigated.

In the current study, a detailed description of the differences between the NCS criteria proposed by Hadden and by Rajabally is provided as well as the impact of these differences on final subtyping in patients included in the International GBS Outcome Study (IGOS). The distribution of the motor conduction data in median, ulnar, peroneal and tibial nerves is described [12]. Lastly,

it is considered how the GBS criteria are related to the revised El Escorial electrodiagnostic criteria (rEEC) in amyotrophic lateral sclerosis (ALS), serving as a surrogate marker of ‘true’ axonal neuropathy [13].

## METHODS

### Study population and protocol, inclusion and exclusion criteria

The current study is based on the first 1500 patients included in IGOS, a prospective observational cohort study [12]. A description of the collection of NCS data in IGOS has been published previously [14]. Inclusion criteria were fulfilment of the diagnostic criteria for GBS (of the National Institute of Neurological Disorders and Stroke) or one of the clinical variants, the presence of NCS with at least two motor nerves examined, and patients presenting within 2 weeks after onset of GBS-related symptoms. Exclusion criteria were study protocol violation, other diagnosis and insufficient clinical and electrophysiological data. Local investigators were free to conduct EDx studies according to their standards, but it was recommended to perform studies twice: the first within 7 days of registration in IGOS, and the second at 4 weeks after. Only the first EDx studies were used for this analysis. For motor conduction the IGOS protocol recommended measuring unilaterally the median, ulnar, peroneal (fibular) and tibial nerves including F-waves (recording sites respectively abductor pollicis brevis muscle, abductor digiti minimi muscle, extensor digitorum brevis muscle and abductor hallucis muscle). Limb temperature control was allowed to be performed by local standards. The study report was uploaded to the online IGOS database and checked.

### Clinical data

Demographic and clinical data were obtained from the IGOS database. Patients were classified into one of the following clinical variants: sensorimotor, pure motor, Miller Fisher syndrome (MFS), MFS-GBS overlap syndrome, ataxic, pure sensory and pharyngeal-cervical-brachial variants [14].

## Electrophysiological data and subtyping

All patients were classified according to the NCS criteria published by Hadden et al. and Rajabally et al. [9, 10], in this paper referred to as the 'Hadden criteria' and 'Rajabally criteria'. Local reference values were used. Each NCS parameter was expressed as a percentage of the upper/lower limit of normal (ULN, LLN). If reference values were lacking, the previously published (mean) reference values collected from the other participating centers in IGOS were used, in accordance with the local methodology used [15]. Motor nerve parameters used in these criteria and hence in this study were distal compound muscle action potential (dCMAP) amplitude, distal motor latency (DML), F-wave latency, motor conduction velocity (MCV) and proximal-to-distal CMAP amplitude ratio (p/dCMAP ratio). NCS variables from the entrapment sites of the ulnar (groove) and peroneal nerve (fibular head) were excluded, but DML from the median nerve (carpal tunnel) was not. The p/dCMAP ratio from the tibial nerve was excluded according to Rajabally subtyping.

See Table S1 for an overview of the Hadden and Rajabally criteria [9, 10]. A summary is as follows. (1) A study is classified demyelinating, according to both Hadden and Rajabally criteria, if at least two parameters fulfilled the demyelinating criteria within two different nerves. One exception is allowed by Hadden criteria (but not by Rajabally): if two demyelinating parameters are present within one nerve, only if all other nerves are inexcitable, this is also classified as demyelinating. In this study, this is named the Hadden 'exception rule'. (2) A study is classified axonal, both for Hadden and Rajabally criteria, if axonal criteria are fulfilled in (at least) two nerves, without demyelinating features. Rajabally criteria considered the F-wave absence and abnormal p/dCMAP ratio as either axonal or demyelinating features, depending on the other NCS findings. However, according to Hadden criteria, an abnormal p/dCMAP ratio is always considered a demyelinating feature and absent F-waves are unclassifiable, as Hadden criteria only provided criteria for prolongation of F-wave latency. (3) The criteria for equivocal and inexcitable studies are the same for both criterion sets. (4) The criteria for a normal study differ slightly in p/dCMAP ratio (p/dCMAP ratio >0.5 considered normal by Hadden, but >0.7 normal by Rajabally criteria).

Because cutoffs for subtyping differed between criteria, the rEEG criteria were applied to our cohort serving as gold standard for axonal neuropathy [13]. The recently published Gold Coast criteria were based on the rEEG, containing a description of NCS parameters consistent with a pure axonal neuropathy [16]. The authors considered certain motor conduction values not consistent with pure axonal loss, which are called 'red flags', suggesting other diseases such as demyelinating neuropathy. These red flags were DML >130% ULN, F-wave latency >130% ULN and MCV <70% LLN [13]. Also, the presence of conduction block was considered non-compatible with ALS, but without defined cutoff. As Hadden and Rajabally criteria defined their own limits for conduction block, p/dCMAP ratio <0.5 and <0.7 respectively, these cutoffs were used.

## Study approval and informed consent

The study was approved by the Medical Ethical Research Committee of the Erasmus University Medical Center Rotterdam, The Netherlands (MEC-2011-477), and by the local institutional review boards of all participating centers. Written informed consent was obtained from all patients or their legal representatives.

## Statistical analysis

IBM SPSS Statistics 28 and RStudio (R Version 4.2.3) were used for the analysis. The one-tailed Spearman's correlation coefficient  $\rho$  was used in order to calculate the correlation between dCMAP amplitude and the different variables representing conduction velocities (DML, F-wave latency, MCV), because variables were not normally distributed.

## RESULTS

Of the first 1500 patients enrolled in IGOS, 203 (13.5%) patients were excluded (52 had chronic inflammatory demyelinating polyradiculoneuropathy; 32 had other diagnoses; 35 because of protocol violation; 84 because of missing clinical and/or electrophysiological data). Of the remaining 1297 patients, 160 patients did not undergo an EDx study. A total of 1137 (87.7%) patients were enrolled in this study. The characteristics of the study population are shown in Table 1. Patients were included from 19 countries, including Argentina ( $N=38$ ), Australia ( $N=9$ ), Bangladesh ( $N=145$ ), Belgium ( $N=25$ ), Canada ( $N=24$ ), China ( $N=14$ ), Denmark ( $N=113$ ), France ( $N=33$ ), Germany ( $N=44$ ), Greece ( $N=8$ ), Italy ( $N=113$ ), Japan ( $N=60$ ), Malaysia ( $N=25$ ), South Africa ( $N=26$ ), Spain ( $N=95$ ), Taiwan ( $N=5$ ), The Netherlands ( $N=109$ ), UK ( $N=133$ ) and United States ( $N=118$ ). All clinical variants were represented, including the predominant sensorimotor variant (60.9%) and pure motor GBS (23.3%). An EDx study was conducted at a median of 7 days (interquartile range 4–11) after onset of GBS-related symptoms.

## Distribution of motor conduction variables

In 190 patients from 23 centers, reference values were lacking and here the IGOS derived reference values were applied, in accordance with local methodology used. The distribution of DML, MCV, F-wave latency and dCMAP amplitudes from the ulnar nerve are presented in Figure 1 (see Figures S1–S3 for median, peroneal and tibial nerves). In all four nerves, conduction slowing (prolongation of DML and F-wave latency and decrease of MCV) was significantly correlated to dCMAP amplitudes. For example, the ulnar nerve DML and F-wave latency were negatively ( $\rho = -0.36$ ;  $\rho = -0.29$ ) and MCV was positively correlated ( $\rho = 0.26$ ),

**TABLE 1** Demographic data of the study population.

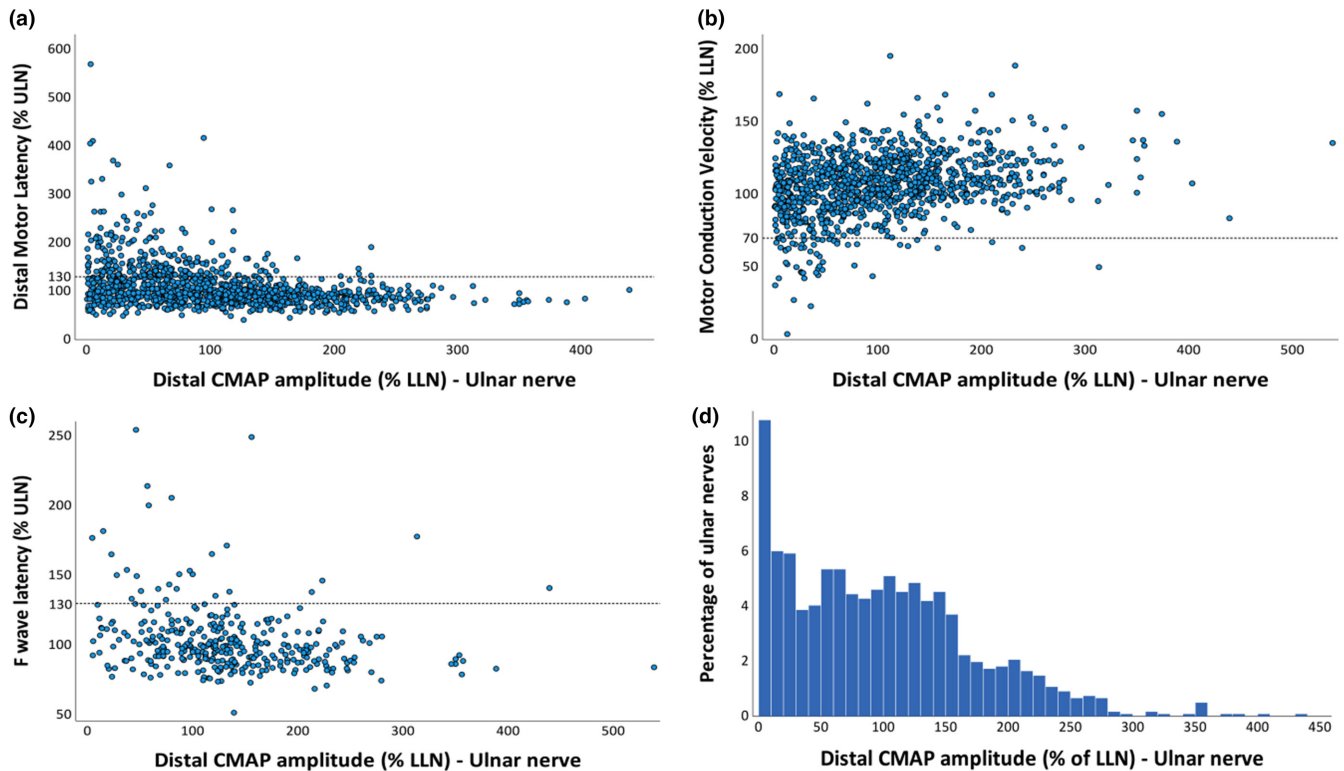
Demography and clinical characteristics	
Total number of patients	1137
Age, median, years (IQR, full range)	51 (35–65; 0–90)
Age below 18 years (%)	68 (6.0%)
Male/female (ratio)	61/39 (1.56)
Continent (%)	
Europe	673 (59.2%)
Asia	249 (21.9%)
North America	142 (12.5%)
South America	38 (3.3%)
Africa	26 (2.3%)
Australia	9 (0.8%)
Clinical variant (%)	
Sensorimotor	672 (60.9%)
Pure motor	257 (23.3%)
Miller Fisher syndrome	63 (5.7%)
Miller Fisher overlap syndrome	60 (5.4%)
Ataxic	19 (1.7%)
Pharyngo–cervical–brachial	14 (1.3%)
Pure sensory	13 (1.2%)
Other <sup>a</sup>	6 (0.5%)
Preceding infection	
No/not tested (%)	440/439 (38.7%; 38.6%)
Present, total	258 (22.7%)
<i>Campylobacter jejuni</i>	158 (13.9%)
Multiple infections	38 (3.3%)
<i>Mycoplasma pneumoniae</i>	33 (2.9%)
Cytomegalovirus	14 (1.2%)
Hepatitis E virus	12 (1.1%)
Epstein–Barr virus	3 (0.3%)
GBS disability score at time of EDx study	
GBS-DS median (IQR)	4 (2–4)
0	2 (0.3%)
1	46 (4.0%)
2	249 (21.9%)
3	215 (18.9%)
4	513 (45.1%)
5	108 (9.5%)
Missing	1 (0.1%)
Electrodiagnostic details	
Median number nerves studied (IQR, full range)	4 (4–6; 2–8)
Median timing EDx study in days (IQR, full range)	7 (4–11; 0–129)

Abbreviations: EDx, electrodiagnostic; GBS, Guillain–Barré syndrome; GBS-DS, Guillain–Barré syndrome disability scale; IQR, interquartile range.

<sup>a</sup>Other overlap syndromes, e.g. with Bickerstaff brainstem encephalitis.

all statistically significant ( $p < 0.01$ ). Of all nerves and variables, the tibial DML and dCMAP amplitude had the highest Spearman's correlation coefficient ( $\rho = -0.54$ ).

The ulnar dCMAP amplitude had a left-skewed distribution with unobtainable ( $< 10\%$  LLN) responses in 10.8% (Figure 1). Unobtainable responses were less common in the median nerve



**FIGURE 1** Distribution of ulnar nerve NCS variables in IGOS. Ulnar nerve NCS variables: (a) distal motor latency versus dCMAP amplitude; (b) motor conduction velocity versus dCMAP amplitude; (c) F-wave minimal latency versus dCMAP amplitude; (d) distribution of dCMAP amplitude of the ulnar nerves. ULN, upper limit of normal; LLN, lower limit of normal. A line was drawn at the cutoffs for DML (130% ULN), MCV (70% LLN) and F-wave latency (130% ULN) derived from the revised El Escorial (exclusion) criteria.

(8.8%) and more common in peroneal (13.4%) and tibial nerves (16.0%). Distal amplitudes were below 80% of LLN in 45.6% of ulnar, 45.8% of median, 45.3% of peroneal and 52.4% of tibial nerves. Ulnar nerves had normal ( $\geq 100\%$  LLN) dCMAP amplitude in 45.4% (median dCMAP amplitude 89.9% LLN). Distal CMAP amplitudes were normal in 46.4% of median nerves (median 90.0%), in 48.5% of peroneal nerves (median 95.0%) and in 40.1% of tibial nerves (median 72.1%).

### Classification according to Hadden criteria

According to the Hadden criteria, 56.6% of the studies were demyelinating, 9.8% axonal, 24.3% equivocal, 3.1% inexcitable and 6.3% normal (Table 5). A prolonged DML in two or more nerves was the most often fulfilled criterion for demyelination (41.7% of total cohort), followed by decreased MCV (24.2%), abnormal p/dCMAP ratio (13.4%) and F-wave prolongation (8.8%) (Table 2). Combining two different variables (DML, F-wave, MCV, p/dCMAP ratio) enabled another 13.4% of studies to be subtyped as AIDP (if both separate variables were demyelinating only once). In some cases, multiple rules for AIDP were fulfilled, so these criteria as shown in Table 2 are not mutually exclusive. For example, if in a study three separate variables were demyelinating (e.g., 1  $\times$  MCV, 1  $\times$  DML, 1  $\times$  F-wave), classifying as AIDP is possible by combining MCV and DML, but also

by DML and F-wave. An additional 0.5% of the cohort was classified as AIDP by the Hadden 'exception rule'.

A description of the proportion of patients and nerves fulfilling specific variables of the Hadden criteria is provided (Table S2). According to Hadden criteria, the top three individual variables most often fulfilling the demyelinating criteria were (1) prolonged median nerve DML (in 40.2% of median nerves), (2) prolonged peroneal DML (33.5%) and (3) prolonged ulnar DML (29.6%). On a patient level, the demyelinating criteria most often met (at least once) were prolonged DML (55.6% of all patients), reduced MCV (42.8%), lowered p/dCMAP ratio (31.8%) and prolonged F-wave latency (22.0%).

Axonal GBS according to Hadden criteria was present in 111 cases (9.8% of cohort). The individual variable and nerve most often fulfilling the axonal criteria was the dCMAP amplitude of the tibial nerve (52.4%).

Inexcitable studies according to Hadden were present in 35 cases (3.1% of cohort). As allowed by the criteria, 10 cases had the presence of dCMAP amplitude below 10% LLN once (six median, one ulnar and three peroneal nerves). Normal studies were present in 72 cases (6.3% of cohort). The remaining 276 cases (24.3%) were classified as equivocal.

In patients with pure sensory GBS ( $N=13$ ) EDx studies were classified by Hadden criteria as demyelinating ( $N=2$ ), equivocal ( $N=6$ ) or normal ( $N=5$ ). For MFS ( $N=63$ ) distribution was as

**TABLE 2** Hadden criteria: final rules for axonal and demyelinating subtypes.

Demyelinating criteria by Hadden criteria <sup>a</sup>	Percentage of cases (number/total number cases <sup>b</sup> )
≥2 × DML prolonged (>110% ULN if dCMAP ≥50% LLN; >120% ULN if dCMAP <50% LLN)	41.7% (452/1084)
≥2 × MCV decreased (MCV <90% LLN if dCMAP ≥50% LLN; <85% if dCMAP <50% LLN)	24.2% (258/1066)
≥2 × p/dCMAP ratio (p/dCMAP ratio <0.5 and dCMAP ≥20% LLN)	13.4% (140/1047)
≥2 × F-wave latency prolonged (latency >120% ULN)	8.8% (83/939)
Combined criteria (two demyelinating variables in two nerves)	
DML and MCV                      1 × DML and 1 × MCV	2.2% (24/1080)
MCV and p/dCMAP ratio        1 × MCV + 1 × p/dCMAP ratio	3.1% (32/1041)
MCV and F-wave                 1 × MCV + 1 × F-wave	2.5% (25/1005)
DML and p/dCMAP ratio        1 × DML + 1 × p/dCMAP ratio	1.7% (18/1048)
DML and F-wave                 1 × DML + 1 × F-wave	1.0% (10/1016)
p/dCMAP ratio and F-wave      1 × p/dCMAP ratio + 1 × F-wave	3.0% (29/979)
Hadden exception rule         Two demyelinating features within one nerve, with dCMAP >10%, others inexcitable	0.5% (6/1110)
<b>Axonal criteria by Hadden</b>	
Distal CMAP <80% LLN in at least two nerves, without demyelinating features (only one demyelinating feature in one nerve allowed if dCMAP <10% LLN)	9.9% (111/1126)

Abbreviations: CMAP, compound muscle action potential; dCMAP, distal compound muscle action potential; DML, distal motor latency; LLN, lower limit of normal; MCV, motor conduction velocity; p/dCMAP, proximal-to-distal compound muscle action potential; ULN, upper limit of normal.

<sup>a</sup>Categories might overlap, for example a patient can fulfill multiple rules: 2 × prolonged DML and also 1 × decreased MCV and 1 × abnormal p/dCMAP ratio.

<sup>b</sup>Each case is only included in the 'total number of cases' if it is possible to fulfill this criterion, for example if only one DML is present in a study, this patient can never fulfill the ≥2 DML rule and therefore is not included in this particular 'total number of cases'.

follows: axonal ( $N=2$ ), demyelinating ( $N=5$ ), equivocal ( $N=33$ ) and normal ( $N=23$ ).

### Classification according to Rajabally criteria

According to the Rajabally criteria, 32.5% of the studies were demyelinating, 30.0% axonal, 28.1% equivocal, 3.1% inexcitable and 6.3% normal (Table 5). A prolonged DML in two or more nerves was the most often fulfilled demyelinating criterion (19.9% of cohort), followed by abnormal p/dCMAP ratio (12.4%), F-wave absence (12.3%), decreased MCV (6.7%) and F-wave prolongation (6.3%) (Table 3). The criteria combining these different variables twice enabled another 4.6% of studies to be subtyped as demyelinating. The different criteria as described in Table 3 are not mutually exclusive: multiple criteria can be met by one patient.

A detailed description on how often individual variables fulfilled the Rajabally criteria in individual nerves is provided in Table S3. The top three individual variables most often fulfilling the demyelinating Rajabally criteria were (1) F-wave absence in peroneal nerve (37.7%), (2) reduced p/dCMAP ratio in peroneal nerve (33.9%) and (3) reduced p/dCMAP ratio in ulnar nerve (25.9%). On a patient level, the demyelinating Rajabally criteria most often met (at least once) were reduced p/dCMAP ratio (52.2%), followed by F-wave absence (43.4%),

prolonged DML (35.1%), F-wave latency prolongation (18.2%) and reduced MCV (16.2%).

For axonal GBS multiple criteria were provided, with a reduced dCMAP amplitude in at least two nerves being the most often fulfilled criterion (26.5% of cohort), followed by absent F-waves (11.4%), abnormal p/dCMAP ratio (9.7%) and combined F-wave absence and abnormal p/dCMAP ratio with reduced dCMAP amplitude (1.2%). The individual variable and nerve most often fulfilling axonal Rajabally criteria was the dCMAP amplitude of the tibial nerve (52.4%). Within the axonal subgroup, the axonal feature most often present was the reduced dCMAP amplitude (87.4%).

Rajabally criteria considered F-wave absence and p/dCMAP ratio as supportive features for both demyelinating and axonal subtypes depending on the rest of the study. Of these two criteria, F-wave absence was most often detected in the peroneal nerve (37.7%).

As criteria for inexcitable NCS were the same for Rajabally and Hadden criteria, the same 35 cases fulfilled these criteria. Normal studies were present in 72 cases (6.3% of cohort). The remaining 319 cases (28.1%) were classified as equivocal by Rajabally criteria: an additional 43 equivocal studies compared to Hadden criteria.

In patients with pure sensory GBS ( $N=13$ ) studies were classified by Rajabally as axonal ( $N=1$ ), demyelinating ( $N=1$ ), equivocal ( $N=6$ ) or normal ( $N=5$ ). For MFS ( $N=63$ ) distribution was as follows: axonal ( $N=4$ ), demyelinating ( $N=3$ ), equivocal ( $N=32$ ) and normal ( $N=24$ ).

**TABLE 3** Rajabally criteria: final rules for axonal and demyelinating subtypes.

Demyelinating criteria by Rajabally criteria <sup>a</sup>	Percentage of cases (number/total number cases <sup>b</sup> )	
≥2 × DML prolonged (>150% ULN)	19.9% (216/1087)	
≥2 × MCV decreased (<70% LLN)	6.7% (72/1068)	
≥2 × F-wave latency prolonged (either latency >120% ULN in dCMAP ≤50% or >150% ULN in dCMAP <50% LLN)	6.3% (58/923)	
≥2 × F-wave absence (dCMAP ≥20% LLN) with additional demyelinating parameter in other nerve	12.3% (113/921)	
≥2 × p/dCMAP ratio <0.7 <sup>c</sup> with additional demyelinating parameter in other nerve <sup>a</sup>	12.4% (129/1039)	
Combined criteria (two demyelinating variables in two nerves)		
DML and MCV	1 × DML and 1 × MCV	1.3% (14/1085)
MCV and F-wave latency	1 × MCV and 1 × F-wave latency	1.4% (14/1007)
DML and F-wave latency	1 × DML and 1 × F-wave latency	1.9% (19/1005)
<b>Axonal criteria by Rajabally</b>		
Distal CMAP <80% LLN in at least two nerves, without demyelinating features (only one demyelinating feature in one nerve allowed if dCMAP <10% LLN)	26.5% (298/1126)	
F-wave absence in two nerves with dCMAP ≥20% LLN, without demyelinating features (only one demyelinating feature in one nerve allowed if dCMAP <10% LLN)	11.4% (105/921)	
p/dCMAP ratio <0.7 <sup>c</sup> in two nerves, without demyelinating features (only one demyelinating feature in one nerve allowed if dCMAP <10% LLN)	9.7% (101/1039)	
F-wave absence in one nerve with dCMAP ≥20% LLN or p/dCMAP ratio <0.7 <sup>c</sup> in one nerve, with in addition dCMAP <80% LLN in one other nerve; without demyelinating features (only one demyelinating feature in one nerve allowed if dCMAP <10% LLN)	1.2% (13/1078)	

Abbreviations: CMAP, compound muscle action potential; dCMAP, distal compound muscle action potential; DML, distal motor latency; LLN, lower limit of normal; MCV, motor conduction velocity; p/dCMAP, proximal-to-distal compound muscle action potential; ULN, upper limit of normal.

<sup>a</sup>Categories might overlap, for example a patient can fulfill multiple rules: 2 × reduced MCV and also 1 × prolonged DML and 1 × prolonged F-wave latency.

<sup>b</sup>Each case is only included in the 'total number of cases' if it is possible to fulfill this criterion. For example if only one DML is present in a study, this patient can never fulfill the ≥2 DML rule and therefore is not included in this particular 'total number of cases'.

<sup>c</sup>Excluding tibial nerve.

**TABLE 4** Classification according to Hadden criteria versus Rajabally criteria.

Hadden classification		Axonal	Demyelinating	Equivocal	Inexcitable	Normal	Total
Rajabally classification	Axonal	111	155	75	0	0	341
	Demyelinating	0	366	4	0	0	370
	Equivocal	0	122	195	0	2	319
	Inexcitable	0	0	0	35	0	35
	Normal	0	0	2	0	70	72
	Total	111	643	276	35	72	1137

### Comparison of classification according to Hadden criteria versus Rajabally criteria

In 68.3% (N=777) of patients, the final NCS classification was the same, and in the remaining 31.7% (N=360) subtyping differed (Table 4). In patients with clinical variants pure sensory GBS (N=13) classification differed in 15.4% (N=2) and in MFS (N=63) in 6.3% (N=4). 277 of studies (24.4%) were classified demyelinating by Hadden criteria but not by Rajabally criteria (N=155 axonal, N=122 equivocal). Therefore, fewer patients fulfilled demyelinating criteria

by Rajabally criteria (N=370) than by Hadden criteria (N=643), making more patients eligible for either axonal or equivocal classification by Rajabally. 75 patients (6.6%) were classified axonal by Rajabally, but equivocal by Hadden criteria, because absent F-waves and reduced p/dCMAP ratio serve as supportive for axonal subtyping by Rajabally criteria only. Four equivocal studies by Hadden were classified demyelinating by Rajabally criteria. Of these, two were based on absent F-waves and two on a p/dCMAP ratio of 0.5–0.7 (both variables supportive of demyelination by Rajabally but not by Hadden). The latter was also responsible for another two cases classified

**TABLE 5** Revised El Escorial criteria in axonal and demyelinating GBS patients, as classified by Hadden criteria and Rajabally criteria.

El Escorial criteria					
	DML >130% (N) <sup>a</sup>	MCV <70% (N)	F-wave latency >130% (N)	Conduction block <sup>b</sup> present (N)	Total percentage of cases (N)
Axonal GBS					
Hadden (N = 111)	0.9% (1)	0.9% (1)	0% (0)	0% (0)	1.8% (2)
Rajabally (N = 341)	23.5% (80)	1.8% (6)	1.2% (4)	62.5% (213)	68.6% (234)
Demyelinating GBS					
Hadden (N = 643)	74.7% (480)	27.8% (179)	22.2% (143)	46.0% (296)	93.3% (600)
Rajabally (N = 370)	86.5% (320)	39.7% (147)	33.2% (123)	65.1% (241)	96.2% (356)

Abbreviations: CMAP, compound muscle action potential; dCMAP, distal compound muscle action potential; DML, distal motor latency; GBS, Guillain–Barré syndrome; LLN, lower limit of normal; MCV, motor conduction velocity; p/dCMAP, proximal-to-distal compound muscle action potential.

<sup>a</sup>Revised El Escorial 'red flag' criteria present in patients (at least once).

<sup>b</sup>Conduction block defined by their own criteria: Hadden criteria p/dCMAP ratio <0.5 and dCMAP ≥20% LLN; Rajabally criteria p/dCMAP ratio <0.7, excluding tibial nerve.

normal by Hadden but equivocal by Rajabally criteria. Finally, two cases were equivocal by Hadden criteria because of abnormal tibial p/dCMAP ratio with the rest of the study being normal. These were classified normal by Rajabally criteria.

## Revised El Escorial criteria

Guillain–Barré syndrome patients were classified according to the rEEC (Table 5). These red flags were fulfilled in 1.8% of axonal GBS by Hadden criteria and in 68.6% by Rajabally criteria. The rEEC most frequently fulfilled in axonal GBS by Rajabally criteria were the presence of a conduction block (62.5% of cases) and prolonged DML (23.5%). In six axonal GBS cases the MCV criterion (<70% LLN) was fulfilled, but this was only possible in the case of reduced dCMAP amplitude (<10% LLN) as this was allowed by both Hadden and Rajabally criteria.

## DISCUSSION

In this study of 1137 patients with GBS, electrodiagnostic neurotyping according to Hadden and Rajabally criteria agreed in 68.3% but there was a significant number in which they did not agree (31.7%). This was explained by the more strictly defined cutoffs for demyelination in the Rajabally criteria. Therefore, fewer patients fulfilled demyelinating criteria by Rajabally (N = 370) than by Hadden (N = 643), making more patients eligible for either an axonal (N = 155) or equivocal (N = 75) classification.

It is confirmed that for all four motor nerves (median, ulnar, peroneal, tibial), variables denoting conduction slowing were significantly correlated with (reduction of) dCMAP amplitudes [17–19]. Whilst more sophisticated criteria could be developed, such as detailed

equations relating the conduction parameters to amplitudes [20], in practice they are difficult to apply.

Our study showed that, for both Hadden and Rajabally criteria, the criterion of prolonged DML (in at least two nerves) was the most frequently met demyelinating criterion (Hadden criteria 41.7%; Rajabally criteria 19.9% of all studies). The most frequently met axonal criterion was the reduced dCMAP amplitude (in at least two nerves) according to both Hadden criteria (9.9% of studies) and Rajabally criteria (26.5% of all studies).

Criteria for demyelinating GBS are crucial in both AIDP and axonal GBS, as exclusion of demyelinating features is a hallmark in axonal GBS, according to both Hadden and Rajabally criteria. Cutoffs for demyelinating criteria varied between the two criteria sets. As ALS is generally considered an axonal motor neuropathy, rEEC and the successive Gold Coast criteria for ALS proposed NCS criteria suggestive of disease processes other than ALS [13, 16]. Using these ALS red flag criteria which suggest that a neuropathy is not axonal, 68.6% of axonal GBS cases according to Rajabally criteria fulfilled these criteria. For Hadden criteria, this was only 1.8% of axonal cases. This underlines the importance of cutoffs showing how the usage of different criteria leads to different conclusions based on the same data. Also, as the rEEC criteria were developed in ALS and not in GBS, and also based on expert opinion, selecting the optimal criteria is not possible.

Subtyping GBS by NCS criteria is complicated by the lack of a gold standard. Multiple criterion sets were published before, including the more recently developed criteria by Uncini et al. requiring a second EDx study and sensory data [11]. Although NCS subtyping is suggested to reflect the underlying pathological process, that is, axonal degeneration or demyelination of peripheral nerves, pathological studies to confirm this are usually not available. Moreover, this dichotomous view as usually stated as AIDP versus acute motor axonal neuropathy is probably too simplistic: axonal degeneration is

often present in demyelinating subtypes and decline in nerve conduction velocities resembling a demyelinating process might also be present in axonal neuropathies with conduction slowing being CMAP amplitude dependent [17–20]. Also, in early stage GBS axonal degeneration and demyelination might be preceded by endoneurial edema, especially in proximal nerve trunks [2]. Our results confirmed these previous findings of amplitude-related conduction slowing, which was explained by loss of large, faster-conducting nerve fibers [21] and the abnormal slow conduction velocities in regenerating motor fibers [22]. In the acute stage of GBS, conduction slowing might represent demyelination or reversible conduction failure [23] as well as loss of fast-conducting motor nerve fibers by Wallerian-like axonal degeneration. Discriminating the role of each process finally resulting in conduction slowing in an individual patient is complex, although some factors might be helpful: (1) excessive temporal dispersion of the CMAP (except the tibial nerve) is generally considered a demyelinating process [24]; (2) follow-up NCS studies might reveal reversible conduction failure but are not useful in the early stages; and (3) conduction slowing in ALS patients showed mild to moderate signs of conduction slowing, but exceptions with severe conduction slowing were present although the European Federation of Neurological Societies/Peripheral Nerve Society chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) criteria were never fulfilled [21]. Therefore, in GBS, unraveling the underlying pathological process based on EDx studies alone is limited. In the classification of GBS, besides the results of EDx studies other features should also be taken into account such as clinical characteristics, anti-ganglioside antibodies, infectious antecedents and biomarkers for axonal loss (e.g., neurofilament light chain, peripherin) in order to get a better understanding of the full spectrum of subtypes and the heterogeneity of GBS, and future studies in IGOS might contribute to this.

This study shows that classifying subtypes in GBS is dependent on the NCS criteria used. Therefore, performing and classifying NCS studies in GBS needs a fundamental reappraisal. First, in the absence of a gold standard it is unknown which are the right criteria to use. The above showed that many axonal studies of Rajabally criteria met red flag criteria for demyelinating neuropathy suggesting an underestimation of demyelinating subtypes. Contrarily, the pathological process in ALS is considered axonal degeneration, whereas axonal GBS might also represent (reversible) axonal dysfunction, which is represented in Rajabally criteria but not in Hadden criteria. Second, GBS classifications should be rethought more holistically, see above, since the NCS classification can be controversial depending on which criteria are used. Third, the preoccupation in clinical trials to use only EDx data to classify subjects seems misguided as subjects can be classified differently depending on the criteria used.

## AUTHOR CONTRIBUTIONS

**Samuel Arends:** Conceptualization; investigation; writing – original draft; methodology; visualization; formal analysis; writing – review and editing; data curation. **Judith Drenthen:** Conceptualization;

writing – review and editing; supervision. **Laura de Koning:** Methodology; data curation; software; validation. **Peter van den Bergh:** Conceptualization; writing – review and editing; supervision. **Robert D. M. Hadden:** Writing – review and editing; supervision; conceptualization. **Satoshi Kuwabara:** Writing – review and editing; supervision; conceptualization. **Ricardo C. Reisin:** Writing – review and editing; supervision; conceptualization. **Nortina Shahrizaila:** Writing – review and editing; supervision; conceptualization. **Senda Ajroud-Driss:** Writing – review and editing. **Giovanni Antonini:** Writing – review and editing. **Shahram Attarian:** Writing – review and editing. **Claudia Balducci:** Writing – review and editing. **Tulio Bertorini:** Writing – review and editing. **Thomas H. Brannagan:** Writing – review and editing. **Guido Cavaletti:** Writing – review and editing. **Chi-Chao Chao:** Writing – review and editing. **Govind Chavada:** Writing – review and editing. **Klaus-Ulrich Dillmann:** Writing – review and editing. **Mazen M. Dimachkie:** Writing – review and editing. **Giuliana Galassi:** Writing – review and editing. **Gerardo Gutiérrez-Gutiérrez:** Writing – review and editing. **Thomas Harbo:** Writing – review and editing. **Badrul Islam:** Writing – review and editing. **Zahurul Islam:** Writing – review and editing. **Hans Katzberg:** Writing – review and editing. **Susumu Kusunoki:** Writing – review and editing. **Fiore Manganeli:** Writing – review and editing. **James A. L. Miller:** Writing – review and editing. **Julio Pardo:** Writing – review and editing. **Yann Pereon:** Writing – review and editing. **Yusuf A. Rajabally:** Writing – review and editing. **Soren Sindrup:** Writing – review and editing. **Mark Stettner:** Writing – review and editing. **Antonino Uncini:** Writing – review and editing. **Camiel Verhamme:** Writing – review and editing. **Michal Vytopil:** Writing – review and editing. **Waqar Waheed:** Writing – review and editing. **Bart C. Jacobs:** Conceptualization; investigation; funding acquisition; writing – review and editing; methodology; supervision; formal analysis. **David R. Cornblath:** Writing – review and editing; methodology; formal analysis; supervision; conceptualization; investigation.

## AFFILIATIONS

<sup>1</sup>Department of Neurology, Erasmus University Medical Center, Rotterdam, The Netherlands

<sup>2</sup>Department of Neurology, HagaZiekenhuis, The Hague, The Netherlands

<sup>3</sup>Department of Neurology, University Hospital St-Luc, Brussels, Belgium

<sup>4</sup>Department of Neurology, King's College Hospital, London, UK

<sup>5</sup>Department of Neurology, Chiba University Hospital, Chiba, Japan

<sup>6</sup>Department of Neurology, Hospital Británico, Buenos Aires, Argentina

<sup>7</sup>Department of Neurology, University of Malaya, Kuala Lumpur, Malaysia

<sup>8</sup>Department of Neurology, Northwestern University Feinberg, Chicago, Illinois, USA

<sup>9</sup>Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University, Rome, Italy

<sup>10</sup>Department Neuromuscular disorders, Hôpital de la Timone, Marseille, France

<sup>11</sup>Department of Neurology, San Gerardo Hospital, Monza, Italy

<sup>12</sup>University of Tennessee Health Science Center, Department of Neurology, Memphis, Tennessee, USA

<sup>13</sup>Department of Neurology, Columbia University, New York, New York, USA

<sup>14</sup>Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan

<sup>15</sup>Department of Neurology, Southern General Hospital, University of Glasgow, Glasgow, UK

<sup>16</sup>Department of Neurology, Universitätsklinikum des Saarlandes, Homburg, Germany

<sup>17</sup>Department of Neurology, University of Kansas Medical Center, Kansas City, Kansas, USA

<sup>18</sup>Department of Neurology, University Hospital of Modena, Modena, Italy

<sup>19</sup>Department of Neurology, Hospital Universitario Infanta Sofia, Universidad Europea de Madrid, San Sebastian de los Reyes, Spain

<sup>20</sup>Department of Neurology, Aarhus University Hospital, Aarhus, Denmark

<sup>21</sup>Department of Neurology and Neurophysiology, BRB Hospital, Dhaka, Bangladesh

<sup>22</sup>International Centre for Diarrhoeal Disease Research (icddr;b), Laboratory of Gut-Brain Axis, Dhaka, Bangladesh

<sup>23</sup>University of Toronto, Department of Neurology, Toronto, Canada

<sup>24</sup>Department of Neurology, Kindai University, Osaka, Japan

<sup>25</sup>Department of Neuroscience, Reproductive Sciences and

Odontostomatology, University of Naples "Federico II", Naples, Italy

<sup>26</sup>Department of Neurology, Royal Victoria Infirmary, Newcastle, UK

<sup>27</sup>Department of Neurology, Complejo Hospitalario Universitario de Santiago, Santiago de Compostela, Spain

<sup>28</sup>Department of Clinical Neurophysiology, Nantes University Hospital, Nantes, France

<sup>29</sup>Aston Medical School, Aston University, Birmingham, UK

<sup>30</sup>Odense University Hospital, Department of Neurology, Odense, Denmark

<sup>31</sup>Department of Neurology and Center for Translational Neuro- and Behavioral Sciences (C-TNBS), University Medicine Essen, Essen, Germany

<sup>32</sup>Department of Neuroscience, Imaging and Clinical Sciences, University 'G. D'Annunzio', Chieti, Italy

<sup>33</sup>Department of Neurology, Amsterdam Neuroscience, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, The Netherlands

<sup>34</sup>Department of Neurology, Lahey Hospital and Medical Center, Burlington, Vermont, USA

<sup>35</sup>Department of Neurology, University of Vermont Medical Centre, Burlington, Vermont, USA

<sup>36</sup>Department of Immunology, Erasmus University Medical Center, Rotterdam, The Netherlands

<sup>37</sup>Department of Neurology, Johns Hopkins University, Baltimore, Vermont, USA

## ACKNOWLEDGEMENTS

The IGOS was funded by the GBS-CIDP Foundation International, gain charity UK ([www.gaincharity.org.uk](http://www.gaincharity.org.uk)), Erasmus University Medical Center Rotterdam, Glasgow University, Prinses Beatrix Spierfonds, CSL Behring, Grifols, Annexon and Hansa Biopharma. Study sponsors had no involvement in data collection, analysis, interpretation and/or writing of the manuscript.

## CONFLICT OF INTEREST STATEMENT

Dr. Dimachkie serves or recently served as a consultant for Abata/Third Rock, Abcuro, Amicus, ArgenX, Astellas, Cabaletta Bio, Catalyst, CNSA, Covance/Labcorp, CSL-Behring, Dianthus, Horizon, EMD Serono/Merck, Ig Society, Inc, Ipsen, Janssen, Medlink, Nuvig, Octapharma, Priovant, Sanofi Genzyme, Shire Takeda, TACT/Treat NMD, UCB Biopharma, Valenza Bio and Wolters Kluwer Health/UpToDate.

Dr. Dimachkie received research grants or contracts or educational grants from Alexion/ AstraZeneca, Alnylam Pharmaceuticals, Amicus, Argenx, Bristol-Myers Squibb, Catalyst, CSL-Behring, FDA/OOPD, GlaxoSmithKline, Genentech, Grifols, Mitsubishi Tanabe Pharma, MDA, NIH, Novartis, Octapharma, Orphazyme, Ra Pharma/

UCB, Sanofi Genzyme, Sarepta Therapeutics, Shire Takeda, Spark Therapeutics, The Myositis Association, and UCB Biopharma / RaPharma.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

## ORCID

Samuel Arends  <https://orcid.org/0000-0003-4279-4657>

Judith Drenthen  <https://orcid.org/0000-0002-2165-6573>

Peter van den Bergh  <https://orcid.org/0000-0003-1954-4617>

Robert D. M. Hadden  <https://orcid.org/0000-0002-9702-0256>

Ricardo C. Reis  <https://orcid.org/0000-0002-7278-4639>

Mazen M. Dimachkie  <https://orcid.org/0000-0002-7148-989X>

Zahirul Islam  <https://orcid.org/0000-0003-0935-8079>

Fiore Manganeli  <https://orcid.org/0000-0001-9478-3744>

Yusuf A. Rajabally  <https://orcid.org/0000-0002-7170-8343>

Antonino Uncini  <https://orcid.org/0000-0002-8131-8912>

Waqar Waheed  <https://orcid.org/0000-0003-3049-5430>

## REFERENCES

- Sejvar JJ, Kohl KS, Gidudu J, et al. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. *Vaccine*. 2011;29:599-612.
- Berciano J, Sedano MJ, Pelayo-Negro AL, et al. Proximal nerve lesions in early Guillain-Barré syndrome: implications for pathogenesis and disease classification. *J Neurol*. 2017;264:221-236.
- Leonhard SE, Van der Eijk AA, Andersen H, et al. An international perspective on preceding infections in Guillain-Barré syndrome: the IGOS-1000 cohort. *Neurology*. 2022;99(12):e1299-e1313.
- Asbury AK, Arnasson BGW, Karp HR, McFarlin DE. Criteria for diagnosis of Guillain-Barré syndrome. *Ann Neurol*. 1978;3:565-566.
- Albers JW, Donofrio PD, McGonagle TK. Sequential electrodiagnostic abnormalities in acute inflammatory demyelinating polyradiculoneuropathy. *Muscle Nerve*. 1985;8:528-539.
- Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barré syndrome. *Ann Neurol*. 1990;27(suppl):S21-S24.
- Ho TW, Mishu B, Li CY, et al. Guillain-Barré syndrome in northern China. Relationship to *Campylobacter jejuni* infection and anti-glycolipid antibodies. *Brain*. 1995;118:597-605.
- Meulstee J, van der Meché FGA, the Dutch Guillain-Barré Study Group. Electrodiagnostic criteria for polyneuropathy and demyelination: application in 153 patients with Guillain-Barré syndrome. *J Neurol Neurosurg Psychiatry*. 1995;59:482-486.
- Hadden RDM, Cornblath DR, Hughes RAC, et al. The plasma exchange/sandoglobulin Guillain-Barré syndrome trial group. Electrophysiological classification of Guillain-Barré syndrome: clinical associations and outcome. *Ann Neurol*. 1998;44:780-788.
- Rajabally YA, Durand MC, Mitchell J, Orlikowski D, Nicolas G. Electrophysiological diagnosis of Guillain-Barré syndrome subtype: could a single study suffice? *J Neurol Neurosurg Psychiatry*. 2015;86:115-119.
- Uncini A, Ippoliti L, Shahrizaila N, Sekiguchi Y, Kuwabara S. Optimizing the electrodiagnostic accuracy in Guillain-Barré

- syndrome subtypes: criteria sets and sparse linear discriminant analysis. *Clin Neurophysiol.* 2017;128:1176-1183.
12. Jacobs BC, van den Berg B, Verboon C, et al. International Guillain–Barré syndrome outcome study: protocol of a prospective observational cohort study on clinical and biological predictors of disease course and outcome in Guillain–Barré syndrome. *J Peripher Nerv Syst.* 2017;22:68-76.
  13. Brooks BR, Miller RG, Swash M, Munsat TL. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. *Amyotroph Lateral Scler Other Motor Neuron Disord.* 2000;1:293-299.
  14. Arends S, Drenthen J, van den Bergh P, et al. Electrodiagnosis of Guillain–Barré syndrome in the international GBS outcome study: differences in methods and reference values. *Clin Neurophysiol.* 2022;138:231-240.
  15. Wakerley B, Uncini A, Yuki N, the GBS Classification Group. Guillain–Barré and Miller Fisher syndromes—new diagnostic classification. *Nat Rev Neurol.* 2014;10:537-544.
  16. Shefner JM, Al-Chalabi A, Baker MR, et al. A proposal for new diagnostic criteria for ALS. *Clin Neurophysiol.* 2020;131:1975-1978.
  17. Daube JR. Electrodiagnostic studies in amyotrophic lateral sclerosis and other motor neuron disorders. *Muscle Nerve.* 2000;23:1488-1502.
  18. Cornblath DR, Kuncl RW, Mellits ED, et al. Nerve conduction studies in amyotrophic lateral sclerosis. *Muscle Nerve.* 1992;15:1111-1115.
  19. Feinberg DM, Preston DC, Shefner JM, Logigian EL. Amplitude-dependent slowing of conduction in amyotrophic lateral sclerosis and polyneuropathy. *Muscle Nerve.* 1999;22:937-940.
  20. Van Asseldonk JTH, Van den Berg LH, Kalmijn S, Wokke JHJ, Franssen H. Criteria for demyelination based on the maximum slowing due to axonal degeneration, determined after warming in water at 37°C: diagnostic yield in chronic inflammatory demyelinating polyneuropathy. *Brain.* 2005;128:880-891.
  21. Souayah N, Pahwa A, Jaffry M, et al. Electrodiagnostic profile of conduction slowing in amyotrophic lateral sclerosis. *Heliyon.* 2023;9:e18400.
  22. Iijima M, Arasaki K, Iwamoto H, et al. Maximal and minimal motor nerve conduction velocities in patients with motor neuron diseases: correlation with age of onset and duration of illness. *Muscle Nerve.* 1991;14:1110-1115.
  23. Kuwabara S, Yuki N, Koga M, et al. IgG anti-GM1 antibody is associated with reversible conduction failure and axonal degeneration in Guillain–Barré syndrome. *Ann Neurol.* 1998;44:202-208.
  24. Uncini A, Kuwabara S. Nodopathies of the peripheral nerve: an emerging concept. *J Neurol Neurosurg Psychiatry.* 2015;86:1186-1195.

## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Arends S, Drenthen J, de Koning L, et al. Electrodiagnostic subtyping in Guillain–Barré syndrome patients in the International Guillain–Barré Outcome Study. *Eur J Neurol.* 2024;31:e16335. doi:[10.1111/ene.16335](https://doi.org/10.1111/ene.16335)

## APPENDIX A

### Members of the IGOS Consortium

James M. Addington, Umesh A. Badrising, Fabio A. Barroso, Kathleen Bateman, Isabelita Bella, Luana Benedetti, Bianca van den Berg, Ratna Bhavaraju-Sanka, Chiara Briani, Jan Buermann, Mark Busby, Steven Butterworth, Carlos Casanovas, Shan Chen, Kristl Claeys, Eugenia Conti, Jeremy S. Cosgrove, Marinou Dalakas, Philip van Damme, Efthimios Dardiotis, Amy Davidson, Alex Doets, Pieter van Doorn, Andoni Echaniz-Laguna, Filip Eftimov, Karin G. Faber, Raffaella Fazio, Thomas E. Feasby, Janev Fehmi, Chris Fokke, Toshiaki Fujioka, Ernesto Fulgenzi, Marcel P.J. Garssen, Cees J. Gijssbers, James M. Gilchrist, Job Gilhuis, Jonathan M. Goldstein, Kenneth C. Gorson, Namita Goyal, Volkan Granit, Ludwig Gutmann, Hans-Peter Hartung, James K.L. Holt, Sung-Tsang Hsieh, Min Htut, Richard A.C. Hughes, Ivonne Jericó-Pascual, Kenichi Kaida, Summer Karafiath, Mohammad Ali Khoshnoodi, Lynette Kiers, Ruud P. Kleiweg, Norito Kokubun, Noah A. Kolb, Rinske van Koningsveld, Anneke J. van der Kooi, Hans Kramers, Krista Kuitwaard, Justin Y. Kwan, Shafeeq S. Ladha, Lisbeth Landschoff Lassen, Victoria H. Lawson, Helmar Lehmann, Luciana Leon Cejas, Sonja E. Leonhard, Linda Luijten, Michael P.T. Lunn, Hadi Manji, Girolama A. Marfia, Celedonio Márquez Infante, Lorena Martín-Aguilar, Eugenia Martínez-Hernández, Giorgia Mataluni, Marcelo Mattiazzi, Christopher McDermott, Gregg Meekins, Quazi Deen Mohammad, Soledad Monges, Germán Moris de la Tassa, Caterina Nascimbene, Eduardo Nobile-Orazio, Richard J. Nowak, Michael Osei-Bonsu, Farah Pelouto, Michael T. Pulley, Luis Querol Gutiérrez, Stephen W. Reddel, Taco van der Ree, Simon Rinaldi, Paolo Ripellino, Rhys C. Roberts, Iñigo Rojas-Marcos, Joyce Roodbol, Stacy A. Rudnicki, George M. Sachs, Johnny P.A. Samijn, Lucio Santoro, Angelo Schenone, Maria José Sedano Tous, Kazim A. Sheikh, Nicholas Joseph Silvestri, Soeren H. Sundrup, Claudia Sommer, Beth Stein, Amro Maher Stino, Robin C.M. Thomma, Paul Twydell, Jay D. Varrato, y, Frederique H. Vermeij, Jan Verschuuren, Leo H. Visser, Christa Walgaard, Yuzhong Wang, Hugh J. Willison, Paul W. Wirtz, Marieke van Woerkom, Sascha A. Zivkovic.