AN ELECTROPHYSIOLOGICAL EXPLORATION OF THE DOUBLE CRUSH HYPOTHESIS

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The double crush hypothesis (DCH) suggests that a peripheral nerve which is compressed proximally is more susceptible to a distal compressive lesion than a nerve that has not sustained a proximal compression. Upton and McComas23 originally suggested the hypothesis, which has been supported by studies in humans10,14,20 and animal models.4,16,19 Nevertheless, it has also been questioned.25 A recent review assessed the supportive animal studies and found various flaws.26 The review also suggested that the most common clinical example of the DCH, an increased predisposition to carpal tunnel syndrome (or median mononeuropathy, MM) in patients with cervical radiculopathy (CR), was physiologically unsound. More specifically, the authors noted that a radicular lesion should have no effect on frequency of MM because a CR should have: (1) no effect on distal sensory conduction studies; (2) no effect on distal myelin; and (3) minimal effect on distal motor axon function of the median nerve, given its multiple levels of innervation. The first two concerns are particularly important because most patients with MM have electrodiagnostic findings characterized by sensory latency prolongation and focal demyelination. Although valid, these concerns do not necessarily disprove the DCH.

We are aware of only one other study that offers detailed systematic human data that explore the DCH.15 That study did so by identifying records of patients with MM (and ulnar neuropathy at the elbow) and then determining the frequency with which an appropriate coexisting CR was present. Although existence of a coexistent CR was not common (435 of 12,736 limbs, 3.4%), approximately 98 of those 435 limbs (22.5%) with both CR and distal compression demonstrated an appropriate anatomical relationship. It is not clear if that frequency is greater than would be anticipated by chance.

We analyzed cases of C6, C7, and C8 CR and exploited the fact that for routine nerve conduction...
studies, the median sensory response is of C6/C7 origin and the median motor response is primarily of C8/T1 origin. We identified cases by reviewing written reports that were computer-recorded as C6, C7, or C8 CR in our institution over the last 9 years. To test the hypothesis that nerve root compression causes a predisposition to distal compressive neuropathy, we evaluated the following:

Primary Hypotheses
1. MM as determined by sensory nerve conduction criteria will be identified more frequently in electrodiagnostic case reports with C6 and/or C7 CR than cases with C8 CR.
2. MM as determined by motor nerve conduction criteria will be identified more frequently in case reports with C8 CR than cases with C6 and/or C7 CR.

Secondary Hypotheses
1. Cases with C6 or C7 CR will have decreased median sensory amplitudes, increased median sensory latencies, or both, compared to cases with C8 CR.
2. Cases with C8 CR will have decreased median motor amplitudes, increased latencies, or both, compared to cases with C6 and/or C7 CR.
3. Cases with C6 and/or C7 CR and electrodiagnostically defined MM will demonstrate decreased median sensory amplitudes compared to cases with C8 CR radiculopathy and MM.
4. Cases with C8 CR and electrodiagnostically defined MM will demonstrate decreased median motor amplitudes compared to cases with C6 and/or C7 CR and MM.

MATERIALS AND METHODS
Using a software system (EMGPRO®, University of Michigan Software, 475 E. Jefferson, Rm.23554, Ann Arbor, MI 48109-1092) which has recorded and categorized written electrodiagnostic reports at the University of Michigan since 1988, we reviewed all studies coded as C6, C7, or C8 CR. Inclusion and exclusion of cases were based on the following criteria.

Inclusion Criteria
1. Unequivocal abnormal spontaneous activity in two limb muscles from the anterior myotome of appropriate root origin, and the appropriate level of the paraspinal cervical musculature.

Exclusion Criteria
1. Electrodiagnostic evidence, even if equivocal, of C8 involvement in the C6 group and of C6 involvement in the C8 group.
2. Electrodiagnostic evidence, even if equivocal, of C6 or C8 involvement in the C7 group.
3. Electrodiagnostic evidence of any other neuromuscular disorder.
4. A history of any medical disorder associated with a generalized peripheral neuropathy.

The nerve conduction studies were performed as follows: The hand was warmed as needed to keep the palmar temperature at or above 32.0°C. The median sensory response was recorded with ring electrodes over the 2nd digit; stimulation was performed antidromically 14 cm proximally over the median nerve. The ulnar sensory response was recorded with ring electrodes over the 5th digit; stimulation was performed antidromically 14 cm proximally over the ulnar nerve. A 3-cm distance between active and reference electrodes was maintained for sensory studies. The median motor response was recorded over the thenar eminence and the ulnar motor response over the hypothenar eminence; stimulation was performed 7 cm proximally over the median and ulnar nerves, respectively.

Analysis of Electrodiagnostic Cases. The frequency of coexistent MM at the wrist among the C6, C7, and C8 CR groups was determined. Median to ulnar sensory latency differentials $\leq 0.5\text{ ms}^5$ and $> 0.8\text{ ms}^{17}$ were used as sensory criteria for MM. The former is probably overly sensitive but was included to maximize the chances of finding a difference in MM frequency among different CR levels. A median to ulnar motor latency differential of $\approx 1.8\text{ ms}^{22}$ was used as motor criteria for MM. A chi-square analysis was performed to identify the possible presence of an association between MM and CR level.

Mean absolute and relative median sensory and median motor amplitudes were determined. Relative amplitudes were calculated by subtracting the ulnar from the median response amplitude in each case so as to control for possible group differences in amplitudes. Mean absolute and relative latencies were similarly determined, the latter by subtracting the ulnar from the median response latency for each case. Analyses of variance (ANOVA$s$) were performed to determine the effect of CR level on the distal nerve conduction parameters; a Bonferroni correction for multiple comparisons was also utilized. A statistical software program (SPSS version 7.5) was used in the analysis.
The electrodiagnostic case studies obtained from EMGPRO also had demographic data including height, weight, age, and gender. These factors [height and weight when converted into a body mass index (BMI kg/m²)] have been associated with a higher prevalence of MM. A series of 2 (MM present versus MM absent) by 3 (C6, C7, C8 CR) ANOVAs was performed to determine if significant differences in age or body mass index were present as a function of MM or CR. Chi-square analysis was also performed to determine if gender was significantly related to the presence of MM or CR.

For all analyses a $P$ value of $<0.05$ was considered significant and a value $\geq 0.05$ but $<0.10$ was considered a trend.

RESULTS

Following application of the inclusion and exclusion criteria, 45 C6 cases, 54 C7 cases, and 55 C8 cases were identified and subjected to analysis.

Primary Hypotheses 1 and 2. The relationship between frequency of sensory and motor MM and level of radiculopathy is shown in Table 1. Using the 0.5-ms differential between median and ulnar sensory responses as electrodiagnostic criteria, MM was significantly more frequent among the C6 (28.9%) and C8 (29.1%) cases compared to the C7 cases (9.3%, $P < 0.02$). These data are consistent with the DCH with regard to the C6 group, but contrary to the hypothesis with regard to the C8 group. Using the 0.8-ms differential between median and ulnar sensory responses as criteria for MM, there was still a minimally increased frequency of MM among the C6 (8.9%) and C8 (9.1%) cases compared to the C7 (3.7%) cases, but the difference was smaller and not significant.

Contrary to DCH, when the C6 and C7 cases were grouped together and compared to the C8 cases there was a trend toward a significantly increased frequency of MM among the C8 cases (29.1%) compared to the grouped C6 and C7 cases (18.2%, $P = 0.088$) using the 0.5-ms differential criteria. Using that same grouping pattern and the 0.8-ms differential criteria, MM was only slightly and not significantly more frequent among the C8 group (9.1%) than the C6/C7 group (6.1%).

When using a 1.8-ms differential between median and ulnar motor responses as electrodiagnostic criteria, MM was somewhat less frequent in the C8 group (7.3%) than the C6 group (15.6%) and not different than the C7 group (5.6%). None of the differences reached statistical significance. Using these same criteria for MM and grouping the C6 and C7 cases together, MM was again slightly less frequent among the C8 cases (7.3%) as compared to the C6/C7 (10.1%, ns).

When all cases were considered together regardless of CR level, the frequency of MM was relatively high. Using the 0.5-ms sensory latency differential criteria, MM was present in 34 of 154 (22.1%) of cases; using the 0.8-ms sensory latency differential criteria, MM was present in 11 of 154 (7.1%) of cases. Lastly, using the 1.8-ms motor latency differential criteria, it was present in 14 of 154 (9.1%) of cases.

Secondary Hypotheses 1 and 2. The relationship between median motor and sensory response parameters and level of CR is shown in Table 2. The median sensory amplitudes [mean, (SD)] among cases with a C6 CR were slightly but not significantly greater than the median sensory amplitudes of patients with C7 and C8 CR. When a relative median sensory amplitude was calculated by subtracting the ulnar sensory response from the median sensory response for each case, a trend consistent with the double crush hypothesis was noted. The C8 cases demonstrated a greater amplitude compared to the C6 and C7 cases ($P = 0.05$); however, when a Bonferroni correction for multiple comparisons was ap-

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**Table 1.** Frequency of median mononeuropathy (MM) defined by different sensory and motor criteria, for different levels of crucial radiculopathy.

<table>
<thead>
<tr>
<th>MM Criteria</th>
<th>C6 (n = 45)</th>
<th>C7 (n = 54)</th>
<th>C6 and C7 (n = 99)</th>
<th>C8 (n = 55)</th>
<th>Significance*</th>
<th>Significance †</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory</td>
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<tr>
<td>0.5 ms</td>
<td>13 (28.9%)</td>
<td>5 (9.3%)</td>
<td>18 (18.2%)</td>
<td>16 (29.1%)</td>
<td>$P &lt; 0.02^|$</td>
<td>$P &lt; 0.088^|$</td>
</tr>
<tr>
<td>0.8 ms</td>
<td>4 (8.9%)</td>
<td>2 (3.7%)</td>
<td>6 (6.1%)</td>
<td>5 (9.1%)</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>Motor</td>
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<tr>
<td>1.8 ms</td>
<td>7 (15.6%)</td>
<td>3 (5.6%)</td>
<td>10 (10.1%)</td>
<td>4 (7.3%)</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Significance at any level.
†Significance of C6 and C7 combined versus C8.
‡ANOVA demonstrated that C6 and C8 CR groups had significantly greater number of cases with MM as compared to C7 radiculopathy group.
§A trend toward C8 CR group with more cases with MM as compared to the combined C6/C7 CR groups.
plied, the finding was not significant. When latencies were evaluated, neither absolute nor relative median sensory latencies in the C6 group were significantly more prolonged than those in the C7 or C8 group. Furthermore, with the C6 and C7 cases grouped together, there was no significant difference from the C8 group between the median sensory response amplitudes or latencies.

The median motor amplitudes in cases of C8 CR were slightly but not significantly decreased compared to cases of CR involving C7 or C6. This minimal decrease was no longer evident when the relative amplitudes (by subtracting the ulnar motor response amplitude for each case) were determined. Similarly, the median motor response latencies in cases with a C8 CR were slightly but not significantly prolonged compared to CR involving the other levels, and this minimal apparent difference was not evident when relative latencies were determined. When the C6 and C7 cases were grouped and compared to the C8 cases, no significant difference between groups was noted for median motor response amplitudes or latencies.

**Secondary Hypotheses 3 and 4.** The relationship between CR level and median response amplitudes among cases with MM is shown in Table 3. Cases with a median to ulnar sensory latency differential of 0.5 ms or greater were analyzed separately. Thirty-four cases met the criteria. Consistent with the DCH, median sensory response amplitudes in cases of C6 CR were decreased compared to C7 and C8 cases but this finding did not approach significance. Contrary to the DCH, median motor amplitudes in the C8 cases were greater than in the C6 cases but again the difference was not significant. When the C6 and C7 cases were grouped and compared with the C8 cases, no significant difference in median sensory or motor response amplitudes were identified.

**Gender, BMI, and Age as Functions of CR and MM.** Although the C8 group was slightly older, there were no significant differences in age, BMI, or gender among the different CR groups (Table 4). Consistent with previous studies, increased BMI and older age were found to be significantly greater among those who met electrodiagnostic criteria for MM (using a median to ulnar sensory latency difference of 0.5 ms or more) than those who did not, as shown in Table 5. However, unlike other studies, MM was not more common among women21 (Table 5).

<table>
<thead>
<tr>
<th>Table 2. Absolute and relative median nerve response parameters [mean (SD)] by radiculopathy level.</th>
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<tr>
<td>NCS parameter</td>
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<td>---------------</td>
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<tr>
<td>MSA (µV)</td>
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<tr>
<td>Absolute</td>
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<td>Relative</td>
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<tr>
<td>MSL (ms)</td>
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<td>Absolute</td>
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<td>Relative</td>
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<td>MMA (mV)</td>
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<td>Absolute</td>
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<td>Relative</td>
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<tr>
<td>MML (ms)</td>
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<tr>
<td>Absolute</td>
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<tr>
<td>Relative</td>
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</table>

NCS, nerve conduction studies; MSA, median sensory amplitude; MSL, median sensory latency; MMA, median motor amplitude; MML, median motor latency.

*Significance at any level.
†Significance, C6 and C7 combined versus C8.

<table>
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<th>Table 3. Median response amplitudes [mean (SD)] by radiculopathy level in cases with electrodiagnostically defined MM.</th>
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<tr>
<td>Radiculopathy level</td>
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<tr>
<td>---------------------</td>
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<tr>
<td>MSA (µV)</td>
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<tr>
<td>MMA (mV)</td>
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</tbody>
</table>

MSA, median sensory amplitude; MMA, median motor amplitude.
*Significance at any level.
†Significance, C6 and C7 combined versus C8.
DISCUSSION

The DCH has some experimental and considerable clinical support. Although this support has been called into question, the DCH is still accepted by many clinicians. However, present understanding of the anatomy and physiology of peripheral nerves is largely inconsistent with the most often suspected clinical double crush, MM superimposed on a CR. As has been pointed out elsewhere, it is difficult to understand how a CR could influence distal sensory nerve conduction studies. CR leading to disruption in axoplasmic flow proximal to the dorsal root ganglion would not be expected to cause distal dysfunction or demyelination of that same axon, and the presence of the dorsal root ganglion within the spinal canal appears to occur primarily in the lumbar-sacral segments and rarely has an impact on nerve conduction studies. However, the spirit of this investigation was simply to assume that a disruption of distal nerve function could exist, through presumably unknown mechanisms, and then determine if nerve conduction data supported its existence.

Which point of view do the data from this study support? The overall incidence of MM among all of the cases of CR (22.1%) appears increased when compared to that of the general adult population (0.52% for men, 1.49% for women) which upon first observation suggests support for the DCH. However, when compared to industrial populations, the difference is less marked. The incidence of MM among applicants for industrial jobs is approximately 12%, and the incidence among active workers is approximately 25%. Although it seems unlikely that all patients in this study repetitively used their hands for 40 or more hours per week, the work/upper extremity usage habits of the population analyzed is unknown. Nevertheless, our data suggest that patients with CR have MM with a frequency that is similar to that in groups at high risk, and greater than the frequency seen in groups at a more intermediate risk.

However, the distribution of the types of MM analyzed by CR level was not consistent with the DCH. Although sensory-defined MM was significantly more frequent in the C6 cases than in the C7, the C8 cases demonstrated the same frequency as the C6 cases. In addition, when the C6 and C7 cases were grouped and compared to the C8 cases, there was a trend toward a significantly greater frequency of MM among the latter. Even if it is assumed that there is a mechanism to link a proximal lesion with distal demyelination at the same root level, a C8 CR should not influence a median sensory response recorded at the 2nd digit. The DCH also predicts that MM defined by motor criteria will occur more frequently in C8 cases, but our data do not demonstrate this.

The DCH was not supported by any of the eight electrophysiological parameters analyzed by CR level. No significant differences were found in median sensory amplitudes or latencies in C6 and/or C7 cases as compared to C7 or C8 cases, and no differences were found in motor responses among C8 cases compared to C6 and/or C7 cases (Table 2). This remained true even when cases whose median to ulnar sensory latency differentials were consistent with MM were analyzed separately (Table 3). Of note, the mean median motor response amplitude in the C8 cases with MM was slightly greater, rather than less, than that of the C6/C7 cases. These data cast particular doubt on the DCH, given that cases with a C8 radiculopathy and MM have two lesions which are distal to the axons’ cell bodies of origin.

Other studies supporting the DCH have often

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<th>Table 4. Characteristics of cases by radiculopathy level.</th>
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<tr>
<td>Radiculopathy level</td>
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<tr>
<td>Mean Age (SD)</td>
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<tr>
<td>No. of Women</td>
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<tr>
<td>Mean BMI (SD)</td>
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<th>Table 5. Characteristics of cases by electrodiagnostically defined MM.</th>
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<tr>
<td>Median mononeuropathy</td>
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<tr>
<td>Mean Age (SD)</td>
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<tr>
<td>No. of Women</td>
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<tr>
<td>Mean BMI (SD)</td>
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*Cases with MM with significantly greater BMI and older.
defined CR by symptoms or radiological evidence. That strategy is imprecise given the propensity for purely muscular lesions to cause radiating symptomatology and for asymptomatic individuals to have significant spinal degenerative changes. We believe that the electrophysiological techniques used in this study are a more reliable and precise means for identifying CR and MM.

The data therefore suggest that the DC may reflect a clinical entity, but not a neurophysiological one. This conclusion is similar to the one drawn by Frith and Litchy who defined CR surgically and found that of the 104 patients, 18 (12.9%) also had MM. As in the present study, it was noted that “nerve conduction abnormalities were common” but the DCH was not supported by “the distribution of the abnormalities in relation to the diseased roots.”

Morgan and Wilbourn also used reports of electrodiagnostic studies to analyze the DCH. They identified two distal compression neuropathies (MM and ulnar at the elbow) and assessed the studies for the presence of an “appropriate” CR that would be anticipated to cause the distal neuropathy if the DCH is correct. Overall an appropriate CR was found infrequently and it was concluded that a CR rarely underlies a distal compression neuropathy; however, the frequency of CR among a control group without MM and ulnar neuropathy was not revealed. Furthermore among those subjects with CR and a distal neuropathy, the CR was appropriate 22.5% of the time. This was true despite the fact that an appropriate CR pattern for MM affecting both sensory and motor nerve conduction studies was considered to be an ipsilateral multilevel radiculopathy involving C6, C7, C8 and T1—an unlikely finding. Therefore, although Morgan and Wilbourn’s data strongly suggest that the DCH is rarely of clinical relevance in the setting of MM and ulnar neuropathy at the elbow, the data do not disprove the DCH. In contrast the data in this study come from cases with known CR and, although coincident MM was relatively common, no changes in distal nerve conduction studies or type of MM consistent with the DCH were found when comparing one level of CR to another. The data directly contradict the DCH.

It is unclear why CR and MM seem to coincide so frequently. It may be that both disorders have a common predisposing influence such as upper extremity overuse or osteoarthritis leading to both cervical foraminal and carpal canal stenosis. Previous work has identified an increased incidence of carpal tunnel syndrome in patients with cervical arthritis and small carpal canal size. Upper extremity weakness and pain in patients with CR may cause changes in biomechanics and usage patterns leading to increased upper extremity edema with resultant increased carpal canal pressures.

Despite its strengths, our study has limitations. The data were obtained from patients who were referred to a tertiary electrodiagnostic laboratory and who may not represent the general population. The MM was determined strictly by electrodiagnostic means, without associated history or physical findings. The criteria for radiculopathy were stringent; many potential cases who probably had a CR were excluded because they did not meet all of our inclusion/exclusion criteria. Therefore our analysis involved an exclusive group and the numbers of cases were relatively modest.

In summary, it appears that electrodiagnostic evidence of MM as defined by sensory criteria is common among cases with CR, particularly at the C6 and C8 level. However the data do not support a neurophysiological explanation; i.e., the distal electrophysiological parameters are not consistent with a proximal disruption in axoplasmic flow at a specific root level leading to distal axonal dysfunction. This suggests that if any relationship between CR and MM exists, it is associational rather than causative. Although the double crush hypothesis may appear to be a clinical entity, at least in the case of CR and MM, it does not appear to be a neurological one.

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