

Evidence-Based Guideline Update: Intraoperative Spinal Monitoring with Somatosensory and Transcranial Electrical Motor Evoked Potentials*

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Objective: To evaluate whether spinal cord intraoperative monitoring (IOM) with somatosensory and transcranial electrical motor evoked potentials (EPs) predict adverse surgical outcomes.

Methods: A panel of experts reviewed the results of a comprehensive literature search and identified published studies relevant to the clinical question. These studies were classified according to the evidence-based methodology of the American Academy of Neurology. Objective outcomes of postoperative onset of paraparesis, paraplegia, and quadriplegia were used because no randomized or masked studies were available.

Results and Recommendations: Four class I and eight class II studies met inclusion criteria for analysis. The four class I studies and seven of the eight class II studies reached significance in showing that paraparesis, paraplegia, and quadriplegia occurred in the IOM patients with EP changes compared with the IOM group without EP change. All studies were consistent in showing all occurrences of paraparesis, paraplegia, and quadriplegia in the IOM patients with EP changes, with no occurrences of paraparesis, paraplegia, and quadriplegia in patients without EP change. In the class I studies, 16% to 40% of the IOM patients with EP changes developed postoperative-onset paraparesis, paraplegia, or quadriplegia. IOM is established as effective to predict an increased risk of the adverse outcomes of paraparesis, paraplegia, and quadriplegia in spinal surgery (four class I and seven class II studies). Surgeons and other members of the operating team should be alerted to the increased risk of severe adverse neurologic outcomes in patients with important IOM changes (level A).

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INTRODUCTION

Paraparesis, paraplegia, and quadriplegia are complications of spinal surgery and certain surgeries of the aorta. Intraoperative monitoring (IOM) of neural function is used to warn of the risk of surgical complications (Fehlings et al., 2010; Harner et al., 1987; Nuwer et al., 1995, 2008; Radtke et al., 1989; Sala et al., 2006). Anesthesiologists and surgeons are able to intervene in a variety of ways when IOM raises warnings. They can modify surgery by interventions such as reducing the degree of distraction, adjusting retractors, removing or adjusting grafts or hardware, reimplanting or unclamping arteries, placing vascular bypass grafts, minimizing the remaining portion of the surgery, or other actions. Surgeons also have the opportunity to check a wake-up test in some patients.

This evidence-based guideline seeks to answer the clinical question: Does IOM with somatosensory evoked potentials (SEP) and transcranial electrical motor evoked potentials (MEP) predict adverse surgical outcomes?

The panel addressed this question on the basis of subgroup analyses of well-defined patient cohorts, comparing the clinical outcomes of those patients who had evoked potential (EP) changes with those who had no EP changes. The panel recognized an inherent limitation in assessing the specificity of IOM changes when those changes resulted in clinical interventions by anesthesiologists or surgeons.

The panel applied the following reasoning:

1. If it can be shown that adverse IOM changes predict increased risk of adverse clinical outcomes consistently, then all adverse IOM changes may represent possible compromise of the spinal cord that might result in an adverse outcome.
2. Nonobjective outcomes are particularly problematic for assessing the usefulness of IOM because of the potential for diagnostic suspicion bias. Patients with abnormal IOM might be more thoroughly evaluated postoperatively than patients without intraoperative changes. Without masked outcome assessment and a standardized method of case ascertainment, only obvious outcomes (e.g., new paraplegia) are likely to be noticed in patients with normal IOM. Subtle changes, such as sensory changes, could easily be missed.

This bias would tend to exaggerate the usefulness of IOM. Therefore, the only outcomes assessed were new paraparesis, paraplegia, and quadriplegia, as these neurologic deficits are more objective signs than are less-severe deficits.

DESCRIPTION OF THE ANALYTIC PROCESS

Seven physician clinical neurophysiologists were appointed to write this guideline (MN, RE, GG, AL, JL, RM, TY) because of their expertise in spinal IOM. The panel members were appointed jointly by the Therapeutics and Technology Assessment Subcommittee (see appendixes 1 and 2) of the American Academy of Neurology (AAN) and the American Clinical Neurophysiology Society (ACNS). Five additional panel members (DG, CA, VC, GG, CH) served as methodology experts.

A research librarian performed literature searches of MEDLINE and EMBASE databases using the following keywords: “monitoring,” “intraoperative,” “evoked potentials,” “paralysis,” and “intraoperative complications.” Additional articles were found from among the references cited in the reports reviewed. Each article was reviewed independently by at least two panel members. Appendix 3 presents the complete MEDLINE search strategy, and appendix 4 presents the complete EMBASE search strategy.

The panel elected to focus on the two most common current spinal cord IOM techniques. The SEP technique evaluated was ankle-wrist stimulation with neck-scalp recording. The MEP technique evaluated was transcranial electrical MEP with muscle recording.

Minimum size for study inclusion was 100 patients for orthopedic procedures and 20 patients for neurosurgical or cardiothoracic procedures. Different numbers were used because the rates of adverse neurologic outcomes are lower for orthopedic spine procedures compared with neurosurgical and cardiothoracic procedures.

A study was included if it represented a consecutive series of a representative group of patients, preferably prospective; if the IOM followed a protocol established in advance; if the IOM changes were identified in real time, before outcomes were known; and if the clinical outcomes of interest (paraparesis, paraplegia, and quadriplegia) were clearly reported. Reports were reviewed and scored independently by all content expert panelists. Those panelists discussed and resolved by consensus the methodology, results, relevance, and conclusions for a few reports for which there was initial panel discrepancy.

Next, these articles were rated using the AAN four-tiered (class I to class IV) classification of evidence scheme for rating diagnostic studies (appendix 5), and conclusions and recommendations were linked to the strength of the evidence (appendix 6). All articles that were rated class I or class II are listed in Table 1. The primary data evaluated were the results from a comparison of the group without EP changes with the group with EP changes in both the number of cases with new postoperative paraparesis, paraplegia, and quadriplegia and the number without these conditions. Descriptive statistics and Fisher's exact test were used for statistical analysis.

ANALYSIS OF EVIDENCE

The search identified an initial set of 604 reports. Of those, 40 articles met inclusion criteria, but 28 were subsequently excluded because they contained class III or IV data; did not address the outcomes of paraparesis, paraplegia, or quadriplegia; primarily

assessed nerve roots instead of the spinal cord; or substantially relied on techniques beyond the scope of this guideline.

Twelve studies (Costa et al., 2007; Cunningham et al., 1987; Etz et al., 2006; Hilibrand et al., 2004; Jacobs et al., 2000; Khan et al., 2006; Langeloo et al., 2003; Lee et al., 2006; May et al., 1996; Pelosi et al., 2002; Sutter et al., 2007; Weinzierl et al., 2007) provide evidence to assess the role of IOM in the prediction of adverse outcomes (Table 1), four of which were class I (Costa et al., 2007; Cunningham et al., 1987; Sutter et al., 2007; Weinzierl et al., 2007). One class I study (Cunningham et al., 1987) found that no events of paraparesis, paraplegia, or quadriplegia occurred in 17 IOM patients without EP changes, but five of these adverse events occurred in 16 IOM patients with EP changes (31%) (Fisher's exact test, $P = 0.0184$). In the second class I study (Sutter et al., 2007), no events of paraparesis, paraplegia, or quadriplegia occurred in 84 IOM patients without EP changes, but among 25 IOM patients with EP changes, four (16%) had adverse outcomes: one had paraplegia, one had quadriplegia, and two had worsening of preexisting paraparesis (Fisher's exact test, $P = 0.00369$). In the third class I study (Costa et al., 2007), no events of paraparesis, paraplegia, or quadriplegia occurred in 45 IOM patients without EP changes, but two adverse events occurred in five IOM patients with EP changes (40%) (Fisher's exact test, $P = 0.0158$). In the fourth class I study (Weinzierl et al., 2007), no events of paraparesis, paraplegia, or quadriplegia occurred in 49 IOM patients without EP changes, but eight adverse events occurred in 20 IOM patients with EP changes (40%) (Fisher's exact test, $P = 0.000148$). Overall, events of paraparesis, paraplegia, or quadriplegia occurred in 16% to 40% of IOM patients with EP changes, but no adverse outcome events occurred in patients without an EP change.

The other eight articles were class II (Etz et al., 2006; Hilibrand et al., 2004; Jacobs et al., 2000; Khan et al., 2006; Langeloo et al., 2003; Lee et al., 2006; May et al., 1996; Pelosi et al., 2002). No events of paraparesis, paraplegia, or quadriplegia occurred in 108 of 1378 IOM patients without EP changes, whereas these severe adverse outcome events occurred in 1% to 100% in the 1 to 72 IOM patients with EP changes. Seven of these studies reached significance by Fisher's exact test ($P < 0.05$) (Etz et al., 2006; Hilibrand et al., 2004; Jacobs et al., 2000; Khan et al., 2006; Lee et al., 2006; May et al., 1996; Pelosi et al., 2002).

All studies were consistent in that all paraparesis, paraplegia, and quadriplegia events occurred in the IOM patients with EP changes, and none occurred in the IOM patients without EP changes.

This assessment did not undertake to evaluate lesser degrees of motor impairment, which would underestimate the overall adverse outcome rate. It did not assess radiculopathy or similar complications of lumbar fusion.

The one prospective comparative study (Sala et al., 2006) of motor outcomes in patients with IOM *versus* those without IOM was excluded from this assessment because it used graded motor power changes rather than the presence of paraparesis, paraplegia, and quadriplegia as its outcome measure. That cohort study measured motor outcome and the decision to monitor, not whether the monitoring showed intraoperative changes. The study showed a significant positive relationship between decision to monitor and better motor outcome.

CONCLUSION

IOM is established as effective to predict an increased risk of the adverse outcomes of paraparesis, paraplegia, and quadriplegia in spinal surgery (four class I and seven class II studies).

TABLE 1. Summary of Evidence

Reference	Methods: Study design, number of patients, type of surgery, definition of intraoperative EP abnormality	Results	Class of Evidence
Pelosi et al., 2002	126 consecutive spinal orthopedic operations in 97 patients: 79 spinal deformity and 18 other spinal procedures Preoperative deficits 76 intact and 21 with deficits SEP criteria for change: $\geq 50\%$ amplitude decrease or $\geq 10\%$ latency increase MEP criteria for change: (a) during propofol maintenance anesthesia $\geq 50\%$ amplitude drop; (b) otherwise loss of response on 2 consecutive trials	EP monitoring in 124 operations in 95 patients, orthopedic spinal surgery SEP in 122, MEP in 106 EP summary (n = 124) No EP changes: 0/108 Yes EP changes: 1/16 (6.3%) Fisher's exact test: $P = 0.129$ (NS)	II
Hilibrand et al., 2004	Retrospective cohort study reviewing 427 consecutive cervical spine procedures EP criterion of change: $> 60\%$ amplitude decrease for ≥ 10 mins	SEP and MEP monitoring in 427 patients during cervical spine surgery EP summary (n = 427) No EP change: 0/415 Yes EP change: 1/12 (8.3%) Fisher's exact test: $P = 0.0281$	II
Jacobs et al., 2000	210 consecutive patients undergoing thoracoabdominal aortic aneurysm repair CSF drainage used Abnormal MEP: reduction of MEP amplitude to $< 25\%$ of baseline	MEP monitoring during 210 cases of thoracoabdominal aortic aneurysm repair MEP summary (n = 210): No EP change: 0/138 Yes EP change: 5/72 (1.4%) Fisher's exact test: $P = 0.00541$	II
Langeloo et al., 2003	Descriptive historic cohort study 132 patients undergoing corrective surgery for spinal deformity MEP criterion of change: $> 80\%$ decrease in amplitude	MEP monitoring during 132 cases of correction of spinal deformity MEP summary (n = 132): No EP change: 0/116 Yes EP change: 1/16 (6.2%) Fisher's exact test: $P = 0.1212$ (NS) Three additional cases of limited leg weakness, each associated with EP changes, were not included here as paraparesis-paraplegia outcomes	II
Cunningham et al., 1987	33 consecutive patients undergoing surgical procedures for lesions of the descending thoracic or thoracoabdominal aorta prospectively evaluated SEP changes criteria of change: persistent EP loss	SEP monitoring in 33 procedures on descending thoracic or thoracoabdominal aorta SEP summary (n = 33): No EP change: 0/17 Yes EP change: 5/16 (31%) Fisher's exact test: $P = 0.0184$	I
May et al., 1996	191 patients undergoing cervical spine procedures Median SEP monitored in all cases; ulnar and/or posterior tibial SEP in 12 cases SEP criterion for change: $> 50\%$ amplitude reduction in N20, occurring suddenly, persisting, without attributable anesthetic or systemic cause	SEP monitoring of upper-limb responses in 182 procedures SEP summary (n = 182): No EP change: 0/149 Yes EP change: 2/33 (6.0%) Fisher's exact test: $P = 0.032$	II
Khan et al., 2006	Retrospective review for 508 patients who underwent anterior cervical fusion with single-level or multilevel corpectomies EP change criteria: $> 50\%$ amplitude decrease or $> 10\%$ latency increase Masking: Motor outcome determined without knowledge of EP changes	SEP monitoring in 508 cases of cervical spine corpectomy surgery SEP summary (n = 508): No EP change: 0/481 Yes EP change: 1/27 (3.7%) Fisher's exact test: $P = 0.032$	II

TABLE 1. (Continued)

Reference	Methods: Study design, number of patients, type of surgery, definition of intraoperative EP abnormality	Results	Class of Evidence
Lee et al., 2006	Retrospective review of 1445 patients who underwent anterior cervical discectomy or corpectomy 573 single-level ACDFs, 375 multilevel ACDFs, 497 corpectomies Criterion for change: $\geq 60\%$ amplitude decrease persisting at least 10 mins	MEP and SEP monitoring in 1445 cases of anterior cervical surgery EP summary (n = 1445) No EP change: 0/1378 Yes EP change: 1/67 (1.5%) Fisher's exact test: $P=0.0464$	II
Weinzierl et al., 2007	Prospective study of EP intraoperative monitoring in 69 consecutive neurosurgical operations Criterion for EP change: $>50\%$ decrease in amplitude or $>10\%$ latency increase	SEP and MEP monitoring in 69 procedures EP summary (n = 69): No EP change: 0/49 Yes EP change: 8/20 (40%) Fisher's exact test: $P = 0.000148$ Excluded from postop motor deficits in patients with EP changes: 1 transient ataxic gait, 1 transient hypoesthesia	I
Costa et al., 2007	Prospective study of 52 patients during spine surgery for trauma, tumor resection, spondylosis, scoliosis, spinal vascular anomaly, dorsal cysts SEP with MEP monitoring in 38 patients MEP alone in 12 patients Criterion for change: $>50\%$ SEP or $>60\%$ MEP amplitude decrease	SEP and MEP monitoring in 50 cases of spine and spinal cord surgery EP summary (n = 50): No EP change: 0/45 Yes EP change: 2/5 (40%) Fisher's exact test: $P = 0.0158$ Deficits included 1 new paraplegia and 1 worsening of preoperative paraparesis	I
Sutter et al., 2007	Prospective study of 109 consecutive patients for whom monitoring was performed during spinal tumor surgery: 23 intramedullary, 41 intradural-extramedullary, 45 epidural Surgical intervention included systemic steroid, local hypothermia, and other interventions Criteria for EP change: $>50\%$ decrease in amplitude or $>10\%$ latency increase	SEP and MEP monitoring in 109 patients with spinal tumors EP summary (n = 109): No EP change: 0/84 Yes EP change: 4/25 (16%) Fisher's exact test: $P = 0.00369$ Adverse outcomes included 1 paraplegia, 1 quadriplegia, and 2 worsening of preexisting paraparesis	I
Etz et al., 2006	Retrospective review of 100 patients during thoracic and thoracoabdominal aortic aneurysm repair involving serial segmental artery sacrifice Criteria for EP change: $>50\%$ decrease in amplitude or $>10\%$ latency increase	MEP and SEP monitoring in 100 patients during aorta repair involving serial segmental artery sacrifice MEP and SEP summary (n = 100): No EP change: 0/99 Yes EP change: 1/1 (100%) Fisher's exact test: $P = 0.0198$ Excludes one paraplegia with an onset after a postoperative respiratory arrest	II

No EP change, number of new adverse postoperative motor outcomes among the cases with no EP changes/all cases with no changes; Yes EP change, number of new adverse postoperative motor outcomes among the cases with EP changes/all cases with EP changes (percent of adverse outcomes when EPs change); MEP, motor evoked potential; SEP, somatosensory evoked potential; EP, evoked potential; ACDF, anterior cervical discectomy and fusion.

RECOMMENDATION

Surgeons and other members of the operating team should be alerted to the increased risk of severe adverse neurologic outcomes in patients with important IOM changes (level A).

CLINICAL CONTEXT

In practice, after being alerted to IOM changes, the operating team intervenes to attempt to reduce the risk of adverse neurologic outcomes. No studies in humans have directly

measured the efficacy of such interventions. However, multiple controlled studies in animals (Bennett, 1983; Cheng et al., 1984; Coles et al., 1982; Kojima et al., 1979; Laschinger et al., 1982; Nordwall et al., 1979) have demonstrated that intervening after IOM alerts (as opposed to not intervening) reduces the risk of permanent neurologic injury. On this basis, it seems reasonable to assume that such interventions might improve outcomes in humans as well. It is unlikely that controlled human studies designed to determine the efficacy of post-IOM alert interventions will ever be performed.

This analysis did not compare MEP with SEP. The two techniques differ slightly. MEP more directly monitors the motor pathway itself. One technique may change while the other remains stable, or one may change earlier than the other. MEP requires more restrictive anesthesia requirements, causes patient movement, and has less-clear criteria for raising an alarm. SEP can localize an injury or site of ischemia more exactly. The transcranial electrical MEPs are often used intermittently because of movements that occur with the stimulus. Sometimes one technique can be accomplished throughout a case, whereas the other techniques cannot. As a result, it may be most appropriate for the surgeon, anesthesiologist, and neurophysiologic monitoring team to choose which technique(s) are most appropriate for an individual patient. Conducting both techniques together is a reasonable choice for many patients. Neither technique can predict the onset of paraplegia that is delayed until hours or days after the end of surgery. Neither technique should be considered to have perfect predictive ability when no EP change is seen; rare false-negative monitoring has occurred (Nuwer et al., 1995, 2008).

The studies reported here varied somewhat in the criteria used to raise alerts. The specific criteria used are reported in Table 1.

These IOM studies involved a knowledgeable professional clinical neurophysiologist supervisor. These studies support performance of IOM when conducted under the supervision of a clinical neurophysiologist experienced with IOM (American Medical Association, 2006, 2008; Nuwer et al., 1995). IOM conducted by technicians alone or by an automated device is not supported by the studies reported here because these studies did not use that practice model and because there is a lack of identified well-designed published outcome studies demonstrating efficacy with those practice models.

RECOMMENDATIONS FOR FUTURE RESEARCH

1. Pooling of results from a large series of well-monitored patients may permit determination if the low false-negative frequency for MEP IOM in the reported studies is a generalizable observation.
2. A better understanding of anterior spinal artery syndrome may help to reduce further the rate of paraplegia and paresis after spinal surgery.
3. If limitations in the techniques reviewed can be identified explicitly and methods to correct those limitations are developed, then comparisons among different monitoring techniques may be desirable.

AUTHOR CONTRIBUTIONS

Dr. Nuwer: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, statistical analysis. Dr. Emerson: drafting/revising the manuscript, analysis or interpretation of data, statistical analysis. Dr. Galloway: drafting/revising the manuscript, study concept or design, analysis or interpretation of data. Dr. Legatt: drafting/revising the manuscript, analysis or interpretation of data. Dr. Lopez: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, acquisition of data. Dr. Minahan: drafting/revising the manuscript, study concept or design, analysis or interpretation of data. Dr. Yamada: drafting/revising the manuscript, contribution of vital reagents/tools/patients, acquisition of data, statistical analysis. Dr. Goodin: drafting/revising the manuscript. Dr. Armon: drafting/revising the manuscript, study concept or design, analysis or interpretation of data. Dr. Chaudhry: drafting/revising the manuscript, analysis or

interpretation of data. Dr. Gronseth: drafting/revising the manuscript, analysis or interpretation of data, statistical analysis. Dr. Harden: drafting/revising the manuscript, statistical analysis.

DISCLOSURES

Dr. Nuwer estimates that 20% of his clinical effort is spent on intraoperative spinal cord monitoring; serves on a scientific advisory board for Corticare; serves on editorial advisory boards for *Clinical Neurophysiology*, *Journal of Clinical Neurophysiology*, *Practical Neurology*, and *Medical Economics*; receives publishing royalties for *Intraoperative Neurophysiologic Monitoring* (Cambridge University Press, 2010); serves as a consultant for Mattel; serves as Local Medical Director for SleepMed-Digitrace; receives research support from Bristol-Myers Squibb; holds stock in Corticare; and has provided depositions and expert testimony in medicolegal cases. Dr. Emerson has filed patents regarding Dynamic adjustable spatial granularity for EEG display and systems and methods for measuring brain activity; serves as a consultant for Persyst Development Corporation; estimates that 85% of his clinical effort is spent on intraoperative monitoring; and receives research support from Cyberkinetics Neurotechnology Systems Inc., the National Institutes of Health, NYS SCIRB, and the Epilepsy Foundation. Dr. Galloway estimates that 60% of her clinical effort is spent on intraoperative monitoring. Dr. Legatt serves on the editorial board of the *Journal of Clinical Neurophysiology*; holds equity in Entremed, Pfizer Inc, Teva Pharmaceutical Industries Ltd., GlaxoSmithKline, Johnson & Johnson, Schering-Plough Corp., GE Healthcare, and Proctor & Gamble; estimates that 65% of his clinical effort is spent on intraoperative monitoring; and has provided expert testimony in medicolegal cases. Dr. Lopez has received funding for travel from Cadwell Laboratories, Inc.; receives publishing royalties for *Intraoperative Neurophysiologic Monitoring* (Cambridge University Press, 2010); estimates that 60% of his clinical effort is spent on intraoperative monitoring; and has provided expert testimony in medicolegal cases. Dr. Minahan estimates that 60% of his clinical effort is spent on intraoperative monitoring and has provided expert testimony in medicolegal cases. Dr. Yamada estimates that 10% of his clinical effort is spent on intraoperative monitoring; serves on the editorial board of the *Journal of Clinical Neurophysiology*; and receives publishing royalties for *Practical Guide for Clinical Neurophysiologic Testing: EEG* (Wolters Kluwer/Lippincott Williams & Wilkins, 2010) and *Practical Guide for Clinical Neurophysiologic Testing: EP, LTM, IOM, PSFG and NCS* (Wolters Kluwer/Lippincott Williams & Wilkins, 2011). Dr. Goodin has served on scientific advisory boards for Bayer Schering Pharma and Merck Serono; has received funding for travel and honoraria for speaking and consulting from Bayer Schering Pharma, Teva Pharmaceutical Industries Ltd., Novartis, and Merck Serono; has received speaker honoraria from Bayer Schering Pharma; has received research support from Bayer Schering Pharma and Novartis; has served as an expert witness in medicolegal cases; and holds equity interest in Teva Pharmaceutical Industries Ltd. and Biogen Idec. Dr. Armon has served on a scientific advisory board for Avanir Pharmaceuticals; serves on the editorial boards of *Neurology* and *emedicine Neurology*; has received honoraria from Medscape Today; receives publishing royalties from emedicine.com for updating electronic chapters and from UpToDate; has received research support from Avanir Pharmaceuticals, Schwartz Biomedical, LLC, the National Institutes of Health, and the Swiss PFO-Consortium; and has served as an expert witness in medicolegal cases. Dr. Chaudhry serves on the editorial board of *Neurologist*; is an inventor on patent(s) regarding Total Neuropathy Score (TNS)—a score for evaluating

peripheral neuropathies, for which he receives technology royalties from Abbott, Johnson & Johnson, and Sanofi-Aventis; receives publishing royalties for *Harrison's Principles of Internal Medicine, 17th edition* (McGraw Hill Companies, Inc., 2008); estimates that 40% of his clinical effort is spent on nerve conduction studies; has given expert testimony for the Department of Health and Human Services Vaccine Injury Compensation program; and receives research support from the Neuropathy Association and Nutricia. Dr. Gronseth serves as an editorial advisory board member of *Neurology Now*; serves on a speakers' bureau for Boehringer Ingelheim; and receives honoraria from Boehringer Ingelheim and the American Academy of Neurology. Dr. Harden serves on a scientific advisory board for Upsher-Smith Laboratories, Inc.; serves on speakers' bureaus for and has received speaker honoraria from Glaxo-SmithKline, UCB, and Lundbeck, Inc.; serves on the editorial boards of *Epilepsy Currents* and *Epilepsy Research*; receives publishing royalties from UpToDate, Inc.; and receives research support from Forest Laboratories, Inc., the Epilepsy Foundation, and the Milken Family Foundation.

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APPENDIX 1

Therapeutics and Technology Assessment Subcommittee Members 2009-2011

Janis M. Miyasaki, MD, MEd, FAAN (Co-Chair); Cynthia L. Harden, MD (Co-Chair); Richard M. Camicioli, MD; Terry D. Fife, MD, FAAN; Jonathan Hosey, MD, FAAN (Ex-Officio); Cheryl Jaigobin, MD; Barbara S. Koppel, MD, FAAN; Jason Lazarou, MD; Alexander Rae-Grant, MD; William H. Theodore, MD, FAAN.

APPENDIX 2

Mission Statement of the Therapeutics and Technology Assessment Subcommittee

The Therapeutics and Technology Assessment Subcommittee provides rigorous, relevant, timely evidence-based reviews of new, emerging, or established therapeutic agents and technologies in the field of neurology.

APPENDIX 3

Complete MEDLINE Search Strategy

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Database: Ovid MEDLINE(R) <1996 to April Week 3 2008>
Search Strategy

1. Monitoring, Intraoperative/ (7608)
2. exp Spinal Cord/ (22700)
3. 1 and 2 (254)
4. spinal cord monitor:.mp. (94)

5. Evoked Potentials, Motor/ (3266)
6. (motor adj2 evoked adj2 response\$1).mp. (132)
7. Evoked Potentials, Somatosensory/ (3871)
8. (somatosensory adj2 evoked adj2 response\$1).mp. (114)
9. (intraoperative adj2 neurophysiology).tw. (15)
10. (intraoperative adj2 somatosensory adj2 monitoring).tw. (3)
11. (sep adj2 monitoring).tw. (62)
12. Scoliosis/ (3578)
13. exp Spinal Cord Neoplasms/ (2248)
14. (spinal adj2 tumor\$1).tw. (868)
15. Spinal Fractures/ (4738)
16. exp Spinal Cord Injuries/ (12944)
17. Arteriovenous Malformations/ (2152)
18. (spinal adj2 avm\$1).tw. (55)
19. scoliosis.tw. (3911)
20. Aortic Coarctation/ (1738)
21. exp Neurosurgical Procedures/ (41808)
22. Operating Rooms/ (2875)
23. exp surgical procedures, operative/ (757407)
24. (21 or 22 or 23) and 2 (3016)
25. (aortic adj2 coarctation).tw. (919)
26. 2 and 17 (148)
27. or/1,3,9-10 (7613)
28. or/12-16,18-20,24-26 (28543)
29. 27 and 28 (429)
30. or/4-8,11 (6853)
31. or/12-16,18-20,25-26 (26249)
32. or/21-23 (759245)
33. 30 and 31 and 32 (221)
34. 29 or 33 (507)
35. limit 34 to (humans and yr="2005 - 2008" and (case reports or clinical trial or comparative study or controlled clinical trial or evaluation studies or journal article or meta analysis or multicenter study or randomized controlled trial or research support, nih, extramural or research support, nih, intramural or research support, non us gov't or research support, us gov't, non phs or research support, us gov't, phs or twin study or validation studies)) (137)
36. limit 34 to (humans and yr="2005 - 2008" and (clinical conference or comment or congresses or editorial or letter or news or practice guideline or "review")) (32)
37. 35 not 36 (109)

APPENDIX 4

Complete EMBASE Search Strategy

While the staff of HealthSearch makes every effort to ensure that the information gathered is accurate and up-to-date, HealthSearch disclaims any warranties regarding the accuracy or completeness of the information or its fitness for a particular purpose. HealthSearch provides information from public sources both in electronic and print formats and does not guarantee its accuracy, completeness, or reliability. The information provided is only for the use of the Client, and no liability is accepted by HealthSearch to third parties.

Database: EMBASE <1980 to 2008 Week 17>
Search Strategy

1. patient monitoring/ (38294)
2. Spinal Cord/ (23301)
3. and/1-2 (94)
4. (spinal adj2 cord adj2 monitor:).mp. (395)

5. neurophysiology/ (11456)
6. and/1,5 (227)
7. (intraoperative adj2 neurophysiology).tw. (15)
8. (intraoperative adj2 somatosensory adj2 monitoring).tw. (6)
9. 1 or 3 or 4 or 6 or 7 or 8 (38561)
10. (sep adj2 monitoring).tw. (145)
11. evoked muscle response/ (3373)
12. (motor adj2 evoked adj2 potential\$1).mp. (2433)
13. exp evoked somatosensory response/ (27328)
14. (somatosensory adj2 evoked adj2 potential\$1).mp. (5097)
15. (motor adj2 evoked adj2 response\$1).tw. (230)
16. (somatosensory adj2 evoked adj2 response\$1).tw. (391)
17. 10 or 11 or 12 or 13 or 14 or 15 or 16 (31104)
18. exp Scoliosis/ (8532)
19. exp Spinal Cord Tumor/ (3992)
20. (spinal adj2 tumor\$1).tw. (1531)
21. scoliosis.tw. (6971)
22. exp Spine Fracture/ (9466)
23. (spin\$2 adj2 fracture\$1).tw. (1911)
24. (spin\$2 adj2 arteriovenous malformation\$1).tw. (274)
25. spin\$2 adj2 avm\$1).tw. (116)
26. exp Spinal Cord Injury/ (23472)
27. Aorta Coarctation/ (4065)
28. (aort\$2 adj2 coarctation).tw. (1607)
29. Arteriovenous Malformation/ (5510)
30. 2 and 29 (115)
31. 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 30 (50565)
32. neurosurgery/ (17898)
33. exp spinal cord surgery/ (12343)
34. dorsal rhizotomy/ (557)
35. 33 not 34 (11786)
36. exp spine surgery/ (23516)
37. exp Surgical Technique/ (467261)
38. operating room/ (5763)
39. 32 or 37 or 38 (484754)
40. 2 and 39 (684)
41. 35 or 36 or 40 (26474)
42. 9 and 31 (656)
43. 17 and 31 and 41 (281)
44. 42 or 43 (801)
45. limit 44 to (human and yr="2005 - 2008" and journal) (227)
46. limit 44 to (human and yr="2005 - 2008" and (book or conference paper or editorial or erratum or letter or note or proceeding or report or "review" or short survey)) (105)
47. 45 not 46 (122)

APPENDIX 5

Classification of Evidence for Diagnostic Accuracy

1. **Class I:** A cohort study with prospective data collection of a broad spectrum of persons with the suspected condition, using an acceptable reference standard for case definition. The diagnostic test is objective or performed and interpreted without knowledge of the patient's clinical status. Study results allow calculation of measures of diagnostic accuracy.
2. **Class II:** A case control study of a broad spectrum of persons with the condition established by an acceptable reference standard compared to a broad spectrum of controls or a cohort study where a broad spectrum of persons with the suspected condition where the data was collected

retrospectively. The diagnostic test is objective or performed and interpreted without knowledge of disease status. Study results allow calculation of measures of diagnostic accuracy.

3. **Class III:** A case control study or cohort study where either persons with the condition or controls are of a narrow spectrum. The condition is established by an acceptable reference standard. The reference standard and diagnostic test are objective or performed and interpreted by different observers. Study results allow calculation of measures of diagnostic accuracy.
4. **Class IV:** Studies not meeting class I, II, or III criteria, including consensus, expert opinion, or a case report.

APPENDIX 6

Classification of Recommendations

1. A = Established as effective, ineffective, or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent class I studies. [In exceptional cases, one convincing class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large {relative rate improved outcome >5, and the lower limit of the confidence interval is >2}].)
2. B = Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one class I study or two consistent class II studies.)
3. C = Possibly effective, ineffective, or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one class II study or two consistent class III studies.)
4. U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

Disclaimer

This statement is provided as an educational service of the AAN and ACNS. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods for care of a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodology. The AAN and ACNS recognize that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved. The clinical context section is made available to place the evidence-based guideline into perspective with current practice habits and challenges. No formal practice recommendation should be inferred.

Conflict of Interest

The AAN and ACNS are committed to producing independent, critical, and truthful clinical practice guidelines (CPGs). Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this CPG. To the

extent possible, the AAN and ACNS keep separate those who have a financial stake in the success or failure of the products appraised in the CPG and the developers of the guidelines. Conflicts of interest forms were obtained from all authors and reviewed by an oversight committee before project inception. AAN and ACNS limit the participation of authors with substantial conflict of interest. They forbid commercial participation in, or funding of, guidelines projects. Drafts of the guideline have been reviewed by at least three committees of the AAN and ACNS: a network of neurologists, *Neurology* peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at www.aan.com.

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