Monitoring of Spinal Cord Perfusion Pressure in Acute Spinal Cord Injury: Initial Findings of the Injured Spinal Cord Pressure Evaluation Study*

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Objectives: To develop a technique for continuously monitoring intraspinal pressure at the injury site (intraspinal pressure) after traumatic spinal cord injury.

Design: A pressure probe was placed subdurally at the injury site in 18 patients who had isolated severe traumatic spinal cord injury (American Spinal Injuries Association grades A–C). Intraspinal pressure monitoring started within 72 hours of the injury and continued for up to a week. In four patients, additional probes were inserted to simultaneously monitor subdural pressure below the injury and extradural pressure. Blood pressure was recorded from a radial artery catheter kept at the same horizontal level as the injured segment of the spinal cord. We determined the effect of various maneuvers on spinal cord perfusion pressure and spinal cord function and assessed using a limb motor score and motor-evoked potentials.

Setting: Neurosurgery and neuro-ICU covering a 3 million population in London.

Subjects: Patients with severe traumatic spinal cord injury. Control subjects without spinal cord injury (to monitor spinal cerebrospinal fluid signal and motor evoked potentials).

Interventions: Insertion of subdural spinal pressure probe.

Measurements and Main Results: There were no procedure-related complications. Intraspinal pressure at the injury site was higher than subdural pressure below the injury or extradural pressure. Average intraspinal pressure from the 18 patients with traumatic spinal cord injury was significantly higher than average intraspinal pressure from 12 subjects without traumatic spinal cord injury. Change in arterial P_{CO_2}, change in sevoflurane dose, and mannitol administration had no significant effect on intraspinal pressure or spinal cord perfusion pressure. Increase in inotrope dose significantly increased spinal cord perfusion pressure. Bony realignment and laminectomy did not effectively lower intraspinal pressure. Laminectomy was potentially detrimental by exposing the swollen spinal cord to compression forces applied to the skin. By intervening to increase spinal cord perfusion pressure, we could increase the amplitude of motor-evoked potentials recorded from below or just above the injury level in nine of nine patients with traumatic spinal cord injury. In two of two patients with American Spinal Injuries Association grade C traumatic spinal cord injury, higher spinal cord perfusion pressure correlated with increased limb motor score.

Conclusions: Our findings provide proof-of-principle that subdural intraspinal pressure at the injury site can be measured safely after traumatic spinal cord injury. (*Crit Care Med* 2014; 42:646–655)

Key Words: autoregulation; perfusion pressure; pressure reactivity index; spinal cord; trauma; vasoreactivity

***See also p. 749.**

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccmjournal).

Supported, in part, by the U.K. Spinal Cord Injury Research Network, Neurosciences Research Foundation, London Deanery, Royal College of Surgeons of England, and National Institute of Health Research (Neuroscience Theme) in Cambridge.

Ms. Werndle's institution received grant support from the Royal College of Surgeons of England and the Neurosciences Research Foundation (Hoseham fellowship). Dr. Saadoun is funded by the Guthy Jackson Charitable Foundation. Mr. Phang received support for article research from the Spinal Cord Injury Research Network, Neurosciences Research Foundation, and London Deanery. ICM+ (http://www.neurosurg.cam.ac.uk/icmplus) is licensed by the University of Cambridge (Cambridge Enterprise). Prof. M. Czosnyka received royalties from ICM+ software (part of the licensing fee). Prof. M. Czosnyka's institutions received grant support from NIHR (Neurosciences Theme) in Cambridge. Dr. Smielewski received royalties from ICM+ software (part of the licensing fee). His institutions received grant support from National Institute of Health Research (Neurosciences Theme) in Cambridge. Prof. Papadopoulos is funded by the Guthy Jackson Charitable Foundation. His institution received grant support from Neurosciences Research Foundation, U.K. Spinal Cord Injuries Research Network, London Deanery, and Royal College of Surgeons of England. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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DOI: 10.1097/CCM.0000000000000028

In the United States, about 40 people per million sustain a traumatic spinal cord injury (TSCI) each year rendering them paralyzed or wheelchair bound (1). The annual cost of care for patients with TSCI, excluding indirect costs such as loss of wages, was estimated at $19 billion in 2011 (2).

In developed countries, the management of acute TSCI is variable (3–5). Although many surgeons aim to realign and fix the spine as soon as possible to restore spinal cord perfusion thus preventing secondary damage, there are no well-designed prospective studies with appropriately matched controls showing that early surgical decompression improves outcome. During surgery, many anesthesiologists do not measure arterial blood pressure (ABP) invasively. The optimal levels of mean arterial pressure (MAP) and $Paco_2$ are unknown. The American Association of Neurological Surgeons (AANS) concluded that there is insufficient evidence to support treatment standards but recommended MAP of 85–90 mm Hg for 5–7 days after TSCI (6), whereas the U.K. National Spinal Cord Injury Strategy Board recommended systolic ABP of 90–100 mm Hg (7) as a treatment option.

In contrast to the variable management of severe TSCI, the management of severe traumatic brain injury (TBI) is more standardized in developed countries (8). Patients with TBI are urgently transferred to a neuro-ICU for intracranial pressure (ICP) and MAP monitoring. ICP is measured by inserting a probe intraparenchymally (and occasionally intraventricularly or subdurally). ICP is the same in the three compartments, and changes in ICP are reflected simultaneously and equally in all three compartments (9). Treatment for TBI aims to optimize cerebral perfusion pressure (CPP = MAP – ICP) with normocapnea, drugs (inotropes, anesthetics, and osmotic agents), or surgery (decompressive craniectomy), to avoid secondary brain damage (8). Low CPP (< 60 mm Hg) and high ICP (> 20 mm Hg) are associated with worse outcome after TBI (10, 11). It has been suggested that the outcome of patients with severe TBI who have ICP-directed management is comparable with those whose management is guided by imaging and clinical examination alone (12). In TSCI, spinal cord imaging may be uninterpretable because of the spinal instrumentation, and sensory-motor examination may be difficult to perform because of intubation/sedation. It may thus be difficult to use imaging and clinical examination for guiding TSCI management.

Currently, there is no method in clinical use for measuring intraspinal pressure (ISP) after TSCI analogous to measuring ICP after TBI. The ability to measure ISP would be a major advance by allowing the spinal cord perfusion pressure (SCPP = MAP – ISP) to be monitored and, if possible, optimized, potentially reducing secondary spinal cord damage. It might also elucidate the effect of interventions (laminectomy, altered $Paco_2$ or ABP, mannitol, and anesthetic) on spinal cord perfusion. Here, we report the initial findings of the Injured Spinal Cord Pressure Evaluation study, which aims to develop a novel technique for continuously monitoring ISP at the injury site after TSCI.

MATERIALS AND METHODS

Institutional Review Board approvals

Approvals were obtained from the St. George's Joint Research Office and the South London, Maudsley, and the Institute of Psychiatry Local Research Ethics Committee (No. 10/H0807/23).

Patients With TSCI

We recruited 18- to 70-year-old patients with severe TSCI (American Spinal Injury Association [ASIA] grades A–C). Exclusion criteria were inability to consent and other major injuries or significant comorbidities. ISP monitoring was started within 72 hours of the TSCI and continued for up to a week. For details, see **Supplemental Methods** (Supplemental Digital Content 1, http://links.lww.com/CCM/A759).

Control Subjects

We monitored the spinal cerebrospinal fluid (CSF) signal in subjects admitted for lumbar infusion studies for suspected normal pressure hydrocephalus who had normal CSF dynamics. We monitored motor-evoked potential (MEPs) at different MAPs in patients who were admitted for surgery for cervical or lumbar radiculopathy.

Surgical Technique

A Codman probe was placed subdurally following laminectomy or small laminotomy (**Fig. 1**). After reducing and fixing the spinal fracture and inserting metalwork to stabilize the spine, a 14-gauge introducer was used to tunnel the Codman probe through the skin into the wound (**Supplemental Video 1**, Supplemental Digital Content 2, http://links.lww.com/CCM/A760). We used a 21-gauge needle bent at 90° to perforate the dura one level below the injury. To monitor ISP, the Codman probe was calibrated and advanced through the dural hole until the probe tip was at the site of maximal spinal cord swelling according to the MRI scan (**Supplemental Video 2**, Supplemental Digital Content 3, http://links.lww.com/CCM/A761). In four patients, a second probe was inserted subdurally below the injury or extradurally. The probes were secured to the skin with silk sutures and a tightening stitch around the exit site to prevent CSF leak. ABP was recorded from a radial artery catheter kept at the same horizontal level as the injured segment of the spinal cord. The probes were connected to a Codman ICP box linked via a ML 221 amplifier to a PowerLab running LabChart v. 7.3.3 (AD Instruments, Oxford, UK). ISP and ABP data were simultaneously captured by LabChart at 100 Hz for up to a week. Satisfactory probe position was confirmed with CT before data collection. Data were retrospectively analyzed using ICM+ (http://www.neurosurg.cam.ac.uk/icmplus) with the investigators blinded to clinical details.

ISP Waveform Analysis

The essential outputs of our monitoring technique are ISP, MAP (monitored), SCPP, spinal pressure reactivity index (sPRx), and spinal reserve capacity index (sRAP) (calculated). ISP and MAP were simultaneously recorded for up to a week. SCPP was

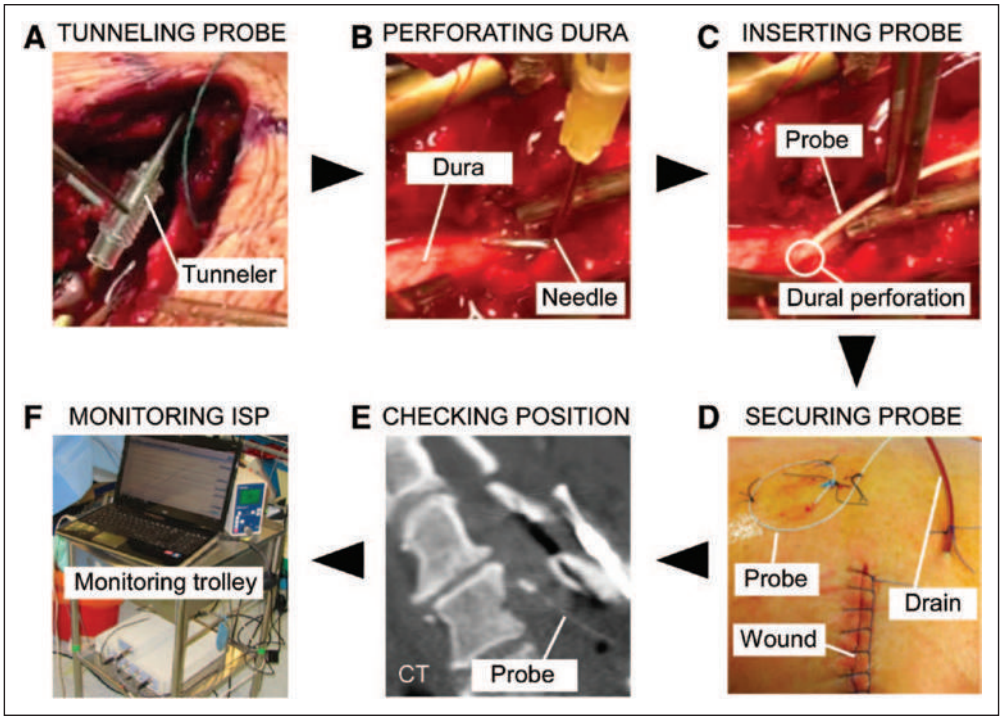

Figure 1. Intraspinal pressure (ISP) monitoring technique. **A**, A tunneler pulls the Codman pressure probe through the skin into the wound. **B**, The dura is perforated with a 90° bent needle one spinal level below the injury. **C**, The Codman probe is inserted through the dural perforation. **D**, The surgical incision is closed and the probe secured to skin using silk sutures. **E**, CT checks probe position. **F**, Data monitoring trolley kept behind the patient bed in ICU. Trolley carries the laptop, Codman intracranial pressure box, and Powerlab system.

computed as MAP – ISP. sPRx, a measure of spinal cord vascular reactivity, is the running correlation coefficient between mean ISP and ABP calculated over a 5-minute period. If the spinal cord vasculature reacts normally, sPRx is less than or equal to 0. If autoregulation is impaired, sPRx is greater than 0. sRAP, a measure of compensatory reserve, is the running correlation coefficient between ISP amplitude and mean ISP. With good compensatory reserve, sRAP is 0. Without compensatory reserve, sRAP approaches +1. sPRx and sRAP are the respective equivalents of pressure reactivity index (PRx) and reserve capacity index (RAP) defined for cerebral vascular reactivity (11). We also determined the time-dependent components of ISP (regular slow, respiratory, and pulse waves) as defined for ICP (11).

MEPs

MEPs were recorded after transcranial electrical stimulation using NVJJB/M5 (NuVAsive, Elstree, UK) or NIM-Eclipse (Medtronic, Watford, UK). We stimulated using a train of five pulses (each pulse 60 µs, 400 Hz, amplitude ≤ 600 V) and recorded from preselected muscles at two SCPPs per patient with three repeats per SCPP. For each MEP, we compared the average peak-to-peak amplitudes at low versus high SCPP. Confounding variables (anesthetic dose, body temperature, patient and electrode position, and stimulus characteristics) were kept constant for each patient. We changed SCPP using noradrenaline or metaraminol. In control experiments, we tested the effect of altering ABP (with metaraminol) on MEPs in subjects without TSCI.

Attempts to Reduce ISP and Increase SCPP

We assessed the response of ISP and SCPP to the following, chosen for their established effect on ICP and CPP in patients with TBI (8): mannitol (100 mL, 20% IV), altered ventilation (change in $Paco_2$ ≥ 7.5 torr [1 kPa] from baseline), sevoflurane (increasing minimum alveolar concentration [MAC] from 1.0 to 1.5 with stable $Paco_2$), and inotropes (noradrenaline or metaraminol to increase MAP > 15 mm Hg). We also assessed the effect of laminectomy at the injury site.

Indocyanine Green Video Angiography

After exposing the dura, we injected indocyanine green (ICG)-Pulsion (10 mg in 10 mL water IV bolus; Pulsion, Hounslow, UK) and recorded using a Leica M525 OH4 microscope (Leica, Milton Keynes, UK) with FL800 optics (excitation 805 nm, recording 835 nm) and a Sony 3CCD camera (Sony, Weybridge, UK) at 752 × 582 pixel resolution. We waited ~30 minutes (for the ICG to be eliminated and for the SCPP to be changed), injected another ICG bolus, and re-recorded. Videos were converted to stacks (256 grayscale jpg images 100 ms apart) using Free Studio Converter v. 5.0.10 (http://dvdvideosoft.com). Image J64 1.5S (http://rsbweb.nih.gov) was used to subtract background (each image minus the first image), amplify images (each image added to itself 4×), synchronize videos (playback started when ICG is about to enter the spinal cord), and color-code (16-color heat map). In six patients, we compared ICG fluorescence of the injured spinal cord at low versus high SCPP.

Limb Motor Score

The neuro-ICU nursing chart records the best motor score of each limb 4–6 hourly as 0 (no movement to command or peripheral pain), 1 (movement to peripheral pain but not to command), 2 (voluntary movement but not antigravity), 3 (weak voluntary movement against gravity), and 4 (normal power). The nurse recording the motor score was unaware of our ISP and SCPP recordings. For ASIA C patients with cervical TSCI, we plotted the total limb score (0–16) versus the corresponding SCPP.

Statistics

Two groups were compared with two-tailed Student *t* test. One-sample *t* test was used to test the effect of treatments on ISP

and SCPP and the effect of changing SCPP on MEP. Pearson coefficient and Spearman rank order were used to determine correlation between variables. For further details, see Supplemental Methods (Supplemental Digital Content 1, http://links.lww.com/CCM/A759).

RESULTS

Patients With TSCI

Eighteen consecutive patients with TSCI were recruited between October 2010 and April 2013. All except one patient who were approached consented for the study. Eleven of 18 patients with TSCI (61.1%) were men. ASIA scores were A in 11 of 18 patients with TSCI (61.1%), B in three of 18 (16.7%), and C in four of 18 (22.2%). Six of 18 patients with TSCI (33.3%) were recruited within 24 hours, six of 18 (33.3%) at 24–48 hours, and six of 18 (33.3%) at 48–72 hours. **Table 1** summarizes the details of the recruited patients with TSCI.

Control Patients

Spinal CSF signal was monitored in 12 control subjects (mean age 58 yr, age range 18–86) and MEPs were monitored in four

TABLE 1. Details of the Patients With Traumatic Spinal Cord Injury at Admission

Age	Sex	Cause	Injury	American Spinal Injury Association Score	Fixation	Laminectomies	Hours Between Spinal Cord Injury and Operation
28	Male	Fall	T5, 6 burst fractures	A	T3, 4, 7, 8 pedicle screws	Yes	52
61	Female	Fall	C6/7 bifacet dislocation	B	C6, 7 lateral mass screws	No	68
68	Female	Fall	C6/7 unifacet dislocation	B	C6, 7 lateral mass screws	No	44
44	Male	RTA	T3 burst fracture	A	T1, 2, 4, 5 pedicle screws	Yes	10
32	Male	RTA	C6/7 bifacet fracture dislocation	A	C6, 7 lateral mass screws	Yes	43
35	Female	Fall	C6, 7 burst fractures	A	C5–7 lateral mass screws, C6 corpectomy/graft/plate/screws	Yes	15
38	Male	Fall	C5 burst fracture	A	C4–6 lateral mass screws, C5 corpectomy/graft/plate/screws	No	28
64	Female	Fall	C5/6 discoligamentous injury	C	No fusion	Yes	53
49	Female	Fall	C5/6 unifacet dislocation	C	C5, 6 lateral mass screws	No	13
54	Male	RTA	T12 burst fracture	C	T10, 11, L1, 2 pedicle screws	No	40
60	Male	Fall	C6/7 bifacet fracture dislocation	A	C6, 7 lateral mass screws	Yes	56
40	Male	Fall	T11/12 fracture disclocation	A	T9-L2 pedicle screws	Yes	72
65	Male	RTA	C4/5 discoligamentous injury	C	C4/5 discectomy/fusion; C4, 5 lateral mass screws	Yes	38
54	Female	Fall	C6/7 bifacet fracture dislocation	A	C5–7 lateral mass screws, C6/7 discectomy/graft/plate/screws	Yes	58
34	Male	Fall	C5, 6 burst fractures	A	C2–7 lateral mass screws, C5, 6 corpectomies/graft/plate/screws	No	18
19	Male	RTA	T6/7 fracture dislocation	A	T4, 5, 8, 9 pedicle screws	Yes	36
32	Male	RTA	C4/5 unifacet dislocation	B	C4, 5 lateral mass screws	No	12
36	Female	Fall	C6/7 bifacet fracture dislocation	A	C6/7 lateral mass screws	Yes	21

RTA = road traffic accident.

control patients (mean age 49 yr, age range 45–53), who had no spinal cord pathology.

Surgery and Complications

Five of 18 patients with TSCI (27.8%) had anterior and posterior cervical fusion, seven of 18 (38.9%) had posterior cervical fusion only, and five of 18 (27.8%) had posterior thoracic fusion (Table 1). Eleven of 18 patients with TSCI (61.1%) had laminectomy. The probe insertion technique is described in the *Materials and Methods* section, Figure 1, Supplemental Video 1 (Supplemental Digital Content 2, http://links.lww.com/CCM/A760), and Supplemental Video 2 (Supplemental Digital Content 3, http://links.lww.com/CCM/A761). There were no complications related to ISP monitoring, such as wound infection, meningitis, CSF leak, pseudomeningocele, spinal cord or subdural hematoma (assessed by MRI), or deterioration in ASIA score (before probe insertion versus after probe removal).

ISP Signal Characteristics

The 18 patients with TSCI had no CSF MRI signal between the swollen spinal cord and dura at the injury site. Based on this, we defined four compartments, three subdural (CSF above the injury, CSF below the injury, and the injury site where ISP is measured), and one extradural (**Fig. 2*A***). ISP at the injury site was higher than pressure simultaneously recorded from the CSF compartment below (two patients) or extradurally (two patients) (**Fig. 2*B***). This finding suggests that the pressure exerted by the swollen injured cord against the dura (ISP) is different from the CSF and extradural pressures.

ISP waveforms comprised three peaks (**Fig. 2*C***), corresponding to arterial pulsation, intracranial compliance, and aortic valve closure analogous to ICP waveforms (11, 13, 14). The ISP signal had slow (0.05–0.0055 Hz), respiratory (0.2–0.3 Hz), and pulse waves. The first pulse wave harmonic corresponds to the heart rate (~1 Hz). Compared with subjects that have normal CSF circulation, the patients with TSCI had significantly higher mean ISP and more prominent slow, respiratory, and pulse waves (**Fig. 2*D***), which also suggests that ISP is not a CSF pressure.

ISP and SCPP Profiles

ISP was initially high (> 20 mm Hg) and then normalized (6 of 18, 33.3% patients), initially normal and then high (4 of 18, 22.2%), high throughout (4 of 18, 22.2%), or normal throughout (4 of 18, 22.2%) (**Fig. 3*A***). **Figure 3**, ***B*** and ***C*** shows the ISP and SCPP from all patients with TSCI. ICU doctors were unaware of ISP; their ABP management aimed to maintain peripheral organ perfusion. After TBI, CPP less than 60 mm Hg causes brain ischemia and is associated with fatal outcome (10, 11). During the first 3 days after TSCI, 33.3–60.0% patients had mean daily SCPP less than 60 mm Hg with MAP more than 65 mm Hg, which is adequate for renal perfusion in young healthy subjects (15). SCPP was less than 60 mm Hg for 16.5% of the time that MAP was within the AANS recommendations (85–90 mm Hg).

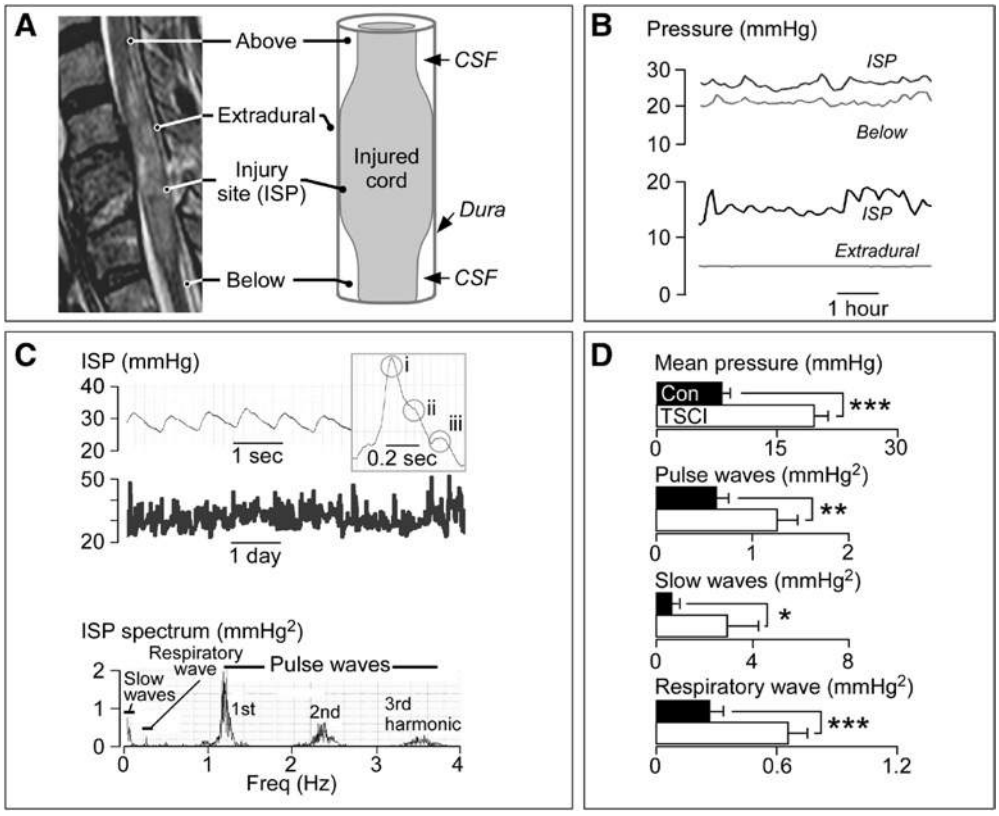

Figure 2. Intraspinal pressure (ISP) signal characteristics. **A**, MR scan (*left*) and corresponding schematic showing four compartments, three intradural (cerebrospinal fluid [CSF] above, CSF below, and injury site), and one extradural (right). **B**, Simultaneous pressure recordings from injury site (ISP) versus below and ISP versus extradural in a laminectomized patient. C, Typical ISP recording over seconds (*upper*) and days (*middle*). Inset shows peaks for i) arterial pulsation, ii) intracranial compliance, and iii) aortic valve closure. ISP frequency spectrum (*lower*) with slow (0.0055–0.05 Hz), respiratory (~0.2 Hz), and pulse (~1 Hz) waves. **D**, Comparison of ISP signal characteristics (mean pressure, pulse wave, slow waves, and respiratory wave) in 18 patients with traumatic spinal cord injury (TSCI) versus 12 control subjects. Mean ± SE, *p* value of less than 0.05*, 0.01**, and 0.001***.

Reserve Capacity (sRAP) and Autoregulation (sPRx)

Figure 4*A* shows a positive correlation between change in ISP amplitude and mean ISP in a patient with impaired compensatory reserve. Data from all 18 patients with TSCI are summarized in **Figure 4** (*right*). Figure 4 shows the relationship between sRAP and ISP and

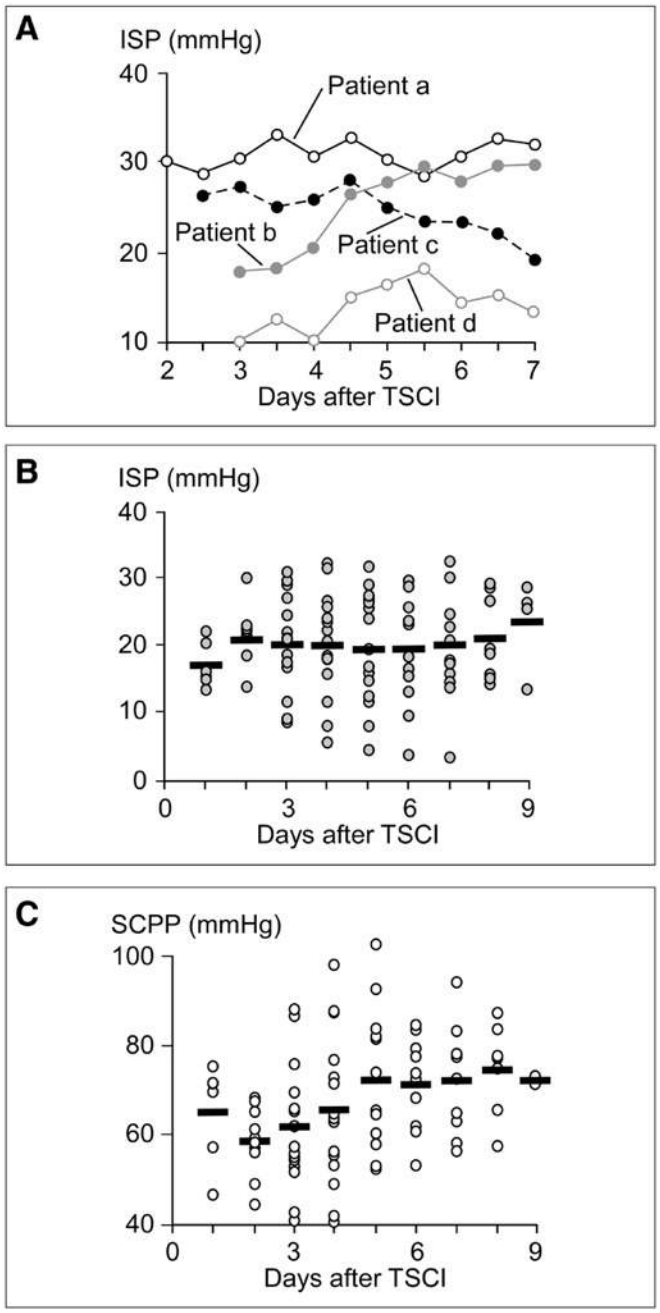

Figure 3. Intraspinal pressure (ISP) and spinal cord perfusion pressure (SCPP) profiles. **A**, Patterns of ISP elevation: high throughout (patient a), initially normal then high (patient b), initially high then normal (patient c), and normal throughout (patient d). Points represent ISP values averaged over 12 hr. **B**, ISP versus days and SCPP versus days (**C**) since traumatic spinal cord injury (TSCI) ($n = 18$). *Points* represent ISP values for each patient averaged over 24 hr. *Lines* indicate means.

between sPRx and ISP. At low ISP, sRAP is ~0 (good compensatory reserve). As ISP increases more than 10 mm Hg, sRAP increases toward +1 (exhausted compensatory reserve). As ISP increases more than 15–20 mm Hg, sPRx increases toward +1 (progressive loss of autoregulation). Figure 4*c* shows the relationship of sRAP versus SCPP and sPRx versus SCPP. As SCPP decreases (spinal cord becomes more ischemic and swollen), sRAP rises indicating progressive loss of compensatory reserve. The relationship between SCPP and sPRx is U-shaped. The optimum SCPP ($SCPP_{opt}$) is ~90 mm Hg. Autoregulation becomes impaired as SCPP decreases below $SCPP_{opt}$ (spinal cord ischemia) and above $SCPP_{opt}$ (spinal cord hyperperfusion). These findings are remarkably similar to trends seen with RAP and PRx versus ICP and CPP in TBI (11, 13, 16), including the U-shaped relationship with PRx versus CPP (17).

Attempts to Alter ISP and SCPP

Change in $Paco_2$ (≥ 7.5 torr [1 kPa]), 100 mL 20% mannitol IV bolus, and increased sevoflurane (from 1.0 to 1.5 MAC) caused no significant change in ISP or SCPP, whereas inotropes increased MAP and ISP with a net increase in SCPP (**Fig. 5**).

Effect of Laminectomy on ISP and SCPP

In patients who had laminectomy, compressing the skin incision caused a significant rise in ISP (up to 60 mm Hg) with a corresponding decrease in SCPP, but in patients without laminectomy, skin compression did not cause changes in ISP or SCPP (**Fig. 6*A***). Although laminectomy adequately decompressed the spinal (bony) canal, there was no CSF between the swollen spinal cord and the surrounding dura on MRI. In nine of 11 laminectomized patients (81.8%), ISP was high (> 20 mm Hg for ≥ 12 hr) and SCPP was low (< 60 mm Hg for ≥ 12 hr). **Figure 6*B*** shows the ISP and corresponding SCPP of all laminectomized patients. These findings indicate spinal cord compression by the surrounding dura rather than bone.

SCPP and Spinal Cord Blood Flow

After obtaining an amendment to our ethical approval, we were able to test the effect of increasing SCPP (using inotropes) on spinal cord blood flow in six laminectomized patients (two ASIA A, one ASIA C). Increased SCPP was associated with significantly increased overall ICG fluorescence from the injured spinal cord (**Fig. 7**). Control experiments (not shown) revealed that more than 95% of the ICG signal is from the spinal cord and less than 5% from the dura.

SCPP and Clinical Motor Response

We investigated the relation between SCPP and limb movement. Only four patients had ASIA C scores and were thus eligible for this analysis, but data from two patients could not be analyzed (one patient had arterial catheter for 9 hr and therefore had only two clinical assessments; the other patient had low SCPP throughout). In the two eligible patients, there was a significant positive correlation between SCPP (averaged for 30 min before the limb examination) and limb motor score (**Fig. 8**).

SCPP and MEPs

MEP amplitudes allow an objective assessment of the severity of corticospinal damage and thus predict the recovery of function mediated by the corticospinal tract (18). We, therefore, asked whether increasing SCPP increases MEP amplitudes. Following an amendment to our ethical approval, we

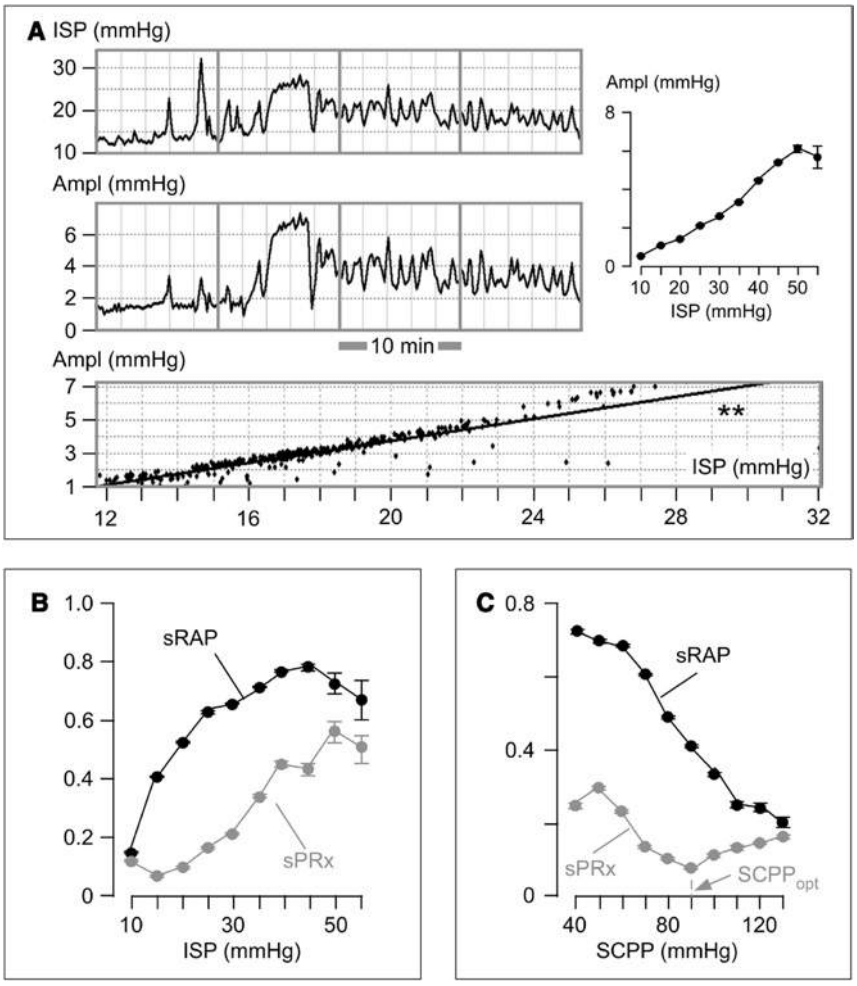

Figure 4. Spinal pressure reactivity (sPRx) and spinal reserve capacity (sRAP). **A**, Intraspinal pressure (ISP) signal (*upper*) and corresponding pulse amplitude (Ampl) signal (*middle*) of a patient with traumatic spinal cord injury (TSCI). Scatter plot of Ampl versus ISP (*lower*) for this patient and best-fit straight line. Each point is a 10-second average, Pearson $r = 0.91$, $p < 0.01$**. Ampl versus ISP (*right*) for 18 patients with TSCI. sRAP and sPRx versus ISP (**B**) and spinal cord perfusion pressure (SCPP) (**c**) for 18 patients with TSCI. Optimum SCPP (SCPP$_{opt}$) corresponds to minimum sPRx. Mean ± 95% CI.

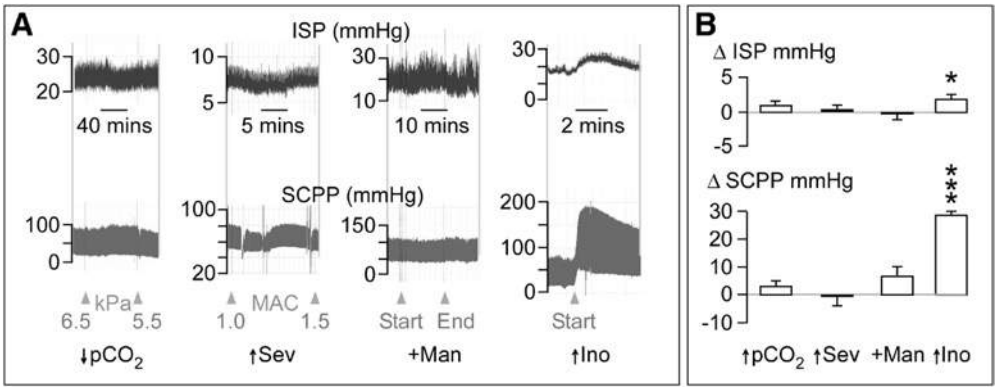

Figure 5. Effect of different maneuvers on intraspinal pressure (ISP) and spinal cord perfusion pressure (SCPP) after traumatic spinal cord injury (TSCI). **A**, Representative ISP and corresponding SCPP traces showing the effect of reducing Paco2 (49–41 torr [6.5–5.5 kPa]), increasing sevoflurane (Sev) (1.0–1.5 minimum alveolar concentration [MAC]), infusing 100 mL 20% mannitol (Man) IV, and increasing inotrope (Ino) infusion. **B** Summary of data showing ΔISP and ΔSCPP produced by ↑P$_{CO_2}$ $n = 17$, ↑Sev $n = 17$, +Man $n = 11$, or ↑Ino $n = 9$. Mean ± SE, p value of less than 0.05* and 0.001***.

monitored MEPs in nine of 18 patients with TSCI (54 muscles) and four control patients (16 muscles) without TSCI (Fig. 8). In patients with TSCI, increasing SCPP by 17–41 mm Hg produced a significant rise in MEP amplitude in muscles at or below the level of injury. The optimal SCPP (to maximize MEP amplitude) varied between patients, and in one patient with TSCI, very high SCPP (> 100 mm Hg) was required to maximize the MEP amplitude. In control patients, increasing MAP by 18–38 mm Hg (with metaraminol) produced no significant change in MEP amplitude. Together, the data suggest that the injured spinal cord is ischemic. By increasing SCPP, motor function at or below the TSCI level improves.

DISCUSSION

Our key finding is that it is possible to continuously monitor subdural ISP for up to a week without complications. The recordings indicate that after severe TSCI, ISP at the injury site is elevated. High ICP in TBI is potentially lethal by causing brain ischemia and herniation (8, 10, 11). Our technique may help elucidate whether high ISP is also harmful in TSCI.

We defined variables (ISP, SCPP, sPRx, and sRAP), which might be used to guide therapy after TSCI. In some respects, these variables behave similarly in TSCI as their brain counterparts (ICP, CPP, PRx, and RAP) do in TBI. For example, the ISP and ICP signal characteristics appear similar, including waveform shape (with three peaks), amplitude, and the presence of slow, respiratory, and pulse waves. The relationships between sRAP and sPRx versus ISP and SCPP are similar to the corresponding relationships

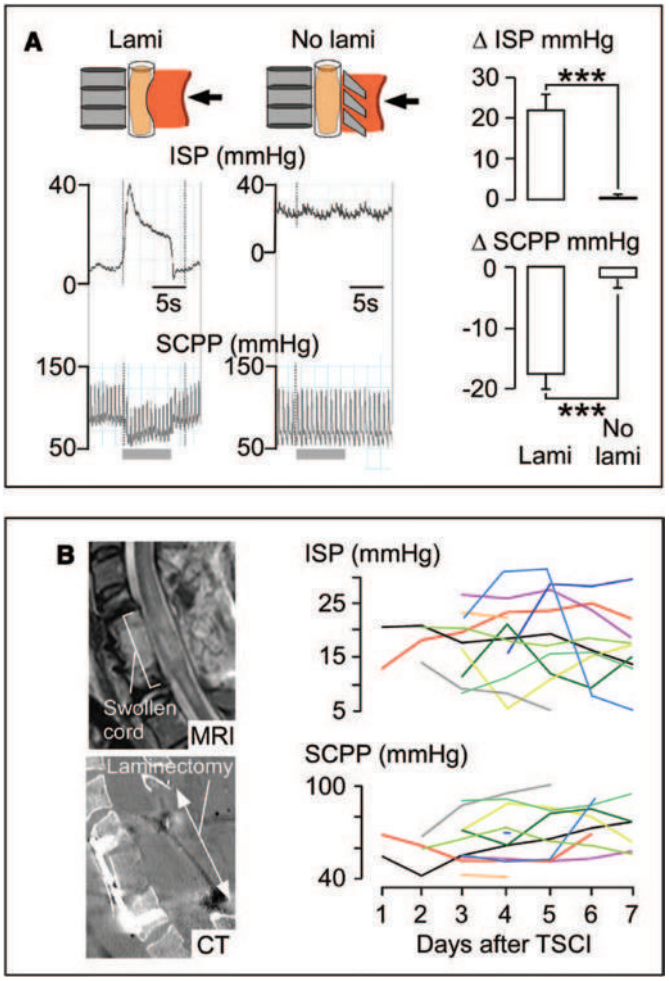

Figure 6. Effect of laminectomy on intraspinal pressure (ISP) and spinal cord perfusion pressure (SCPP). **A**, Effect of compressing skin incision on ISP and SCPP in a laminectomized (Lami) (*left*) and a nonlaminectomized (No lami) (*middle*) patient. ΔISP and ΔSCPP (*right*) caused by compressing the skin incision (Lami $n = 10$, No lami $n = 7$). **B**, ISP in laminectomized patients. MR and CT scans (*left*) of a laminectomized patient with ISP more than 20 mm Hg. ISP and SCPP of the 11 laminectomized patients (*right*). Each *line* represents a patient with ISP and SCPP averaged over 24 hr. Mean ± SE, *p* value of less than 0.001***. TSCI = traumatic spinal cord injury.

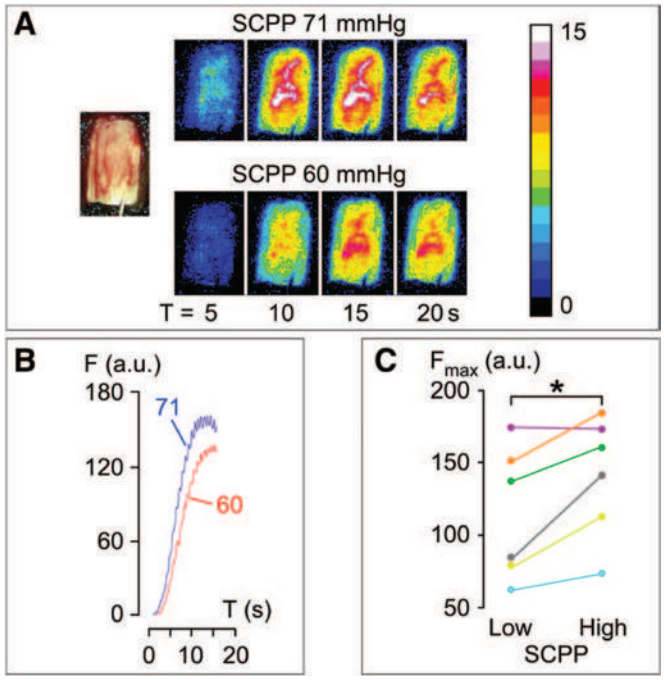

Figure 7. Increasing spinal cord perfusion pressure (SCPP) improves spinal cord perfusion. **A**, Brightfield photo of exposed dura (*left*). Corresponding indocyanine green (ICG) fluorescence at 5, 10, 15, and 20 s from the onset of fluorescence (*right*). Spinal cord perfusion was assessed at SCPPs of 71 mm Hg (*right top*) and 60 mm Hg (*right bottom*). **B**, Time course of ICG fluorescence (arbitrary units [a.u.]) of injured spinal cord at SCPPs 71 and 60 mm Hg. **C**, Peak ICG fluorescence (a.u.) of injured spinal cord at low versus high SCPPs (in mm Hg) for six patients with traumatic spinal cord injury (SCPP: yellow 60 vs 90, blue 64 vs 101, purple 50 vs 65, orange 66 vs 92, green 60 vs 71, and gray 52 vs 81). *p* value of less than 0.05*.

between RAP and PRx versus ICP and CPP (11, 13, 17). There are also differences between the spinal cord and brain variables. For example, ICP (but not ISP) responds to mannitol, $Paco_2$, and sevoflurane. Further studies are required to compare the behavior of the variables defined here for TSCI with the behavior of the analogous variables for TBI.

ISP monitoring is technically simple. With experience, pressure probe insertion took less than 10 minutes. Previous attempts to measure SCPP after TSCI had little success. Lumbar drains were inserted to measure CSF pressure below the injury (19), which (as shown here) differs from the ISP at the injury site. Pressure in a spinal radicular artery has been recorded (20), but it is technically difficult, risks vascular damage to the spinal cord, and does not measure SCPP at the injury site.

Based on our data, we propose the following sequence of events after severe TSCI. The injured section of the spinal cord swells so that there is no CSF between the spinal cord and the nondistensible dural sac. Four compartments are created each with a different pressure profile: the injury site (swollen spinal cord against dura), the CSF compartment above, the CSF compartment below, and the extradural compartment. At the injury site, the lack of CSF around the spinal cord decreases the local reserve capacity (quantified using sRAP). Further spinal cord swelling causes a rapid local rise in ISP (as the spinal cord becomes compressed against the dura), which causes loss of autoregulation (quantified using sPRx). By analogy to intracranial dynamics (17), too high SCPP (hyperperfusion) and too low SCPP (hypoperfusion) are associated with impaired autoregulation, which may cause secondary damage to the spinal cord.

Maneuvers that influence ICP after brain injury (8)—change in $Paco_2$, mannitol, sevoflurane—had little effect on ISP and SCPP after TSCI. To explain the difference between the brain and spinal cord, we propose that, after TBI, some brain regions are damaged and unresponsive to these maneuvers, whereas other regions, which are less damaged, are responsive. Therefore, after TBI, the ICP responds to these maneuvers because of the less damaged brain regions. In contrast, ISP is measured from the injury site only, which is unresponsive to these maneuvers. We showed that inotropes raised MAP and ISP, but with a significant net increase in SCPP. The primary effect of inotropes is likely a rise in MAP, which increases spinal cord blood flow at the injury site (evident

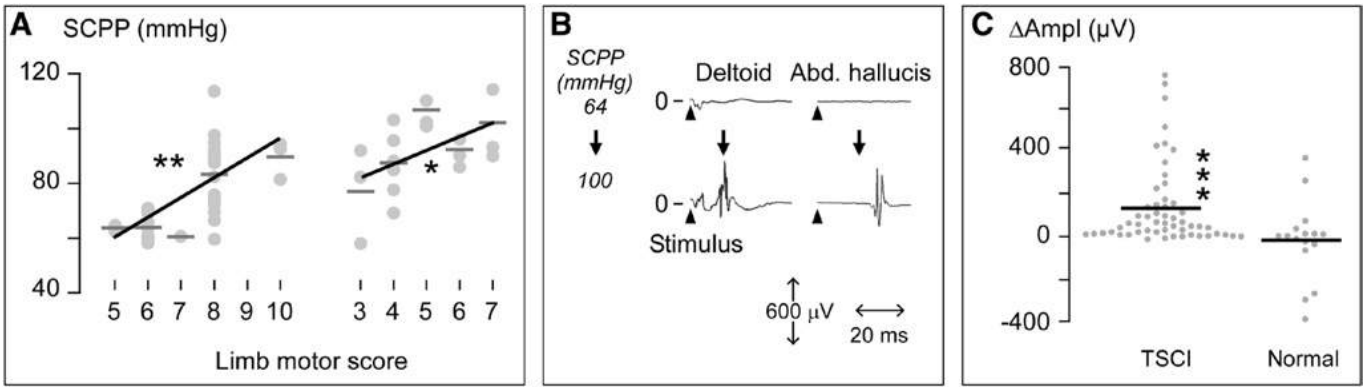

Figure 8. Increasing spinal cord perfusion pressure (SCPP) improves limb motor function. **A**, SCPP versus total limb motor score (0–16) for two American Spinal Injury Association (ASIA) C patients with cervical spinal cord injury, Spearman $r = 0.65$ (*left*) and 0.48 (*right*). Points represent neurological assessments, lines are SCPP means. **B**, Motor-evoked potentials (MEPs) in a patient with cervical ASIA C traumatic spinal cord injury (TSCI) recorded from deltoid and abductor (Abd.) hallucis at SCPP 64 versus 100 mm Hg. **c**, Change in amplitude (Ampl) of MEP recorded at high versus low SCPP (ΔAmpl) for 54 muscles in nine patients with TSCI (six ASIA A, three ASIA C) and 16 muscles in four normal subjects. *Points* represent different muscles. *Lines* are means. In the nine patients with TSCI, SCPP was changed (in mm Hg) 52→80, 62→79, 50→84, 55→86, 47→81, 77→118, 64→100, 63→83, and 50→78, respectively. In the four normal subjects, mean arterial pressure was changed (in mm Hg) 84→111, 84→122, 73→91, and 54→80, respectively. *p* value of less than 0.05*, 0.01**, and 0.001***.

as increased ICG fluorescence), which in turn increases ISP. Whatever the underlying mechanisms, our data show that the available therapies to increase SCPP after TSCI are limited.

We investigated the effect of laminectomy after TSCI. Our data show that laminectomy does not reduce ISP efficiently because the swollen spinal cord remains compressed by the surrounding dural sac. Laminectomy for TSCI is equivalent to a decompressive craniectomy without durotomy for TBI, which does not effectively reduce ICP (21). Therefore, to reduce ISP, durotomy and duraplasty might be required in addition to the laminectomy. Our findings also indicate that laminectomy is potentially detrimental by allowing skin compression to be transmitted to the injured spinal cord. To avoid transmission of external forces to the injured spinal cord, the patient could be nursed on the side, prone on a ring-shaped pillow.

Our data suggest that ISP and SCPP vary widely between patients and raise the possibility of individualized therapy to optimize SCPP (to maximize MEP amplitude and minimize PRx). For incomplete TSCI, the aim is to improve function below the level of injury and for complete TSCI, to limit cranial extension of the neurological deficit. It is unclear, however, whether prophylactically increasing SCPP has side effects, such as acute respiratory distress syndrome or exacerbation of spinal cord edema.

We conclude that ISP monitoring is feasible and safe after severe TSCI. ISP monitoring might also be applicable in other conditions that cause marked spinal cord edema, such as longitudinally extensive transverse myelitis (22).

ACKNOWLEDGMENTS

We thank P. Rich, T. Jones, M. Crocker, J. Poloniecki (St. George's Hospital), M. Belci (Stoke Mandeville Hospital), D. Choi (National Hospital for Neurology and Neurosurgery), K. Rezajooi (Royal National Orthopaedic Hospital), D. Bell and N. Thomas (King's College Hospital), M. Sofroniew (University of California at Los Angeles), and N. Burr (Lay person).

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