Microdialysis to optimize cord perfusion and drug delivery in spinal cord injury

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ABSTRACT

OBJECTIVE: There is lack of monitoring from the injury site to guide management of patients with acute traumatic spinal cord injury. Here we describe a bedside microdialysis monitoring technique for optimizing spinal cord perfusion and drug delivery at the injury site.

METHODS: 14 patients were recruited within 72 hours of severe spinal cord injury. We inserted intradurally at the injury site a pressure probe, to monitor continuously spinal cord perfusion pressure, and a microdialysis catheter, to monitor hourly glycerol, glutamate, glucose, lactate and pyruvate. The pressure probe and microdialysis catheter were placed on the surface of the injured cord.

RESULTS: Microdialysis monitoring did not cause serious complications. Spinal cord perfusion pressure 90 – 100 mmHg and tissue glucose >4.5 mM minimized metabolic derangement at the injury site. Increasing spinal cord perfusion pressure by ~10 mmHg, increased the entry of intravenously administered dexamethasone at the injury site three-fold.

INTERPRETATION: This study determined the optimum spinal cord perfusion pressure and optimum tissue glucose concentration at the injury site. We also identified spinal cord perfusion pressure as a key determinant of drug entry into the injured spinal cord. Our findings challenge current guidelines, which recommend maintaining mean arterial pressure at 85 – 90 mmHg for a week after spinal cord injury. We propose that future drug trials for spinal cord injury include pressure and microdialysis monitoring to optimize spinal cord perfusion and maximize drug delivery at the injury site.

INTRODUCTION

Traumatic spinal cord injury (TSCI) is a devastating condition that, each year, affects about 15 – 40 people per million[1]. The surgical, anesthetic and neurointensive care unit management of patients with acute TSCI is variable[2,3]. To guide management, we recently developed a novel technique to continuously monitor intraspinal pressure (ISP) at the injury site and compute spinal cord perfusion pressure (SCPP)[4,5]. Intraoperatively, a pressure probe is inserted subdurally to measure ISP at the injury site, which is the same as intraparenchymal ISP[6]. Monitoring ISP and SCPP for up to a week is safe based on a review of 42 patients[7].

Data obtained from human[8,9] and mouse[10] studies show that, after TSCI, the injured spinal cord swells and becomes compressed against the dura. Three intradural compartments form (above, at and below the injury site) each with a different ISP[11]. The low SCPP at the injury site[5,8] suggests that the injured spinal cord is ischemic. We showed that SCPP can be increased by increasing the mean arterial pressure with inotropes[5] or by reducing ISP with expansion duroplasty[8]. It remains unclear whether increasing SCPP is beneficial for the injured spinal cord.

Microdialysis is widely used to monitor brain metabolism in brain-injured patients[12]. Microdialysis catheters monitor hourly the levels of brain tissue glucose, lactate, pyruvate, glutamate and glycerol in the extracellular space. Low glucose, high lactate, high lactate-to-pyruvate ratio (LPR) and high lactate-to-glucose ratio (LGR) indicate metabolic derangement[13-15]. Glutamate is released during ischemia and causes neuronal death (excitotoxicity) whereas glycerol is a marker for cell membrane lipid degradation[12]. Microdialysis has also been used to quantify penetration of drugs including vigabatrin[16], metronidazole[17] and cefotaxime[18] into injured human brain. Microdialysis monitoring has not previously been used in TSCI patients. Here, we describe a simple technique for simultaneous bedside monitoring of SCPP and microdialysis at the injury site. This technique

was used to determine the SCPP and tissue glucose level that minimize the metabolic

derangement at the injury site; these are termed the optimal SCPP and the optimal tissue

glucose level, respectively. We also determined the effect of altering SCPP on the entry of

intravenously administered drugs into the damaged spinal cord.

MATERIALS AND METHODS

Institutional research board approval. Approval for the Injured Spinal Cord Pressure

Evaluation (ISCoPE) study, including the patient information sheet and consent form was

obtained from the St George's Joint Research Office and the National Research Ethics

Service London – St Giles Committee (No. 10/H0807/23). The study conforms with The

Code of Ethics of the World Medical Association (Declaration of Helsinki).

Patient recruitment. Inclusion criteria are: 1. Severe TSCI defined as American spinal

injuries association Impairment Scale (AIS) grade A, B or C; 2. Age 18 – 70 years; 3. Timing

between TSCI and surgery not more than 72 hours. Exclusion criteria are: 1. Patient unable to

consent; 2. Other major injuries or co-morbidities; 3 Penetrating TSCI. Surgery and early

management took place at the neurosurgery unit of St. George's Hospital. Recruitment into

the study was discussed with all eligible patients and their families on admission, the patient

information sheet was given and the consent form was signed by each patient. Recruitment

for microdialysis monitoring was between May 2014 and September 2015.

Insertion of ISP probe and microdialysis catheters. Following bony realignment and

posterior fixation, the ISP probe (Codman Microsensor Transducer®, Depuy Synthes, Leeds,

UK) and microdialysis catheter(s) (CMA61, CMA Microdialysis AB, Sweden) were

tunnelled through skin into the wound cavity. We chose the CMA61 microdialysis catheter,

which has a 3 cm long membrane, long shaft and 20 kDa cut-off rather than the CMA70 or
CMA71 brain catheters, which are too short to tunnel for spinal cord monitoring. Details of
the CMA61 catheter are in the Supplement. Under the operating microscope, the dura and
arachnoid membranes were opened one level below the injury (Fig. 1A). The ISP probe was
inserted through the durotomy and placed under the arachnoid on the spinal cord surface. We
inserted a microdialysis catheter at the injury site in 14 patients. The microdialysis catheter
was inserted until the tip was at the site of maximal spinal cord swelling. The dural opening
was sutured and supplemented with fibrin glue (Tisseel®, Baxter, UK). ISP probes and
microdialysis catheters were secured to the skin with silk sutures. A wound drain was
allowed to drain under gravity for a week. Patients were given 5,000 units dalteparin daily
starting on the day after the surgery. Dalteparin was omitted 24 hours before removing the
probes and wound drain.

ISP and SCPP monitoring. The ISP probe was connected to a Codman ICP box linked via a
ML221 amplifier to a PowerLab running LabChart v.7.3.5 (AD Instruments, Oxford, UK).
Arterial blood pressure was recorded from a radial artery catheter connected to the Philips
Intellivue MX800 bedside monitoring system (Philips, Guildford, UK) in turn connected to
the PowerLab system. The ISP and arterial blood pressure signals were sampled at 1 kHz for
up to seven days. LabChart was used to analyse the signals and compute SCPP, defined as
mean arterial pressure minus ISP.

Microdialysis monitoring. Microdialysis monitoring was started postoperatively in the
neurointensive care unit. CNS perfusion fluid (CMA Microdialysis AB, Sweden) was
perfused at a rate of 0.3 µL/min, unless otherwise stated, using the CMA106 or CMA107
infusion pump (CMA Microdialysis AB, Sweden). The transit time from the microdialysis

membrane to the vial collection chamber is 24 minutes. Microdialysis vials were changed

hourly, stored at 4 °C, and batched analysed up to 24 hours later using ISCUS Flex (CMA

Microdialysis AB, Sweden). The first two samples from each patient were discarded to allow

priming of the microdialysis catheter and stabilisation of the metabolite concentrations. All

samples were analyzed for glucose, lactate, pyruvate, glycerol and glutamate. LPR and LGR

were calculated. 100-fold changes in metabolite concentration, compared with the preceding

hour, were excluded from analysis. After analysis, samples were stored at -80 °C.

Patient assessments. Neurological examinations were done on admission and at two weeks

postoperatively, i.e. before discharge to the rehabilitation facility. A CT and MRI of the

whole spine were done on admission. Another CT was done within 48 hours of surgery to

check screw and probe positions (Fig. 1B). MRI of the injured spinal cord was done at about

2 weeks and at 6 – 12 months after surgery.

Metabolite recovery. The extrapolation to zero flow method was used to determine

metabolite recoveries[19]. Data were collected on the last day of monitoring when metabolite

levels were stable. Flow rate was changed every 2 hours and samples were collected every 30

minutes. The first sample of each 2-hour period was discarded to allow for the transit time of

the microdialysis fluid from the exchange membrane to the vial. We used flow rates of 0.3,

1.0, 2.0 and 5.0 μL/min. The experiment was repeated in three patients and the following

equation was fitted to the data: $R = 100 \times [1 - exp(-K/f)]$, where R is metabolite recovery, K

is exchange membrane surface area times mass transport coefficient and f is flow rate[19].

Dexamethasone assay. In three TSCI patients, a bolus of 4 mg dexamethasone was given

intravenously. Venous blood was withdrawn before giving dexamethasone (0 min) and at 10

minutes, 1, 2, 4 and 8 hours after dexamethasone administration. Blood was allowed to clot

for 30 minutes at room temperature, tubes were centrifuged at 7,000 revolutions per minute

for 10 minutes and sera were collected and stored at -80 °C. In each patient, a microdialysis

catheter at the injury site was perfused at 0.3 μL/min and samples were collected hourly. The

experiment was done with SCPP kept high. At 24 hours later, the experiment was repeated

with SCPP kept low. Serum and microdialysis samples were analysed using an enzyme-

linked immunosorbent assay kit (IDELISA-F016, ID-Labs, London, ON, Canada) according

to the manufacturer's instructions. For serum dexamethasone concentration, we fitted the

exponential decay equation $D_t = D_o \times exp(-\lambda t)$ where D_t is dexamethasone concentration at

time t, D_o is dexamethasone concentration at time 0 and λ is the exponential decay constant.

Serum dexamethasone half-life was calculated as $t_{1/2} = ln(2)/\lambda$. We determined the Area

Under the Curve at 0 – 8 hours (AUC_{0-8h}) for serum and spinal cord dexamethasone.

Statistics. We used http://mycurvefit.com to fit $R = 100 \times [1 - exp(-K/f)]$ (extrapolation to

zero flow) and $D_t = D_o \times exp(-\lambda t)$ (dexamethasone kinetics) to the data. Two-way ANOVA

(XLSTAT Premium, Addinsoft, New York, USA) was used to model each metabolite

concentration (first factor injury site *vs.* below and second factor hours, or first factor AIS A

vs. B/C and second factor hours) and dexamethasone concentration (first factor high *vs.* low

SCPP and second factor time). Statistical significance was $P < 0.05$*, 0.01**, 0.005[†],

0.001[††], 0.0005[#], 0.0001[##].

RESULTS

Patient details. We recruited 14 consecutively admitted TSCI patients with mean age 38

years (Table 1). After surgery, patients were kept in the neurointensive care unit throughout

the monitoring period. Most (92.9 %) were male, most (57.1 %) had thoracic injuries and

most (71.4 %) had no motor or sensory response below the level of injury on admission (AIS A). TSCI resulted from a fall in 42.9 % and a road traffic accident in 57.1 %. Mean time from injury to surgery was 1.5 days after TSCI. 71.4 % patients had posterior spinal fixation with laminectomy and 28.6 % had posterior fixation without laminectomy. The duration of microdialysis monitoring ranged from less than a day to 6 days. On average, patients had microdialysis monitoring for 4 days. Within 2 weeks of surgery, 14.3 % patients improved from AIS A to B; AIS grade did not worsen in any patient.

Metabolite recovery. Plots of metabolite concentration at different flow rates are in Fig. 1C. For each metabolite, there was excellent goodness-of-fit ($r < -0.95$) with the theoretical curve. Relative recoveries were calculated from the theoretical curves as the metabolite concentration at 0.3 µL/min divided by the estimated metabolite concentration at no flow. Our data indicate relative recoveries at 88 – 100 % (Fig. 1D).

SCPP *vs.* metabolite levels. During the microdialysis monitoring period the average SCPP of all patients was 60 – 80 mmHg (Fig. 2A). Figs. 2B-E show the average daily metabolite concentrations, LPR and LGR at the injury site at different SCPPs. SCPP 90 – 100 mmHg was associated with the least abnormal metabolic profile i.e. lowest glutamate, highest glucose as well as lowest LPR and LGR. Below 90 – 100 mmHg the metabolism of the injury site progressively worsened, i.e. negative correlation between SCPP *vs.* glutamate, LPR or LGR and positive correlation between SCPP *vs.* glucose. SCPP > 100 mmHg was associated with more deranged metabolism at the injury site than SCPP 90 – 100 mmHg, i.e. higher glutamate, lower glucose, higher LPR and higher LGR. Glycerol concentration was high (~55 mM) with SCPP below 60 – 70 mmHg and low (~40 mmM) with SCPP > 70 mmHg. There was no correlation between average daily metabolite concentrations, LPR or LGR at the

injury site *vs.* ISP (not shown). We also plotted tissue glucose concentration at the injury site *vs.* LPR (Fig. 2F). Tissue glucose concentration >4.5 mM was associated with the lowest LPR; below 4.5 mM, glucose concentration inversely correlated with LPR. Glucose concentration at the injury site was 35.5 ± 1.0 % of serum glucose. Fig. 2G shows the relationship between serum glucose and microdialysis glucose. The data suggest that, after TSCI, optimum SCPP is 90 – 100 mmHg and optimum tissue glucose is >4.5 mM.

Metabolites in complete *vs.* incomplete injuries. In Fig. 3 we compare average daily metabolite concentrations, LPR and LGR for patients with complete (AIS A) *vs.* incomplete (AIS B/C) neurological deficit. Metabolism at the injury site was more deranged for AIS A than AIS B/C, with markedly higher glycerol, glutamate, lactate, pyruvate, LPR and LGR as well as lower glucose for AIS A. The differences in metabolite levels between AIS A *vs.* AIS B/C were more marked during the first 72 h after injury. Within 3 – 4 days, glycerol and glutamate concentrations were comparable in AIS A *vs.* AIS B/C patients, though lactate, pyruvate, LPR and LGR remained higher and glucose remained lower throughout the monitoring period in AIS A than AIS B/C. These findings suggest that the severity of TSCI correlates with the degree of metabolic disturbance at the injury site.

Dexamethasone kinetics. The low and high SCPP time profiles following administration of dexamethasone are in Fig. 4A. Over 8 hours, mean low (SCPP (72 ± 1 mmHg, mean ± standard error) was significantly lower than mean high SCPP (84 ± 1 mmHg). The correlation coefficient of the dexamethasone standards curve was 0.99 and the assay coefficient of variation was 14 %. After administration of the 4 mg dexamethasone bolus, serum dexamethasone concentration decayed exponentially with no significant difference in dexamethasone concentrations between high *vs.* low SCPP. The correlation coefficient for the

best-fit exponential decay curve was -1.00 for high and low SCPP (Fig. 4B). The $AUC_{0-8h(serum)}$ and $t_{1/2}$ for serum dexamethasone were comparable at high *vs.* low SCPP: $AUC_{0-8h(serum)}$ was 1,091 *vs.* 942 ng.h/mL and $t_{1/2}$ was 2.1 *vs.* 2.3 hours. Significantly more dexamethasone entered the injured spinal cord at high *vs.* low SCPP with $AUC_{0-8h(cord)}$ at 17 *vs.* 6 ng.h/mL and peak spinal cord concentration at 4.8 *vs.* 2.0 ng/mL (Fig. 4C). Only a small proportion of the intravenous dexamethasone entered the spinal cord with $AUC_{0-8h(cord)}/AUC_{0-8h(serum)}$ = 1.62 *vs.* 0.64 % at high *vs.* low SCPP. Therefore, increasing SCPP markedly increases the entry of dexamethasone from the blood into the injured spinal cord.

Complications. Table 2 summarizes patient complications. On average, patients were followed up for 4.1 ± 1.1 months (mean ± standard error). There was no immediate postoperative deterioration in AIS grade. Probe-related complications, noted in 28.5 % patients, were asymptomatic pseudomeningocele or CSF leak through the probe skin exit site. All pseudomeningoceles resolved spontaneously and the CSF leak stopped after we sutured the skin. We did not observe meningitis, spinal cord damage or hematoma. Complications unrelated to the probes include pneumonia, vertebral artery dissection from the original trauma, superficial wound infection and a sacral pressure ulcer. One patient died from pulmonary embolism after he was discharged. In another T12 AIS B patient the mean arterial pressure dropped to 60 mmHg (SCPP 20 mmHg) for 35 minutes. He developed arm weakness and the sensory level ascended. When the SCPP was increased with norepinephrine, power in the arms normalized and the sensory level descended.

DISCUSSION

We showed that, in patients with acute TSCI, simultaneous monitoring of SCPP and microdialysis from the injury site is feasible and safe. The microdialysis catheter was easily

inserted during spinal fixation surgery and was removed in the neurointensive care unit. Complications related to the microdialysis catheter were minor; they include CSF leak from the catheter exit site that resolved by suturing the skin and asymptomatic pseudomeningocele that resolved spontaneously. Since our patient sample is small, complications may appear in a larger sample. Our microdialysis data suggest that the optimal SCPP is 90 – 100 mmHg and the optimal tissue glucose is more than 4.5 mM because these values minimize the metabolic derangement at the injury site. We also showed that simultaneous monitoring of SCPP and microdialysis could be used to enhance drug entry at the injury site. Based on our current findings and earlier studies[4-9,20,21], a large-scale study of outcome from TSCI in patients who have monitoring *vs.* those who do not is warranted.

There are technical nuances. First, a long (3 cm) exchange membrane was inserted to achieve near complete metabolite recovery at 0.3 µL/min flow rate, compared with a 1 cm long microdialysis membrane at 0.3 µL/min, which only achieves 70 % metabolite recovery[22]. Second, we placed the microdialysis catheter under the arachnoid because diffusion across the arachnoid is limited by inter-cellular tight junctions[23] and is greatly reduced for hydrophilic substances[24]. Third, we used surface rather than intraparenchymal microdialysis. Surface microdialysis was originally described in pig liver[25] and myocardium[26] with excellent correlations between surface and intraparenchymal levels of lactate, glucose and glycerol. We advocate using surface rather than intraparenchymal microdialysis monitoring to minimize the risk of probe-related hematoma and mechanical spinal cord damage.

We found more profound metabolic derangement in AIS A than AIS B/C patients. These findings suggest that the severity of TSCI correlates with the metabolic derangement at the injury site. A microdialysis study in a pig TSCI model concluded that the metabolic response at the injury site depends on the biomechanical nature of the injury[27]. Further

studies are required to determine if the metabolic derangement at the injury site accurately predicts AIS grade conversion after TSCI.

Microdialysis was used to characterize the relationship between SCPP, ISP, glucose and metabolism at the injury site. SCPP pressure below 70 mmHg was associated with cell lysis (high glycerol). As SCPP increased to 90 – 100 mmHg, metabolism improved (lower glutamate and lactate, lower LPR and LGR and higher glucose). Interestingly, when SCPP increased above 100 mmHg the metabolic profile worsened (higher glutamate and lactate, higher LPR and LGR and lower glucose). Therefore, not only hypoperfusion (SCPP below 90 mmHg), but also hyperperfusion (SCPP above 100 mmHg) may be detrimental for the injured spinal cord. This is consistent with our earlier report of a U-shaped relationship between the spinal pressure reactivity index and SCPP, which also indicated optimum SCPP around 90 mmHg[5,8,21]. After TSCI, ISP is 20 – 30 mmHg and therefore SCPP 90 – 100 mmHg corresponds to mean arterial pressure 110 – 130 mmHg. Our findings thus challenge current guidelines, which recommend maintaining mean arterial pressure at 85 – 90 mmHg for a week after TSCI[28]. Elevating mean arterial pressure after TSCI requires inotropic support, which is associated with several complications[29]. To reduce inotrope requirements and, therefore, inotrope-related complications when aiming for SCPP 90 – 100 mmHg, expansion duroplasty could be performed to lower the ISP[8]. No clear correlation was found between ISP and metabolite levels at the injury site; therefore, unlike changes in SCPP, changes in ISP may not be detrimental for the injured spinal cord. The microdialysis data also showed that the optimum glucose level at the injury site is more than 4.5 mM because this minimizes the LPR. Since acute hyperglycemia impairs functional improvement after TSCI[30], it may be safer to elevate the tissue glucose concentration at the injury site by increasing the SCPP rather than by increasing the serum glucose concentration. Future studies employing

rapid sampling microdialysis may determine if the optimum SCPP and optimum tissue glucose concentration vary between TSCI patients.

We showed that SCPP is a major determinant of drug entry into the injured spinal cord. The serum half-life of dexamethasone was 2 – 3 hours, in agreement with earlier studies[31]. By increasing SCPP by about 10 mmHg, we increased dexamethasone entry into the injured spinal cord three-fold. Completed[32,33] and on-going[34,35] trials of neuroprotective drugs in TSCI do not monitor SCPP or drug entry at the injury site. Our data suggest that failure to optimize SCPP and drug delivery at the injury site may lead to the erroneous conclusion that the tested drug does not improve outcome after TSCI, even if the drug is neuroprotective. A way to increase drug entry at the injury site is by localized delivery through the microdialysis catheter [36]. Given the spatial limitations of microdialysis, further studies employing several microdialysis catheters are required to compare drug entry at the injury site *vs.* the penumbra.

We conclude that multi-modality monitoring from the injury site after TSCI is helpful for guiding clinical management to reduce secondary damage. Further studies are needed to determine if interventions to optimize SCPP and tissue metabolite levels improve outcome.

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AUTHOR CONTRIBUTIONS

Conception and design of the study (MCP, SS), patient surgery (MCP, AZ), acquisition and

analysis of data (MCP, SS, IP, AZ), drafting the manuscript or figures (IP, MCP, SS).

POTENTIAL CONFLICTS OF INTEREST

None.

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FIGURE LEGENDS

Fig. 1. Insertion of microdialysis catheter at injury site and metabolite recovery. A. i. Insertion of ISP probe and microdialysis (MD) catheter under dura and arachnoid. **ii.** Magnified view of dural entry site. Arrowheads show arachnoid. **iii.** Sutured dural entry site. **iv.** Prone patient with cervical TSCI at end of surgery. S, screw; ISP, intraspinal pressure probe. **B.** Coronal postoperative CT scan through injury site. **C.** Plots of metabolite concentration *vs.* flow rate and best-fit theoretical curve. Mean ± standard error. r = correlation coefficient. **D.** Percent recovery at flow rate 0.3 μL/min.

Fig. 2. Metabolite concentrations at injury site at different SCPPs. A. Mean hourly SCPP *vs.* time. **B.** Glycerol, **C.** Glutamate, **D.** Glucose, Lactate, Pyruvate, **E.** LGR and LGR *vs.* mean hourly SCPP. **F.** Glucose *vs.* LPR. **G.** Serum glucose *vs.* microdialysis glucose. B – G include the metabolite measurements obtained throughout the monitoring period from all patients. Mean ± standard error.

Fig. 3. Metabolite concentrations at injury site of AIS A *vs.* AIS B/C patients. A. Glycerol, **B.** Glutamate, **C.** Glucose, **D.** Pyruvate, **E.** Lactate, **F.** LPR, and **G.** LGR. Mean ± standard error. 10 AIS A *vs.* 4 AIS B/C patients. Mean ± standard error; $P < 0.01$**, 0.0001##

Fig. 4. Effect of SCPP on penetration of dexamethasone into injured spinal cord. A 4 mg bolus of dexamethasone was given intravenously at time 0 at low SCPP. After 24 h, another 4 mg dexamethasone bolus was given intravenously at time 0 at high SCPP. **A.** High and low SCPP during the experiment. Concentration of dexamethasone **B.** in serum, and **C.** at injury site at high and low SCPP. Mean ± standard error; *NS*, not significant; $P < 0.05$*, 0.0001##

FIGURE 1
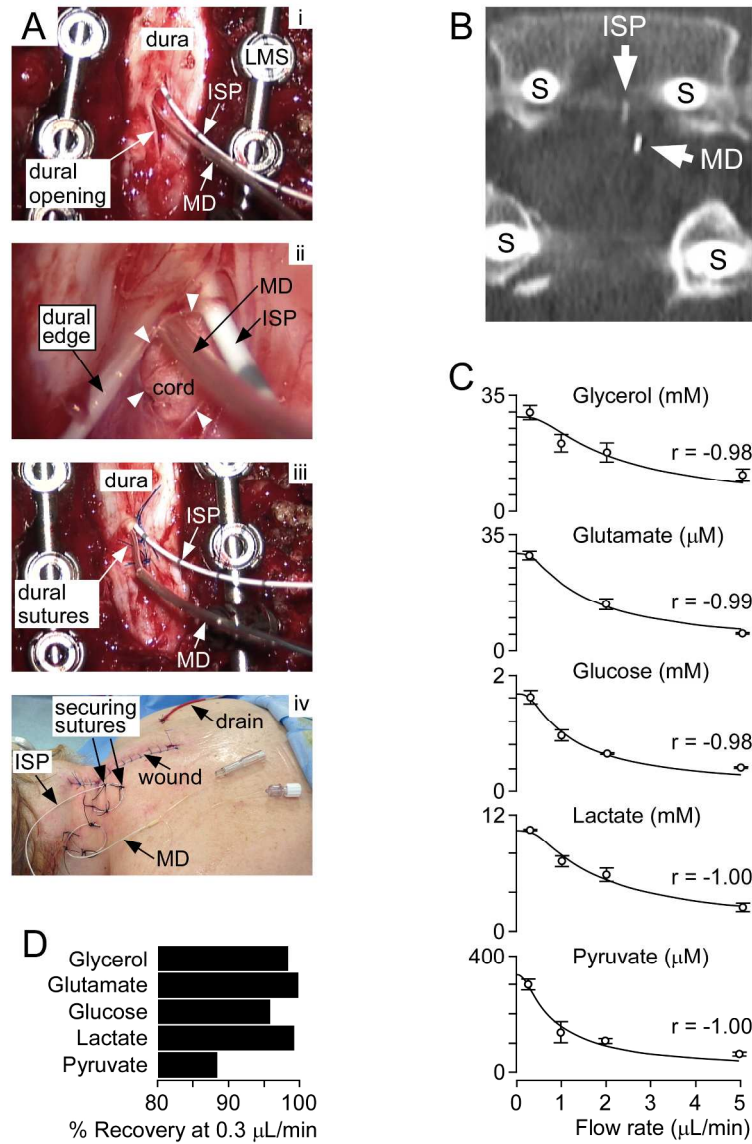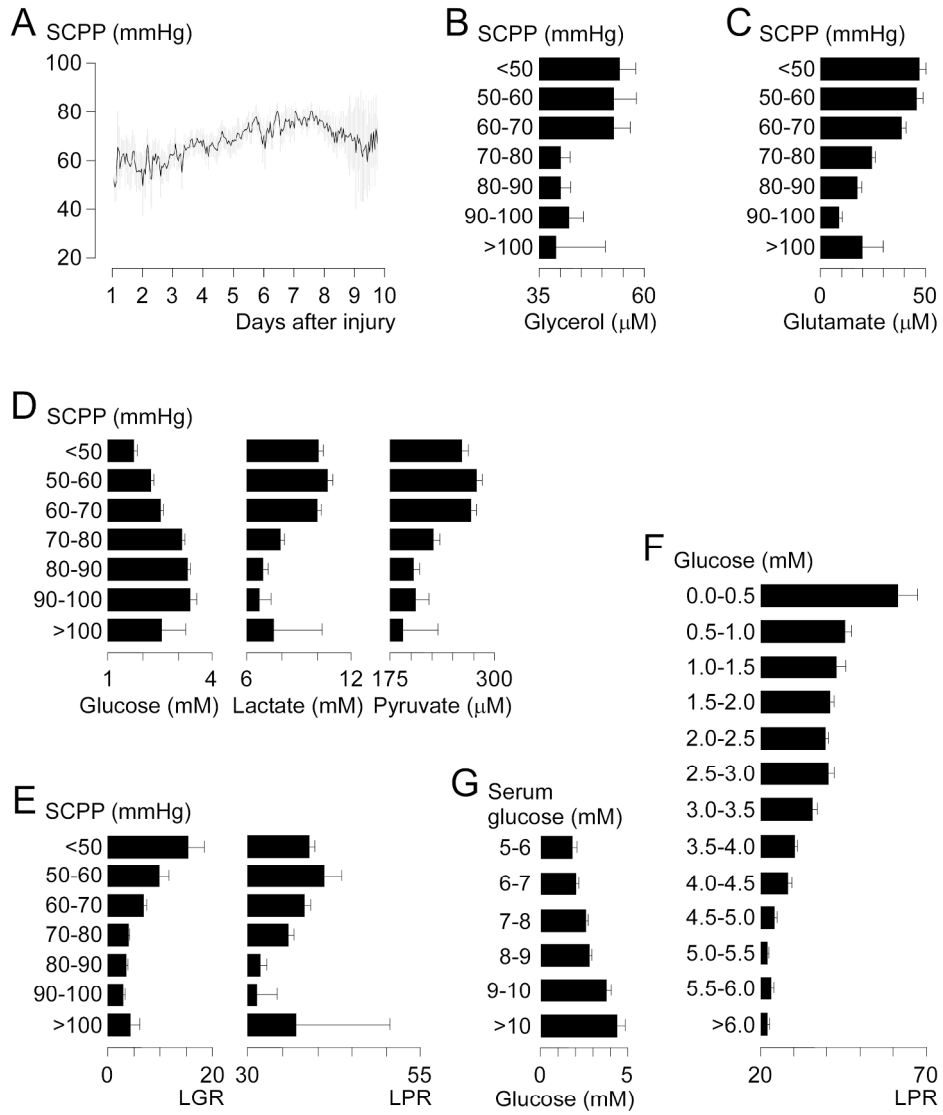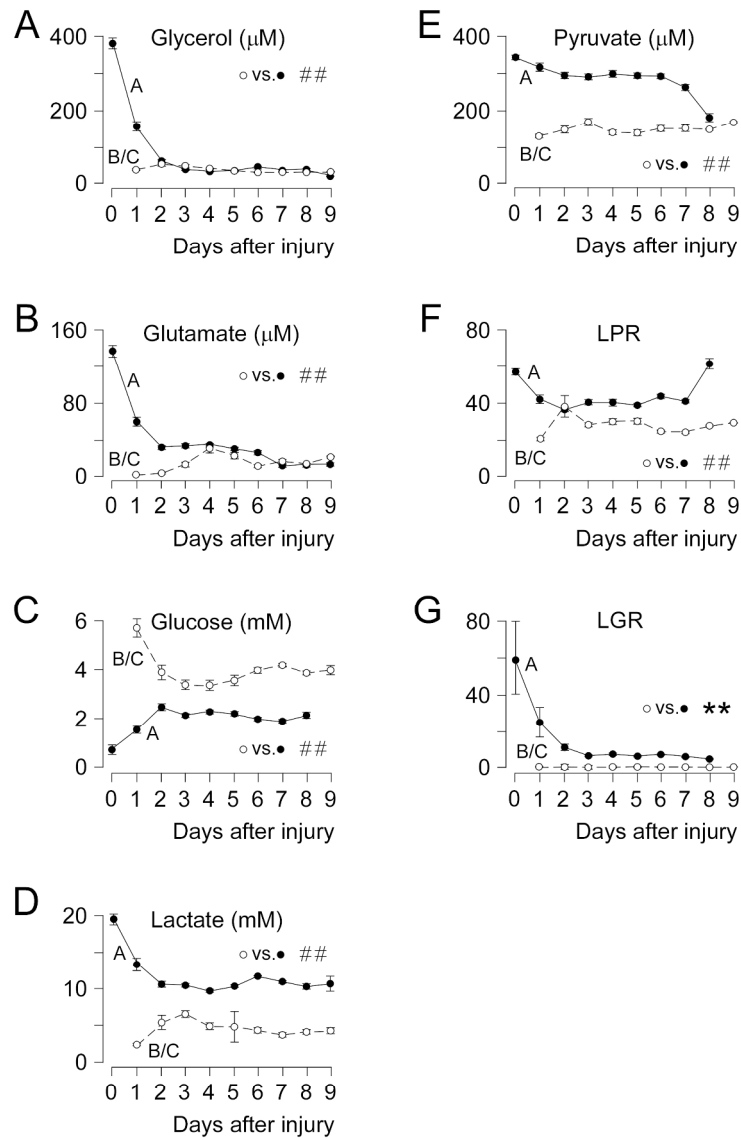
193x273mm (300 x 300 DPI)

FIGURE 2

209x267mm (300 x 300 DPI)

A Glycerol (μM)

B Glutamate (μM)

C Glucose (mM)

D Lactate (mM)

E Pyruvate (μM)

F LPR

G LGR

FIGURE 3

182x264mm (300 x 300 DPI)

A

SCPP

B

Serum dex (ng/ml)

C

Cord dex (ng/ml)
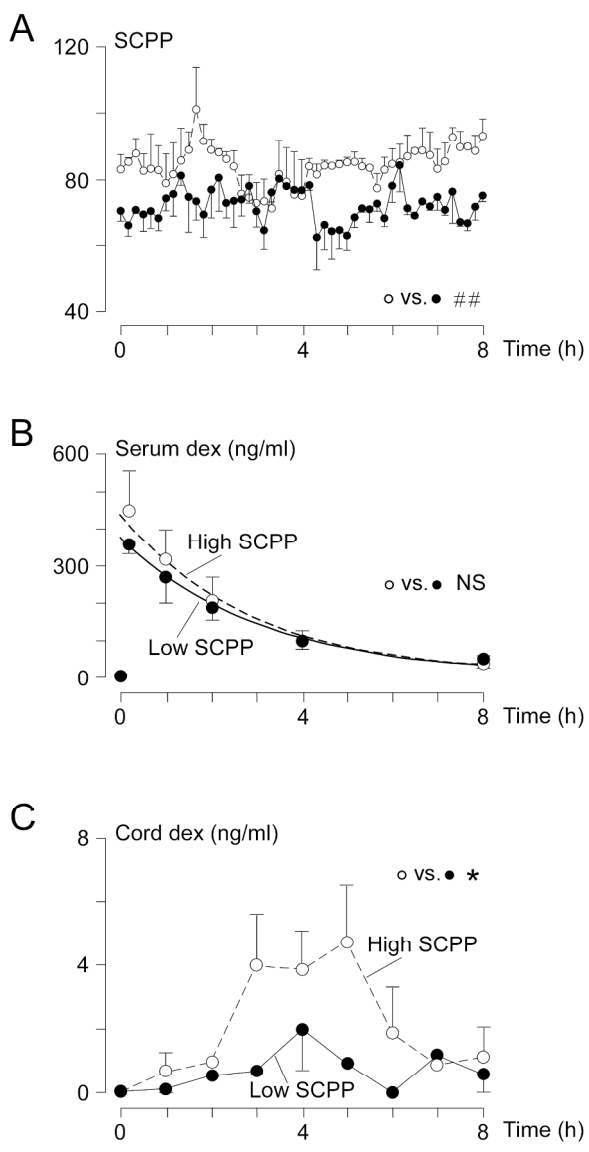
FIGURE 4

164x270mm (300 x 300 DPI)

Table 1. Patient characteristics.

Number of patients	14
Mechanism of injury (number of patients)	Fall (6), Road traffic accident (8)
Age in years, mean (range)	38 (19 – 70)
Male : female	13 : 1
Pre-operative AIS (number of patients)	A (10), B (3), C (1)
AIS at 2 weeks after surgery (number of patients)	A (8), B (5), C (1)
Level of injury (number of patients)	Cervical (6), Thoracic (8)
Hours to surgery, mean (range)	36.5 (9 – 72)
Laminectomy? (number of patients)	Yes (10), No (4)
Hours of microdialysis monitoring, mean (range)	100 (19 – 145)

AIS = American spinal injuries association Impairment Scale

Table 2. Complications in patients who had microdialysis monitoring.

COMPLICATION	NO. OF PATIENTS	%
Associated with microdialysis catheter		
CSF leak[a]	1	7.1
Asymptomatic pseudomeningocele[b]	3	21.4
Probe associated hematoma[c]	0	0.0
Meningitis	0	0.0
Not associated with microdialysis catheter		
Death[d]	1	7.1
Pneumonia	10	71.4
Traumatic vascular injury[e]	1	7.1
Hypotension causing spinal cord ischemia[f]	1	7.1
Superficial wound infection[g]	1	7.1
Pressure ulcer	1	7.1

[a]Resolved by suturing microdialysis catheter exit site. [b]MRI at 2 weeks. Pseudomeningoceles resolved on MRI at 6 – 12 months. [c]MRI from 11/14 patients. [d]Patient died from pulmonary embolus at 28 days at a different hospital. [e]Vertebral artery dissection. [f]T12 TSCI AIS B. The sensory level ascended from L1 to T5 on day 3 during hypotensive episode (mean arterial pressure 60 mmHg, SCPP 20 mmHg for 35 min). MRI showed spinal cord ischemia at T4. At 2 weeks the sensory level improved and AIS grade was B. [g]Resolved with antibiotics.