

# Journal Club: Improved diagnosis of spinal cord disorders with contact heat evoked potentials

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**BACKGROUND AND SIGNIFICANCE** Spinal cord disorders (SCD) comprise a group of traumatic injuries, vascular diseases, and infectious and inflammatory processes that cause spinal cord damage or dysfunction.<sup>1</sup>

Neurophysiologic tools, including evoked potentials, were shown to improve the sensitivity of clinical sensory testing in spinal cord injury. Dermatome somatosensory evoked potentials (dSSEP) are recorded from the CNS following stimulation of sense organs elicited by tactile/electrical stimulation of a sensory/mixed nerve in the periphery. This technique is widely used in clinical routine as the gold standard for evaluation of the dorsal column pathways.<sup>2</sup> In cases in which pain is in the foreground of the symptoms, laser evoked potentials (LEP) have proven suitable to study nociceptive pathways.<sup>3</sup> Contact heat evoked potentials (CHEP) have been introduced recently to study nociceptive pathways. This technique allows studying the cerebral response to thermal stimuli mediated by A $\delta$  and C fibers by using a contact thermode that rapidly increases skin temperature.<sup>4</sup> A strong similarity between CHEP evoked potentials and LEP has been described.<sup>5</sup> CHEP are advantageous with regard to obtaining reliable scalp potentials and absence of pain and cutaneous lesions compared to LEP. Thus, the function of ascending pathways of the spinal cord can be comprehensively investigated by combining dSSEP and LEP/CHEP.<sup>4</sup> Recent guidelines including the recommendations from the European Federation of Neurological Sciences, however, recommend LEP but could not identify studies that demonstrate the diagnostic value of CHEP.<sup>6</sup>

**HYPOTHESIS AND DESIGN** The primary aim stated by Ulrich et al.<sup>7</sup> was to assess the diagnostic value of CHEP in SCD. The authors investigated the sensitivity of CHEP compared with the current gold standard techniques (dSSEP, light touch [LT], and pinprick [PP]) to individuate specific ascending pathways involved in focal disorders of the spinal cord. This is a relevant question, as it has been speculated

that CHEP offer a higher sensitivity but are currently not used routinely in clinical practice.<sup>8</sup>

The significance of this study is related to the large cohort of patients with SCD studied in a prospective study. Patients recruited were adults with different spinal cord lesions defined by MRI. They were studied in 3 different groups (complete, incomplete, diffuse and central-anterior) and further distinguished by the injury levels (cervical and thoracic cord), causes (traumatic and nontraumatic), and clinical impairment of SCD. The sensitivity of each test was assessed separately and was defined as the percentage of patients with at least one impaired dermatome at or below MRI lesion level.

**METHODS** All subjects underwent routine MRI of the spine (1.5T). Seventy-five patients (76% female) were enrolled (complete lesion n = 7, incomplete/diffuse n = 33, central/anterior n = 35). Patients were classified as incomplete-diffuse if they had an incomplete lesion of the spinal cord with a diffuse lesion pattern according to MRI. The larger patient groups were represented by traumatic SCD (n = 29) and chronic compressive myelopathies (n = 27), whereas the other groups were spinal cord ischemia (n = 7), myelitis (n = 5), and syringomyelia (n = 5). The mean age of the patients was 48.6 years (SD 18.5). CHEP and dSSEP were tested at the same dermatomes in each individual above and below the spinal lesion as defined by MRI. C3 was the most rostral dermatome tested. CHEP control values for peak latencies and amplitudes were established in a cohort of 31 healthy volunteers with an age range of 25–75 years. The normal values could be readily recorded in the cohort of healthy subjects in the predefined dermatomes. The normal peak latencies of N1 were the reference for the interpretation of dSSEP. The authors performed clinical sensory examination on the grounds of LT and PP testing. The examination was based on the protocol provided by the American Spinal Injury Association and performed according to

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the International Standards for the Neurological Classification of Spinal Cord Injury.<sup>9</sup>

**RESULTS** CHEP, dSSEP, and clinical sensory testing were comparably sensitive to detect the spinal cord injury in complete and incomplete-diffuse SCD ( $p \geq 0.05$  for all comparisons) as defined by the presentation of MRI findings.

Notably, the number of dermatomes needed to test was lower for CHEP than dSSEP in incomplete-diffuse SCD (1.5 compared with 1.9,  $p = 0.030$ ). Best results were found in central/anterior SCD, where CHEP showed a higher sensitivity (89%) compared with dSSEP (24%,  $p \leq 0.001$ ), PP (62%,  $p = 0.013$ ), and LT testing (57%,  $p = 0.003$ ). In this group, the number of dermatomes needed to test was lower for CHEP (mean = 1.5) compared to dSSEP (6.4,  $p \leq 0.001$ ).

The authors performed receiver operating characteristic (ROC) curve analysis for each type of test and patient group to illustrate the performance of each technique. The ROC curve is a graphical plot used to investigate 2 essential characteristics for the accuracy of a diagnostic test: the sensitivity and the specificity. Of note, ROC curve revealed that CHEP as well as dSSEP and clinical sensory testing have comparable diagnostic accuracy with all area under the ROC curve (AUC) values  $>0.75$  in the group with complete and in the group with incomplete/diffuse SCD. This demonstrates an adequate diagnostic accuracy of all 3 techniques in these types of SCD. In central/anterior cord lesions, only CHEP had diagnostic power (AUC = 0.86), whereas this was not the case for dSSEP, PP, and LT.

Clinical sensory testing and evoked potentials showed consistent correlation with evoked potentials in 69% (CHEP/PP) and 65% (dSSEP/LT) of tested dermatomes. Interestingly, CHEP detected a subclinical sensory impairment more frequently than dSSEP ( $p \leq 0.001$ ). On the other hand, 8 patients with focal central cord lesions presented with normal rated LT and PP sensation, and in 5 of them the clinical motor examination was normal. Three other patients presented with partially impaired motor function. Remarkably, the dSSEP were normal in these patients, whereas CHEP were impaired in 7 patients (87.5%).

**INTERPRETATION** This is a prospective cohort study that systematically investigated the value of CHEP in focal disorders of the spinal cord. The findings underscore the high sensitivity of CHEP to individuate the affection of spinothalamic pathways in myelopathic disorders complementary to MRI, dSSEP, and clinical examinations. In central and anterior cord lesions, CHEP complementary to dSSEP allows to distinguish the affection of spinothalamic from dorsal column pathways. In addition, the sensitivity of CHEP was confirmed in different forms of SCD. Another

key finding was the capacity of CHEP to demonstrate sensory impairment in patients with a single dermatome affected and in those with apparently negative neurologic examination. Indeed, the most challenging incentive in the use of CHEP in clinical practice lies in the clarification of potential differential diagnoses in patients with a myelopathic syndrome but normal MRI findings. Furthermore, CHEP may be valuable in the assessment of somatoform disorders, especially in the group of patients with sensory symptoms. Taken together, these results encourage the use of CHEP in clinical practice as important support to clinical examination and neuroimaging.

The weakness of this study, as stated by the authors, includes the choice of the cutoff level to consider CHEP as abnormal. This was defined as the mean 1 SD of the N2/P2 latency measured in the control group, which is rather loose for evoked potential analysis. Indeed, more than 70% of pathologic CHEP had no detectable N2/P2 peak. Concomitant intake of sedative or analgesic medications may have influenced the findings. It has been shown that the routinely recorded N2/P2 vertex component in CHEP correlates with perceived intensity of the heat stimulus and alertness. A possible influence of central neuropathic pain can be also argued, since it was not an exclusion criterion. Another limitation of the study was the recruitment bias. The major patient groups studied were traumatic spinal cord injuries and chronic compressive myelopathies. The current study does not reflect the spectrum of SCD in the general population of SCD. Further studies should not only focus on the potential dynamics in the course of SCD but also on individual characteristics in SCD such as different forms of spinal cord inflammation, cerebrovascular disorders, or developmental anomalies. This limitation compromises the opportunity to expand our knowledge on individual disease characteristics. Not only the group of controls needs to be expanded for the establishment of thresholds but also aging needs to be considered in this regard. Recent studies indicate that aging interferes with the nociceptive threshold.<sup>10</sup> In addition, the initial negative latency correlates with sex, with shorter latencies noted in female patients.

The authors have shown that CHEP can provide a noninvasive additional clinical tool of potential utility in the evaluation of nociceptive pathways in SCD. The findings indicate that CHEP possess properties that are desired for an appropriate diagnostic test in SCD. Further research, including on use in patients with central neuropathic pain, and studies reporting applicability in clinical practice will disclose the value of CHEP over time.

#### **AUTHOR CONTRIBUTIONS**

Antonella Macerollo: design and conceptualization of the study, analysis and interpretation of the data, drafting and revising the manuscript.

Johann Sellner: design and conceptualization of the study, analysis and interpretation of the data, drafting and revising the manuscript.

### STUDY FUNDING

No targeted funding reported.

### DISCLOSURE

The authors report no disclosures relevant to the manuscript. Go to [Neurology.org](http://Neurology.org) for full disclosures.

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*Neurology* 2014;83:e45-e47  
DOI 10.1212/WNL.0000000000000598

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