SHORT REPORT

ABSTRACT: Complex repetitive discharges (CRDs) are a striking, infrequent finding on needle electromyography (EMG), but their significance is debated. This retrospective case-control study of 486 patients evaluated in a general hospital–based EMG laboratory examined the association of CRDs with specific diagnostic categories, duration of symptoms, and comorbid diabetes mellitus. No CRDs were identified in patients without other evidence of neuromuscular disease. Myopathy was associated with an increased risk of CRDs (adjusted odds ratio, 5.98; 95% confidence interval, 2.38 to 14.99). In general, neuropathic conditions were not associated with either an increased or decreased risk of CRDs compared with other neuromuscular diseases, although confidence intervals were wide. Similarly, neither the chronicity of symptoms nor the presence of diabetes yielded odds ratios that differed significantly from unity. In clinical populations similar to the one we studied, the positive predictive value of CRDs for any of the diagnoses we evaluated is low. However, the absence of CRDs can be of diagnostic value in that it reduces the likelihood of myopathy or motor neuron disease. The likelihood of finding CRDs in acute conditions is the same as that in chronic conditions.

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CLINICAL SIGNIFICANCE OF COMPLEX REPETITIVE DISCHARGES: A CASE-CONTROL STUDY

LESLEY K. FELLOWS, MD, CM, DPhil,[1] BETHANY J. FOSTER, MD,[2] and COLIN H. CHALK, MD, CM, FRCPC[3]

[1] Center for Cognitive Neuroscience, University of Pennsylvania, Philadelphia, Pennsylvania, USA
[2] Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Philadelphia, Pennsylvania, USA
[3] Montreal General Hospital, 1650 Cedar Avenue, Room L7-313, Montreal, Quebec H3G 1A4, Canada

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Complex repetitive discharges (CRDs) are striking bursts of spontaneous electromyographic (EMG) activity, comprising trains of complex polyphasic potentials that repeat at a regular frequency (range, 5–100 Hz) and that characteristically begin and terminate abruptly.[1,8] Single-fiber EMG recordings suggest that these discharges represent ephaptic activation of a small group of muscle fibers through a re-entrant mechanism, with one fiber acting as a pacemaker.[8] The clinical significance of CRDs is unclear. They have been described in both myopathic and neuropathic conditions, as well as in subjects without overt neurological disease, and are often taken to suggest a chronic process.[1,3]

The data in support of these generalizations are relatively scant, however. The majority of previous studies of CRDs were case series; the lack of a control group in this type of study prevents meaningful conclusions about association.[3,4,6,7] Furthermore, the largest case series originates from a specialized center with a preponderance of subjects suffering from congenital disorders of nerve or muscle, limiting the generalizability of the findings.[3] One prospective study of 162 patients with a variety of neuropathic diagnoses, which did include a control group, found that CRDs are common in the iliopsoas, particularly in diabetic patients with polyneuropathy.[5] However, the study was restricted to neuropathic conditions of the lower limb, involved a very detailed EMG examination, and did not control for potential confounders. The findings from existing studies are not necessarily applicable to the clinical setting in which the majority of electrodiagnostic studies are performed.

Are these striking discharges simply electrophysiological curiosities, or do they suggest a specific diagnosis or pathophysiological process? The aim of the current case-control study was to clarify the diagnostic implications of CRDs when they are observed in the course of routine examination, in an unselected patient population presenting to a tertiary-

Abbreviations: CRD, complex repetitive discharge; EMG, electromyography

Key words: complex repetitive discharges; electromyography; motor neuron disease; myopathy; spontaneous activity

Correspondence to: Colin H. Chalk; e-mail: colin.chalk@mcgill.ca

care hospital–based EMG laboratory. Specifically, we sought to characterize the relative risk of CRDs in a variety of diseases of nerve or muscle and to determine whether there is an association between CRDs and the chronicity of the disease process, or between CRDs and diabetes mellitus.

MATERIALS AND METHODS

The cohort of all patients examined in the Montreal General Hospital EMG laboratory over a 5-year period (1994–1998; $n = 9058$) was identified; the case-control study was nested within this cohort. Defined by standard criteria,[1] CRDs were identified by the examining neurologist at the time of the EMG study. All patients in whom CRDs were recorded in at least one muscle were identified as cases ($n = 93$). A consecutive series of patients who underwent needle EMG examination over a 7-month period in 1998, excluding those with CRDs, served as the comparison group ($n = 775$). The comparison group was subdivided into those with normal electrophysiological results ($n = 375$) and those who with abnormalities ($n = 393$). The 393 patients with abnormal electrophysiological findings served as the control group for analysis (see below).

Nerve conduction studies were performed using standard techniques, with surface electrodes for stimulation and recording.[2] The EMG examinations were performed with Medtronic DCN 37 disposable 37×0.46 mm concentric-needle electrodes (Dantec, Skovlunde, Denmark), using Nicolet Viking IV-P and Nicolet Spirit EMG machines (Nicolet Biomedical, Madison, Wisconsin). Spontaneous electrical activity and voluntarily activated motor unit potentials were sampled in three or more areas in each muscle examined. Most of the patients were examined by two neurologists, both of whom were trained in clinical neurophysiology in the same program (Mayo Clinic, Rochester, Minnesota); the balance of patients were examined by two other neurologists who had been trained by the first two. As a consequence, there was a general consistency of technique and approaches used to examine patients.

Data for both cases and controls were collected through retrospective review of the clinical information and electrophysiological findings documented in the records of the EMG laboratory. Diagnoses were those made by the examining neurologist at the time of the study, based on the results of the clinical and electrophysiological examination. Diagnoses were confirmed for the cases by reviewing all available data in hospital and outpatient charts, although in no case did this supplementary information lead to a change in the diagnostic category to which the subject had been assigned.

Preliminary analysis of the data indicated that whereas all the cases had other evidence of neuromuscular disease on the basis of history, physical findings, and electrodiagnostic examination, almost half the comparison group (i.e., 382 of 775) did not have evidence of disease. Based on this finding, we conclude that CRDs will rarely be detected in patients with no other evidence of neuromuscular disease, at least as assessed by the techniques used in the routine clinical practice of EMG. This is not to say that CRDs can never be found in otherwise normal individuals; only that in clinical populations similar to ours undergoing routine EMG examination, this occurs only rarely. Because of the absence of CRDs in our normal patients, we chose to focus the analysis on those patients with evidence of neuromuscular disease. The controls for the analysis presented here therefore comprised the 393 patients in the comparison group who had evidence of neuromuscular disease but in whom no CRDs were recorded. The conclusions of this study are thus applicable only to interpreting the finding of CRDs in patients with other evidence of neuromuscular disease and not in otherwise normal subjects.

A wide range of disorders of nerve or muscle was represented in both cases and controls. To maximize statistical power, these were grouped into broad, neuroanatomically based diagnostic categories for the purposes of analysis. Similarly, the duration of disease was categorized as acute ($\leq$3 months) or chronic ($>$3 months). If the time of symptom onset was uncertain, duration was classified as chronic.

Data were analyzed with STATA statistical software, version 7.0 (Stata Corporation, College Station, Texas). Logistic regression analysis was performed to determine the odds ratio for CRDs for each diagnostic category compared with all other diagnostic categories combined, adjusted for potential confounders. Age, sex, duration of symptoms (dichotomized as acute or chronic), number of muscles examined by needle EMG, and presence of diabetes were entered into the model as potential confounders. Logistic regression was also performed to determine the odds ratio for CRDs in the presence of diabetes, and for acute versus chronic conditions, controlling for age, sex, number of muscles examined, and diagnostic category. Because CRDs are a rare finding in all diagnostic categories, the odds ratio approximates the relative risk.

Table 1. Prevalence of diagnoses for cases and controls, by category, and the odds ratio for CRDs for each diagnostic category.*

Diagnosis	Cases (%)	Controls (%)	Total (%)	Unadjusted odds ratio for CRDs (95% CI)	Adjusted odds ratio for CRDs (95% CI)
Radiculopathy	41 (45)	166 (42)	207 (43)	1.07 (0.68 to 1.70)	0.68 (0.41 to 1.13)
Plexopathy	9 (10)	22 (6)	31 (6)	1.81 (0.80 to 4.07)	1.92 (0.78 to 4.70)
Mononeuropathy	11 (12)	126 (32)	137 (28)	0.28 (0.14 to 0.55)	0.47 (0.23 to 0.95)†
Polyneuropathy	14 (15)	59 (15)	73 (15)	1.00 (0.53 to 1.89)	1.71 (0.79 to 3.68)
Motor neuron disease	5 (5)	7 (2)	12 (3)	3.13 (0.97 to 10.1)	0.57 (0.14 to 2.34)
Myopathy	13 (13)	13 (3)	26 (5)	4.75 (2.12 to 10.63)	5.98 (2.38 to 14.99)†

Bracketed values are the 95% confidence intervals.
†Highlights categories in which the 95% confidence interval does not include 1.00.

RESULTS

There were 93 cases and 393 controls. There was no significant difference in sex ratio, prevalence of diabetes mellitus, or proportion with duration of symptoms ≤3 months (cases, 23%; controls, 26%) between the two groups (Fisher's Exact test, $P > 0.1$). Cases were significantly older than controls (mean ± standard deviation: 65.7 ± 14.3 versus 55.0 ± 16.4 years, $P < 0.01$, Student's unpaired *t*-test). The duration of the neurological condition was longer in cases with CRDs (3.38 ± 6.0 vs. 2.07 ± 4.6 years, $P < 0.05$, Student's unpaired *t*-test), and they had on average one additional muscle examined by EMG (mean ± standard deviation, 5.1 ± 1.9 versus 4.0 ± 1.6; $P < 0.01$, Student's unpaired *t*-test). Diagnoses were subsumed into six neuroanatomically based categories; prevalence rates are shown in Table 1. All patients exhibiting CRDs had other evidence of neuromuscular disease on neurological examination, electrodiagnostic evaluation, or both.

The unadjusted and adjusted odds ratios for each diagnosis are also shown in Table 1. The most striking finding is that the risk of CRDs with a diagnosis of myopathy is 6 times that with any other diagnosis. There was no clear association between CRDs and any of the other diagnostic categories, except mononeuropathy. The risk of finding CRDs in a patient with mononeuropathy is about half that for other diagnoses.

Table 2 provides the sensitivity, specificity, and positive and negative predictive values of the finding of CRDs for each diagnostic category. These values highlight the low positive predictive value of CRDs for any of the diagnoses.

No definite association could be demonstrated between coexistent diabetes mellitus and the presence of CRDs (crude odds ratio, 0.69; adjusted odds ratio, 0.52; 95% confidence interval, 0.22 to 1.24), although the best estimate is that individuals with diabetes are less likely to have CRDs than are nondiabetics. Similarly, there was no evidence of an altered risk of CRD in patients with acute (duration ≤ 3 months) compared with chronic conditions (crude odds ratio, 1.08; adjusted odds ratio, 0.82; 95% confidence interval, 0.45 to 1.49).

DISCUSSION

This case-control study was designed to assess the association between CRDs and anatomically based diagnostic categories in a population presenting to a tertiary-care hospital EMG clinic. It should be emphasized that CRDs were not found in any of the 382 subjects who were not given a neuromuscular diagnosis upon full assessment in the EMG laboratory. Furthermore, these discharges were never the only abnormality on EMG examination. This study compared patients with CRDs with patients who were assigned a neuromuscular diagnosis on the basis of

Table 2. Sensitivity, specificity, and positive and negative predictive values of CRDs for each diagnostic category.

Diagnosis	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Radiculopathy	0.20	0.81	0.44	0.58
Plexopathy	0.29	0.82	0.10	0.94
Mononeuropathy	0.08	0.77	0.12	0.68
Polyneuropathy	0.19	0.81	0.15	0.85
Motor neuron disease	0.42	0.81	0.05	0.98
Myopathy	0.50	0.83	0.14	0.97

the clinical and electrophysiological assessment but in whom CRDs were not detected.

The study design permitted the determination of odds ratios for CRDs for six major diagnostic categories, controlling for potential confounders. The main finding is an increased risk of CRDs in myopathy. In contrast, the confidence intervals for the odds ratios in diseases of nerve root, plexus, or motor neurons all include 1.00. Two interpretations can be offered: that diseases of nerve root, plexus, or motor neurons are not strongly associated with CRDs; or that the study has inadequate ability to detect either an increased risk or a protective effect of any of these diagnoses for CRDs. Given the relatively wide confidence intervals, we favor the latter. In contrast to the other diagnostic categories, with mononeuropathy we found an odds ratio for CRDs that is less than 1.00, indicating a protective effect.

Similarly, when controlling for diagnosis and other potential confounders, we found neither elevated risk of CRDs in diabetics nor an association of CRDs with chronicity of disease (defined as a duration greater than 3 months). Although the wide confidence intervals indicate that these results must be interpreted with caution, we found neither evidence for a preponderance of CRDs in chronic conditions nor a particular proclivity for these discharges in diabetics.

An important consideration in interpreting the results of this study is whether the finding of CRDs influenced diagnosis. In no case were CRDs found in isolation; other abnormalities that supported the primary diagnosis were invariably present on EMG, making this an unlikely source of error. The results of this study cannot be readily generalized to populations in which the prevalence rates for the various diagnoses are very different from those we report, or when EMG practices differ markedly from those used here. The results of this study indicate that in a hospital-based EMG laboratory setting, the finding of CRDs in a given patient is strong evidence for neuromuscular disease. However, the positive predictive value of these discharges is low for any specific diagnosis. In fact, CRDs may be most useful diagnostically when absent, given the high negative predictive values we found for motor neuron disease and myopathy. The presence of CRDs does not provide information about the chronicity of the underlying process.

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