**Isoflurane anaesthesia impairs remote neocortical memory**

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Postoperative cognitive dysfunction (POCD) is a common complication after surgery in elderly patients, although the role of surgery-induced inflammation, anaesthesia, or both on the development of POCD remains elusive. The aim of the present study was to investigate the impact of isoflurane-induced anaesthesia on hippocampal and neocortical-dependent memory in mice in comparison with lipopolysaccharide (LPS)-induced inflammation which is well documented to induce a hippocampal-dependent memory impairment.

Young adult naive mice (male 10–12 weeks) were trained with contextual fear conditioning, and then randomly allocated to different experimental groups either immediately after training (experiment 1) or 3 days after training (experiment 2). The experimental groups were: naive, no intervention; anaesthesia, 20 min of general anaesthesia with isoflurane+buprenorphine for analgesia; LPS was injected i.p. at a concentration of 100 μg kg⁻¹. Mice were placed in the fear-conditioning box either 3 (experiment 1) or 32 days after training (experiment 2), to assess memory function.

**First experiment:** in the context test, mice in the LPS group displayed the greatest reduction of the contextual freezing response [35.0% (4.29) vs control, P<0.05]. Isoflurane-induced anaesthesia does not result in hippocampal memory impairment [49.67% (6.87), P>0.05 compared with control].

**Second experiment:** the control mice displayed the greatest levels of generalization of freezing, while LPS group had reduced freezing levels [74.63% (16.09) vs control, P<0.05], similarly isoflurane-induced anaesthesia results in reduced freezing responses [62.13% (16.42) vs control, P<0.05].

Cognitive function dependent on the hippocampus, where long-term memory is initially stored, is disrupted after LPS-induced inflammation. LPS-induced inflammation and isoflurane-induced anaesthesia both have a detrimental effect on neocortical memory recall, suggesting that the transference of memory between the hippocampus and the neocortex, the ultimate storage site of long-term memory, is affected by isoflurane anaesthesia or LPS.

**Acknowledgements**

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**References**


**Magnetic resonance imaging measures of cerebral perfusion after subarachnoid haemorrhage**


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Delayed cerebral ischaemia (DCI) is the main cause of morbidity and mortality after subarachnoid haemorrhage (SAH). Vasoconstrictive processes have been considered...
fundamental in the pathophysiology behind DCI. Recently, other mechanisms have been proposed. In this preliminary study, we investigate the feasibility of using the non-invasive magnetic resonance imaging (MRI) technique, arterial spin labelling (ASL), to track cerebral blood flow (CBF) changes in the acute period after SAH.

Six SAH patients (5 × Grade I and 1 × Grade II, World Federation of Neurosurgeons) were scanned on a 3 T Siemens MRI scanner with a 12-channel head coil. Patients were scanned on varying days post-endovascular coiling. A pseudo-continuous ASL sequence was used to assess CBF. The sequence consisted of a 1.4 s labelling duration followed by five post-labelling delays and a gradient-echo echo planar imaging readout (TR = 3.75 s, TE = 13 ms). Additional scans included a time-of-flight angio image (1.5 min duration) and two ASL calibration scans (2 × 11 s) to allow quantification of CBF in absolute units (ml 100 g⁻¹ min⁻¹). CBF was quantified by fitting the data to the ASL kinetic model, using a Bayesian inference approach.

The average grey matter CBF values obtained across all subjects was 45.06 (7.36) ml 100 g⁻¹ min⁻¹. Figure 1 shows the trend in CBF in the three patients (3, 4, and 6) who were scanned on three occasions. Patient 4 demonstrated a global CBF reduction on the second scanning day that occurred at the same time as a deterioration in clinical symptoms. This patient scored 15 points on the Glasgow coma scale (GCS) that is routinely used to assess SAH patients. This preliminary study demonstrates the feasibility of using ASL MRI to reproducibly and non-invasively track changes in CBF in SAH. The CBF decrease shown in Figure 1 was not detected by routine clinical assessment. Clinical scales such as GCS are not sensitive to subtle changes in cerebral perfusion in SAH patients that may be an important predictor of deterioration, the onset of DCI, or both. The role of novel MRI techniques such as ASL in assessing SAH patients during the acute phase requires further investigation in a larger clinical study.

**Fig 1** CBF measured with ASL MRI in three patients after subarachnoid haemorrhage.

### Acknowledgements
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### References

### Using propofol to differentiate between mixed populations of recombinant GABAA receptors expressed in HEK cells

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Neuronal GABA<sub>A</sub> receptors (GABA<sub>AR</sub>s) mediate the sedative, hypnotic, and immobilizing effects of the general anaesthetic propofol. GABA<sub>AR</sub>s are heterogeneous pentameric proteins drawn from a repertoire of 19 different subunits, with the α1β2γ2 configuration being the most abundant. However, there is increasing evidence for the existence of mixed GABA<sub>AR</sub> subtypes within individual neurones. For example, GABA<sub>AR</sub>s located within the synapse have a different subunit combination and differing functional properties compared with those located extrasynaptically. It remains unclear whether propofol affects these neuronal GABA<sub>AR</sub> subtypes in the same way, or whether different aspects of propofol’s actions may be mediated through distinct receptors. In this study, we examined whether functionally distinct GABA<sub>AR</sub> subtypes assemble in HEK293 cells by transiently expressing either α1, β2, and γ2 subunits or α1, β3, and γ2 subunits. We characterized the pharmacological properties of recombinant GABA<sub>AR</sub>s using the agonists GABA and propofol in conjunction with the antagonists gabazine and bicuculline methiodide.

Single cells expressing either α1β2γ2 or α1β3γ2 receptors were clamped at −60 mV and activated with GABA or propofol using a rapid application technique. Under these conditions, both GABA and propofol induced bicuculline- and gabazine-sensitive inward currents. Further experiments demonstrated that bicuculline could accelerate the deactivation of propofol-activated currents mediated by α1β2γ2 receptors (deactivation time constant 271 ± 64 ms vs 14 ± 5 ms). However, bicuculline was less effective in this regard for α1β3γ2 receptors (390 ± 44 ms vs 86 ± 15 ms).
was a surprising result as β3 and β2 subunits are structurally very similar; however, β3 subunits contain an extracellular amino acid motif (GKER) not found in β2 subunits, which enables homomeric assembly. Expression of the β3 subunit alone or in combination with the γ2 subunit produced receptors that were activated by propofol (−3.6 ± 1.1 pA/pF) and, interestingly, also by the antagonist bicuculline (−3.1 ± 1.5 pA/pF). GABA displayed weak agonism (−1.3 ± 0.5 pA/pF) and gabazine weak antagonist activity (−0.2 ± 0.1 pA/pF). Expression of the β2 subunit alone or with the γ2 subunit did not produce functional receptors. However, a β2(GKER) mutant subunit, containing β3 subunit residues required for homomeric assembly, produced receptors that shared similar pharmacology with β3 receptors. Furthermore, bicuculline was less effective at accelerating the deactivation of propofol-induced currents mediated by α1β2γ2 receptors (14 ± 5 ms).

These data suggest that cells expressing α1, β3, and γ2 subunits are composed of a mixed population of homomeric and heteromeric receptors and those lacking α1 subunits (either β3γ2 or β3) may be distinguishable by the agonist actions of propofol and bicuculline.

References

Position of the tips of conus medullaris in Chinese adult population with low backache: a magnetic resonance imaging study
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Spinal puncture is commonly performed below the second lumbar vertebra (L2) to avoid spinal cord injury. Increasing evidence indicates that the lower end of the conus is located at the body of L1 or between L1 and L2.1–3 Therefore, the primary objective of this observational study was to determine the tip of the conus in our Chinese population using magnetic resonance imaging (MRI).

The MRI images of 718 patients with low backache were obtained from a single centre between September 2009 and December 2009. Images were obtained in the sagittal plane using T2-weighted imaging (T2WI) and three-dimensional-constructive interference in steady state. Reimann positioning of the spinal cord conus was used.4 Anatomical sections of each lumbar level (x) were defined as: (i) upper vertebral body (Lx:U), (ii) middle vertebral body (Lx:M), (iii) lower vertebral body (Lx:L), and (iv) intervertebral disc. The position of the cone tip was defined as the most distal point of the spinal cord identified in the mid-sagittal MRI image. For analysis, patients were stratified into three groups according to age: Group A, 18–29 yr; Group B, 30–59 yr; and Group C, ≥ 60 yr.

The median conus tip position for males was L1:L and L1:M for females. However, the conus tip was located at L2 and below in 190 (26%) patients and L3 and below in 12 patients. The position of the conus correlated with age; the older the patients, the lower the conus, Spearman’s correlation, r=0.11, P=0.001 (Table 1).

The results of the study indicate that the spinal puncture should not be performed higher than the L3–4 intervertebral space in Chinese patients with low backache unless the position of the lower end of the spinal cord is identified using prior MRI images.

Acknowledgement
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Interobserver reproducibility of measurements of the supraclavicular ultrasound view of the brachial plexus
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The performance of successful ultrasound-guided supraclavicular blocks currently relies upon appropriate two-dimensional ultrasound visualization, accurate interpretation of that image, and effective operator technique. Failure to do so can result in harm (inadequate block, local anaesthetic...
toxicity, pneumothorax) to patients. The aim of this study was to evaluate how the acquisition of a standardized ultrasound image and its subsequent interpretation differs among anaesthetists.

Four anaesthetists of differing levels of experience with these blocks independently scanned 21 volunteers’ right-sided supraclavicular fossae, so that the subclavian artery, first rib, and brachial plexus were all visible. The images were saved and analysed using imageJ v1.43u. The cross-sectional areas of the artery and plexus were measured and used as surrogate markers of image interpretation. All anaesthetists interpreted their own scans and one set of scans from the most experienced. Analysis was made using Stata/SE v11.0.

Our data (Table 2) show that when interpreting one anaesthetist’s scans, the intraclass correlation coefficients (ICCs) for the plexus area were low and for the artery area were high. When interpreting their own scans, the ICC was low for both measurements. When interpreting one set of scans, the variability in measurements are 44% and 10% for the plexus and artery, respectively; when interpreting individual scans, variability for the plexus measurement is similar at 42% but for the artery is higher at 23%.

Comparing these data sets suggests that the main source of error in the plexus area measurement is in the interpretation rather than acquisition of the scan image. However, with the artery, the opposite appears to be the case. This is perhaps due to the artery being pulsatile and the plexus being a more static image to capture. Our method of standardizing the image capture by ensuring all three structures (artery, rib, and plexus) were in view simultaneously does not appear to result in any extra variability in plexus measurement compared with having a single anaesthetist acquire all images. Nevertheless, the ICC is poor for most measurements. This could imply that what actually constitutes nerve or vascular tissue is open to interpretation when using two-dimensional ultrasound, thus needle placement and drug deposition could be variable.

### Table 2 Scan interpretation data

<table>
<thead>
<tr>
<th></th>
<th>Interpreting one set of scans</th>
<th>Interpreting own scans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean plexus area</td>
<td>0.79 cm²</td>
<td>0.97 cm²</td>
</tr>
<tr>
<td>Mean artery area</td>
<td>0.35 cm²</td>
<td>0.33 cm²</td>
</tr>
<tr>
<td>ICC for plexus area</td>
<td>0.18</td>
<td>0.12</td>
</tr>
<tr>
<td>ICC for artery area</td>
<td>0.83</td>
<td>0.24</td>
</tr>
<tr>
<td>Estimated error of plexus area measurement</td>
<td>0.35 cm² (CI: 0.29–0.42 cm²)</td>
<td>0.41 cm² (CI: 0.35–0.48 cm²)</td>
</tr>
<tr>
<td>Estimated error of artery area measurement</td>
<td>0.035 cm² (CI: 0.029–0.042 cm²)</td>
<td>0.076 cm² (CI: 0.060–0.091 cm²)</td>
</tr>
</tbody>
</table>

### Comparison of intraneural and extraneural shear modulus in the Thiel-embalmed human cadaver

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Direct nerve damage still occurs during ultrasound-guided regional anaesthesia. However, a marked disparity exists between the incidence of inadvertent intraneural injection and overt nerve damage; the latter may be attributable to injection of small volumes of local anaesthetic into subperi-neural rather than subepineurial tissue. Illogically perhaps, clinical testing of needle-tip location relies on the injection of a 1 ml volume of local anaesthetic and the possibility exists of endoneural or intrafascicular injection. Thus, there is a clear need for novel technology to clearly identify intra- and extraneural anatomy in order to make regional anaesthesia safer.

Shear wave elastography is a quantitative and reproducible ultrasound technology increasingly used to differentiate between ‘hard’ breast cancer masses and ‘soft’ normal tissue. Unlike strain elastography, shear wave elastography applies a non-compressive longitudinal acoustic radiation force to underlying tissues, inducing transverse shear waves. Because standard ultrasound systems cannot image shear waves, frame rates up to 20 kHz are used. By measuring the shear wave at several locations and time of travel between points, the shear wave speed is measured. Therefore, the primary objective of the study was the comparison of shear modulus in intra- and extraneural tissue in Thiel-embalmed human cadavers. Secondary objectives included measurement of shear modulus and reproducibility of shear modulus between raters.

B-mode imaging was overlaid with a colour map of shear wave modulus (Supersonic Imagine, Aix-en-Provence, France) and two paired circular regions of interest (ROIs).

### Reference


712P
were selected over the appropriate nerves and adjacent muscle. The paired ROI measures were defined as the statistical units for this study in cadavers. Two anaesthetists measured the shear modulus for intra- and extraneural pairs at the same three anatomical block sites—interscalene, median, and sciatic. Two cadavers were selected for imaging and 20 paired measures taken of each block site by both anaesthetists for the first cadaver. Twenty-five paired measurements were taken in the second cadaver. As the standard deviation of data increased with the modulus, log transformation of data was also undertaken. Linear mixed models with maximum likelihood estimation were used to assess effects. Significance was defined at $P < 0.05$ (two-tailed).

A total of 167 measurements were eligible for analysis. The results are shown in Table 3. Significant effects were identified for the cadaver, operator, block site, and intra-neural vs extraneural measures, the latter having the largest effect. Intraclass correlation coefficient was 0.73 among raters.

In conclusion, differences exist in shear modulus for intra- and extraneural measures and for different block sites. Further studies in human volunteers and patients are required to determine if shear modulus can be used to detect and avoid accidental intraneural injection and damage.

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References

Development and validation of a quantitative phenotype model for malignant hyperthermia susceptibility

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Phenotype–genotype analyses strongly suggest that some $RYR1$-variants only partially contribute to malignant hyperthermia (MH) risk.\(^1\) We previously used four separate quantitative phenotypes derived from data collected during the diagnostic in $vitro$ contracture testing (IVCT) to explore phenotype–genotype correlations.\(^1\) These previous analyses showed that if we wished to use IVCT data to estimate the contribution of mutations to the MH susceptibility phenotype, it would be preferable to develop a composite quantitative phenotype. We have conducted and published a similar study previously,\(^2\) but that was confounded by the need to use the IVCT itself to define true-positive and true-negative cases, thus invoking a circular argument. We are now in a position to use $RYR1$ mutation status of individuals from families with identified causative mutations to define ‘true’ positive and negative cases.

We selected 301 patients (195 MH susceptible, 106 MH negative) who had undergone IVCT testing and had been tested for a familial $RYR1$ mutation associated with MH susceptibility. Using data from 137 of these patients, we generated logistic regression probability (backward conditional and forward conditional) models for a composite quantitative phenotype. For construction of each model, the dependent variable was $RYR1$ mutation status and the predictor variables entered were the pre-drug twitch heights and the muscle contractures at each concentration of test agent for

\[\text{Table 3 Shear modulus as geometric mean (95% confidence interval)}\]

<table>
<thead>
<tr>
<th>Block site</th>
<th>kPa</th>
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<tbody>
<tr>
<td>Intra-</td>
<td>Extraneural</td>
</tr>
<tr>
<td>Intraneural</td>
<td>26.8 (24.6–29.2)</td>
</tr>
<tr>
<td>Extraneural</td>
<td>6.2 (5.7–6.8)</td>
</tr>
<tr>
<td>Sciatic</td>
<td>3.5 (3.0–4.0)</td>
</tr>
</tbody>
</table>

\[\text{Fig 2 ROC curves for (a) model generation and (b) test data sets.}\]
each of the static halothane, dynamic halothane, and static caffeine tests (www.emhg.org). The model providing the optimal combination of face validity and best fit was then prospectively validated using the data from the remaining 164 patients. The accuracy of the models was determined using receiver operating characteristic (ROC) curves. SPSS v19.0 (IBM) was used for analyses.

The model generated using the backward conditional algorithm classified 93.6% of cases correctly, but the forward conditional model produced fewer anomalies and classified 92.6% of cases correctly. The ROC curves for this model in the two sets of patients are shown in Figure 2.

Using the validated model, we will next apply quantitative linkage analyses to families with uncharacterized RYR1 variants in order to estimate the contribution of these variants to the phenotype.

Acknowledgement
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References

Do malignant hyperthermia-susceptible patients have higher baseline core body temperature?
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Preliminary data suggest that mutant RYR1 transgenic knock-in mice susceptible to malignant hyperthermia (MH) have a higher baseline core body temperature than wild-type mice and this is associated with increased energy expenditure (IN Pessah and PD Allen, personal communication). The aim of this study was to compare overnight rectal temperature measurements in patients testing positive for MH and those testing negative.

Table 4 Age, sex and temperature for MH-positive and MH-negative patients.

<table>
<thead>
<tr>
<th></th>
<th>MH-positive</th>
<th>MH-negative</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr, mean, range)</td>
<td>29.7, 5–75</td>
<td>26.5, 5–75</td>
<td>0.26</td>
</tr>
<tr>
<td>Sex (m:f)</td>
<td>29:36</td>
<td>35:30</td>
<td>0.38</td>
</tr>
<tr>
<td>Mean temperature (°C, median, IQR)</td>
<td>36.83, 36.68–37.0</td>
<td>36.69, 36.67–36.7</td>
<td>0.013</td>
</tr>
<tr>
<td>Maximum temperature (°C, median, IQR)</td>
<td>37.4, 37.0–37.7</td>
<td>37.25, 37.0–37.6</td>
<td>0.41</td>
</tr>
<tr>
<td>Temperature range (°C, median, IQR)</td>
<td>1.0, 0.6–1.3</td>
<td>1.17, 0.89–1.49</td>
<td>0.028</td>
</tr>
</tbody>
</table>

For the first 20 yr (1971–1991) of our MH diagnostic service, we used a rectal probe to monitor the core body temperature of patients attending for muscle biopsy from 21.00 h the evening before biopsy until discharge from the recovery room the following morning. The temperature was recorded every 1–2 h by the nursing staff. For the purposes of this study, preoperative temperature data were extracted from the MH Unit records of 130 patients (MH-positive, n=65, MH-negative, n=65) and entered into an anonymized database for analysis. We compared the mean and maximum temperatures and the range for each patient between the groups (Mann–Whitney U-test, IBM SPSS 20 software).

The patients’ ages, sex, and temperatures are shown in Table 4.

Although this was not a tightly controlled thermoregulatory study, our data suggest that MH-positive patients may have higher average core body temperatures than MH-negative patients. The differences we observed are small and of no direct relevance to the clinical context of these patients, but our findings are consistent with a growing body of evidence that the metabolic profile of MH muscle is altered even in the absence of triggering drugs.

Is the nociceptin/orphanin FQ peptide receptor system dysregulated in asthma?
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The nociceptin/orphanin FQ (N/OFQ) receptor (NOP) is a non-opioid member of the opioid receptor family. N/OFQ is the endogenous ligand for NOP and exerts a variety of physiological effects in the nervous system (central and peripheral), the cardiovascular system, the airways, the gastrointestinal tract, the urogenital tract, and the immune system.1 Asthma is a chronic inflammatory airway disease characterized by variable degree of airflow obstruction and airway hyper-responsiveness.2 Current evidence from animal model studies suggests that N/OFQ reduces airway hyper-responsiveness and thus could potentially play a key role in asthma.

Table 4 Age, sex and temperature for MH-positive and MH-negative patients.
role in regulating airway inflammation. To date, there are no data on N/OFQ–NOP expression in structural and immune cells from the normal or diseased human airways. Therefore, the potential role of N/OFQ–NOP system in asthma is unknown. The main objective of this project was to determine NOP and N/OFQ precursor prepro-nociceptin (ppN/OFQ) mRNA and protein expression in primary inflammatory and structural cells from the normal and asthmatic airways and then investigate their functional role.

RNA extracted from the airway cells were specifically probed with nociceptin receptor, ppN/OFQ, and GAPDH (housekeeping gene) TaqMan primers by qRT–PCR. The data were expressed as difference in cycle threshold relative to GAPDH mRNA expression. To determine NOP receptor protein expression, radioligand saturation binding assays were performed using [3H]UFP-101 and [125I]N/OFQ where there was sufficient tissue.

No ppN/OFQ mRNA expression could be detected in any of the human airway cells. Average $\Delta C_t$ values recorded for NOP mRNA expression were 11.37 (1.25) [mean (so); $n=6$] in normal human airway smooth muscle cells (HASMs) and 10.77 (1.04) [mean (so), $n=7$] in asthmatic HASMs. However, using radioligand saturation binding assays, we failed to detect NOP receptor protein expression on normal and asthmatic HASMs ($n=4$ each). As a control for these experiments were able to detect high levels of expression in cell line expressing recombinant human NOP. With human bronchial epithelial cells, $\Delta C_t$ values observed in normal cells for NOP mRNA were 11.39, 11.36, 8.12, and 8.10 (mean $\Delta C_t$=9.75, $n=4$) and those recorded in asthmatic cells were 12.12, 9.61, 10.31, and 10.46 (mean $\Delta C_t$=10.63, $n=4$). Similarly, $\Delta C_t$ values observed for human lung mast cell NOP mRNA were 4.63, 7.65, and 6.95 (mean $\Delta C_t$=6.41, $n=3$) and those recorded in human lung fibroblasts were 4.10, 4.70, and 5.01 (mean $\Delta C_t$=4.60, $n=3$).

This is the first study to investigate the expression of NOP receptors on human airway structural and immune cells. These studies revealed that human lung mast cells and lung fibroblasts express relatively higher amounts of NOP mRNA. None of the cells expressed ppN/OFQ mRNA. Further functional studies on these cells would reveal their physiological role in regulating inflammation within the airways. This could potentially identify novel molecules for the management of airway inflammatory diseases, including asthma.

Acknowledgement

Funded by Asthma UK.

References

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Randomized crossover trial comparing a single-use polyvinyl chloride laryngeal mask with a single-use silicone laryngeal mask made by the same manufacturer

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Single-use polyvinyl chloride (PVC) laryngeal masks (LMs) have increased in use since their introduction in 1997, mainly due to concerns regarding possible prion transmission with reusable silicone LMs. 1, 2 Silicone potentially offers increased flexibility when compared with PVC, which may reduce airway trauma. 3 A number of single-use silicone LMs are now available, but are more expensive than PVC versions. We compared a single-use PVC (pLM) with a single-use silicone (sLM) LM, both produced by Flexicare Medical and identical in design except for the material from which they were manufactured.

After local ethical approval, 72 ASA I and II patients, aged 18–79, undergoing elective surgery and suitable for LM insertion, were recruited. I.V. access and full monitoring was instituted before induction of anaesthesia with fentanyl 1 $\mu$g kg$^{-1}$ and propofol 1%, titrated until loss of the eye lash reflex. Sevoflurane was titrated until jaw relaxation was achieved. The LM size was chosen and inserted according to the manufacturer’s guidance. The order of insertion was randomly assigned. Insertion success, insertion time, leak pressure, position (Brimacombe score), subjective ease of insertion, and ease of ventilation were recorded, as were pre- and post-insertion vital signs. After 3 min of steady-state anaesthesia, the first LM was removed, the second LM inserted, and identical tests were performed. Intra- and postoperative complications were recorded.

The mean (so) age was 39 (17) yr and BMI was 25.9 (4.9) kg m$^{-2}$. The male:female ratio was 54:18 and the ASA I:II ratio was 52:20.

McNemar's test did not demonstrate a significant difference for first-time insertion rate ($P=0.39$) (Table 5). There was no difference between the performance of the LMs with respect to the Brimacombe score, insertion time, or ease of ventilation. The mean seal pressures for the sLM were higher ($P=0.017$, difference of 1.6 cm H$2$O). The pLM was easier to insert ($P=0.025$).

In conclusion, we did not find a difference in the first-time insertion rates of single-use PVC and silicone LMs made by the same manufacturer. The higher seal pressure for the

| Table 5 First-time insertion rate (n=72) |
|-----------------|-----------------|
| pLMA            | sLMA            |
| Success         | 68 (94%)        | 64 (89%)        |
| Failure         | 4 (6%)          | 8 (11%)         |
sLM is unlikely to be clinically significant. Subjectively, the pLM was easier to insert, which may be due to user familiarity.

References

Dexmedetomidine pretreatment reduces the cardiac adverse events of intravenous administration of ropivacaine in rats
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D. Y. Wang+1 and G. A. McLeod2

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Cardiac toxicity is a serious side-effect of amide local anaesthetics such as ropivacaine. Our hypothesis in this laboratory study was that dexmedetomidine, an α2- adrenoceptor agonist, prevented cardiac adverse effects during the administration of ropivacaine in a small animal model.1–6

Forty Wistar rats were randomly allocated to four groups of increasing dose of dexmedetomidine infused via a femoral vein over 10 min and monitored with ECG and mean arterial pressure (MAP). The groups were: A (0 μg kg−1), B (5 μg kg−1), C (10 μg kg−1), and D (15 μg kg−1). Thereafter, ropivacaine 1% was infused at 1 ml h−1 via a femoral vein until an adverse cardiac event occurred, defined as: QRS >20% of the baseline, cardiac arrhythmia or MAP or heart rate <25% of the baseline. The plasma concentration of ropivacaine was measured at the time of the cardiac adverse event.

In the control group, cardiac adverse events occurred at mean (so) 846.7 (124.7) s after ropivacaine infusion. In contrast, cardiac adverse events occurred later in Groups B, C, and D, respectively (Table 6).

These results show that dexmedetomidine pretreatment can delay the onset of cardiac adverse events in a dose-dependent manner during ropivacaine i.v. administration. However, further investigation is required to determine the optimal dose of dexmedetomidine.

Table 6 Mean (so) ropivacaine dose, plasma concentration, and time to onset of cardiac adverse event. *P<0.05 compared with the control group A, ANOVA

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ropivacaine dosage (mg)</td>
<td>2.36 (0.34)</td>
<td>3.98 (0.17)*</td>
<td>3.44 (0.34)</td>
<td>3.63 (0.57)*</td>
</tr>
<tr>
<td>Ropivacaine concentration in plasma (μg kg−1)</td>
<td>0.59 (0.07)</td>
<td>3.36 (0.49)*</td>
<td>2.78 (0.43)</td>
<td>3.50 (0.40)*</td>
</tr>
<tr>
<td>Time to onset of cardiac adverse event</td>
<td>847 (125)</td>
<td>1433 (66)*</td>
<td>1235 (124)*</td>
<td>1300 (209)*</td>
</tr>
</tbody>
</table>

Patients’ inability to perform a preoperative cardiopulmonary exercise test risk predicts inferior medium-term mortality after major colorectal surgery
R. A. Struthers+1,2,3, C. Lai+2,3, C. P. Chlland+2,3, K. B. Hosie*1, J. R. Sneyd1,2,3 and G. W. Minto*1,2,3

1 Department of Anaesthesia, 2 GI Directorate, Derriford Hospital, and 3 Peninsula Medical School, Plymouth, UK

Patients with poor functional capacity secondary to comorbidity or physical de-conditioning may be at higher risk of mortality after major surgery.1 We studied the outcomes of patients whose functional capacity was characterized by cardiopulmonary exercise testing (CPET) and of those who were unable to perform the test.

All patients undergoing elective major colorectal surgery at our Colorectal Specialist Unit undergo preoperative CPET to assist in the planning of perioperative care. With ethics committee approval, we followed the outcomes of 238 patients stratified into ‘Fit’ (Group 1, n=161), ‘Unfit’ (Group 2, n=62), and ‘Very Unfit’ (Group 3, n=15) on the basis of their CPET results and a further 17 patients who were unable to cycle a stationary bicycle at all or sufficiently long to provide an interpretable result, ‘Unable to CPET’.

Acknowledgement
This study was supported by departmental funds and there were no conflicts with other sources of funding.

References

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References
(Group 4, n=17). All patients were followed to 500 days after surgery (Fig. 3).

Seven patients from Group 4 were unable to cycle due to lower limb osteoarthritis, seven due to general physical infirmity, two from perineal pain, and one refused.

In this study, patients who were unable to perform a CPET had appreciably high medium-term mortality after elective major colorectal surgery. This is an important consideration when consenting such patients for surgery.

Reference


Protocol presentation: evaluation of a device to detect early respiratory deterioration

S. Rodgers1, G. Drummond2, J. Tocher1, D. Arvind3, A. Waite4, C. Weir5 and J. Smith5

1 School of Health in Social Science, Edinburgh, UK. 2 Department of Anaesthesia and Pain Medicine, Edinburgh, UK. 3 Centre for Speckled Computing, Edinburgh, UK. 4 NHS Lothian, Edinburgh, UK.

We have developed a small non-invasive device that senses body movement and reliably measures respiratory rate in patients after abdominal surgery.1 Respiratory rate is a good marker of developing illness2 and can predict ITU referral and outcome.3 Intensive surveillance with pulse oximetry can reduce emergencies and ITU admission.4 If reliable frequent measures of respiratory rate are included into a routine physiological warning score, it is possible that:

- the ‘weak link’ in the early detection of deterioration might be strengthened;
- early detection would allow prompt escalation of care and improve outcome.

We present the plans we have for testing these hypotheses. We propose:

- validation of the device in acute medical patients (problem: consent in acute illness).

In this time period, we hope to obtain CE marking and MHRA approval.

We propose:

- A feasibility study to define several aspects of use of a new device:
  - staff attitude, response, and use of a new monitor,
  - influence of more intensive monitoring on interventions,
  - methods to measure outcome.

Population: we plan to study ‘level 1’, that is, patients receiving ward-based care, because patients considered at risk of substantial postoperative morbidity are generally given higher levels of care which include more intensive monitoring. Patients would be studied before and after routine and emergency colorectal and urological surgery (we have two suitably sized local units) with a phased introduction and assessment using the following: Surgical Apgar, P-Possum, Charlson age–comorbidity index, Duke activity status Index, Scottish index of multiple deprivation 2009 followed by measures after surgery, using: calls to hospital at night team, postoperative morbidity score, EuroQol EQ-5D and SF-12, dependency-weighted LOS and 28 day mortality, TrakCare electronic patient record system, and other clinical management indicators.

We would value general comments but specifically comments on consent procedures, assessment tools, and study design.
Radial artery to digit pressure transit time is affected by low-pass filter features

J. Koch* and G. B. Drummond

Department of Anaesthesia and Pain Medicine, Royal Infirmary, Edinburgh, UK

We are studying the timing of vascular events in the hand to allow non-invasive measurements of arterial pressure and assessment of vascular responses in the finger. We found that measurements are substantially affected by processing of the signal. Our previous study used recordings of non-invasive radial artery pressure (Colin CBM-700) and finger photoplethysmograph in 12 volunteers. Signals were digitized at 10 kHz. We detected waveform troughs and peaks using second derivatives. Data were analysed with Octave and Prism5 (GraphPad). The photoplethysmograph device we used had no high-pass filter but contained a low-pass filter (2-pole Butterworth, 8.5 Hz) to remove 50 Hz noise.

We measured time delay, using the upsweep of the radial artery pressure and the corresponding point recorded in a non-compliant pressure cuff applied to the finger. The wrist to digit delay was much less than the delay in the photoplethysmograph signal. The delay from the radial artery to photoplethysmograph was 68 (5) ms, but the delay from the radial artery to digital pressure changes was only 4 (5) ms. To assess the impact of the low-pass filter on the photoplethysmograph signal, we applied an equal filter to the digital pressure recordings.

Figure 4 shows a representative subject. Low-pass filtering caused a substantial delay in the digital pressure wave. Measurements of peripheral arterial transmission time depend substantially on the characteristics of the signal processing. One useful application of DC photoplethysmograph measurements is generating pressure-volume plots for finger vessels, but this requires accurate knowledge of exact timing of events distal to the radial artery. Previous studies have simply aligned pressure and volume signals using a recognizable marker such as the turning point. Our measurements show that delays in all parts of the measurement system should be evaluated before accurate measurements are possible.

References


Dexamethasone prolongs the duration of brachial plexus block: a meta-analysis

A. Banerjee*, B. J. Morton* and J. M. Hunter

Royal Liverpool University Hospital, Prescot Street, Liverpool, UK
There has been recent interest in using adjuncts to local anaesthetics to prolong analgesia after peripheral nerve blockade. Dexamethasone has been an adjunct of particular focus in a number of prospective randomized controlled trials (RCTs) examining its efficacy in brachial plexus block. This meta-analysis examines the findings from these RCTs.

The keywords: human, brachial plexus, interscalene, supravclavicular, infraclavicular, nerve block, and dexamethasone were used to search Medline, EMBASE (from 1980 to 2011), and Google Scholar to identify RCTs and published abstracts from scientific meetings. No language restrictions were applied. The Jadad scale was used to assess the quality of the RCTs. RevMan statistical software utilized inverse variance and a random effect model to calculate weighted mean difference with 95% confidence intervals for continuous variables. The primary outcome measure was duration of analgesia, with the secondary outcomes, times to onset of maximum motor and sensory block, and to recovery of motor function.

Seven studies comprising 563 patients published from 2006 to 2011 were included. The Jadad score for the studies was 1–5. Addition of dexamethasone to the local anaesthetic (levobupivacaine, mepivacaine, lidocaine ± epinephrine, or a combination) increased the duration of postoperative analgesia. Recovery of motor function was delayed in patients who received dexamethasone, but there was no significant difference in time to onset of sensory or motor block (Table 7).

The addition of dexamethasone to brachial plexus blocks increases the length of analgesia with no delay in time to onset of sensory or motor block. A delay in recovery of motor function may occur. Dexamethasone has a role as an adjunct in brachial plexus blockade.

### Table 7

<table>
<thead>
<tr>
<th>Duration of analgesia</th>
<th>Number of studies/patients</th>
<th>Mean difference and CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>-418.3 (−555.4, −281.2)</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Onset of sensory block</td>
<td>5/259</td>
<td>1.49 (−0.06, 3.04)</td>
<td>0.06</td>
</tr>
<tr>
<td>Onset of motor block</td>
<td>5/259</td>
<td>0.97 (−0.4, 2.3)</td>
<td>0.16</td>
</tr>
<tr>
<td>Recovery motor function</td>
<td>3/180</td>
<td>−465.57 (−782.02, −149.13)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### Table 8

Perioperative microvascular flow indices, haemodynamic measurements and selected clinical outcomes. Data are presented as medians. No significant difference between T1 or T6–12 and preoperative values by Mann–Whitney U-test.

<table>
<thead>
<tr>
<th>n</th>
<th>Perfused vessel density</th>
<th>Microvascular flow index</th>
<th>Stroke volume (ml)</th>
<th>Intraop. fluid (ml kg⁻¹)</th>
<th>Length of stay (days)</th>
<th>Pts with day 5 POMS score &gt;0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T0 T1 T6–12</td>
<td>T0 T1 T6–12</td>
<td>Pre-op. End-op.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>6 13.3 12.5 11.5 2.9 2.9 2.5</td>
<td>89 98</td>
<td>30.5 8.9 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GDT</td>
<td>7 13.7 12.7 14.4 3.0 2.8 2.8</td>
<td>67 101</td>
<td>89.6 7.9 3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### References

1. Thornton PC, Grant SA, Breslin DS. Int Anesthesiol Clin 2010: 48; 59–70

### Effects of goal-directed fluid therapy during colorectal surgery on the sublingual microcirculation

S. M. Brown*1,3, C. Challand*2,3, J. R. Sneyd1,3, R. Struthers1,3, and G. Minto1,3

1 Directorate of Anaesthesia, 2 Directorate of Gastroenterology, Derriford Hospital, and 3 Peninsula Medical School, Plymouth, UK

We have previously reported that intraoperative goal-directed fluid therapy, GDT, had no impact on clinical outcomes for 179 patients having major elective colorectal surgery. We performed side-stream dark-field imaging of the sublingual capillaries at specified perioperative time points on 27 of these patients to investigate the effects of GDT on microcirculatory blood flow.

Side-stream dark-field imaging was undertaken using a microcamera (Microscan, Microvision, Amsterdam, The Netherlands) at three specified time points: T0 immediately before anaesthesia, T1 immediately after surgery, and T6–12, between 6 and 12 h after operation. The first three images suitable for study at each time point were analysed according to consensus methodology using AVA 3.0 software (Microscan, Microvision).

Fifty-three patients were assessed for inclusion. Twenty-six were excluded (15 refused, 7 no suitable investigator, 4 other reasons) and 27 randomized: 13 GDT and 14 control. Six GDT and 8 control patients were excluded from analysis due to poor video clip quality (Table 8).

This pilot work illustrates the difficulties involved acquiring microvascular images of sufficient quality for studies in awake patients. The results mirror the clinical outcomes of our previous study; however, power is limited. These pilot data have been
used in the power calculation of a follow-up GDT randomized trial on 220 patients undergoing major abdominal surgery.

**Acknowledgement**

Funded by AAGBI through the NIAA, and South West Regional Innovation Fund.

**References**


**Assessment of a non-invasive haemoglobin monitor (Masimo SpHb) in infants and small children undergoing craniofacial surgery**

H. Gill* and M. Sury
Great Ormond Street Hospital for Children, London, UK

Major haemorrhage and haemodilution are common during craniofacial surgery in small children and may be better managed with a continuous monitor of haemoglobin (Hb) concentration. The Masimo Pulse CO-Oximeter™ is a pulse oximeter that monitors SpHb®, yet its accuracy during haemorrhage is uncertain. A recent study in 20 adults showed that 22% of laboratory Hb (LabHb) was >2.0 g dl⁻¹ different from SpHb; no patients had Hb <7.5 g dl⁻¹. We present our preliminary data comparing LabHb with SpHb during craniofacial surgery.

This is a prospective observational study in children <6 yr of age and under 20 kg. Transfusion practice was not changed by the study. Ethics committee approval was obtained and parents gave written informed consent. Timing of blood samples was dictated by clinical judgement. The SpHb probe was attached to a toe and SpHb data were stored on a PC for analysis later. The monitor was hidden from the clinical team. We aimed to determine the confidence interval of the limits of agreement when LabHb was <7 g dl⁻¹. Assuming that the difference between SpHb and Lab Hb was <1 g dl⁻¹, we estimated we needed to study >40 children.

Twelve patients have been studied; mean weight was 11.34 kg (range 9.65–14.1). Forty-five Hb pairs were analysed. The range of LabHb was 5.5–12.9 g dl⁻¹. Five children had at least one LabHb below 7 g dl⁻¹. Using all Hb pairs, the mean bias of SpHb was 0.93 g dl⁻¹ (SD = 0.98). In one patient, the SpHb trace failed to identify a LabHb of 5.5 g dl⁻¹ (Fig. 5).

The level of agreement was wide, although in most patients, the SpHb followed the trend of the LabHb. On average, the SpHb was 1 g dl⁻¹ higher than LabHb. More data are needed.

**Reference**


**Differences in the lumbar epidural pressure between full-term pregnant and non-pregnant women**

H. C. Ma*1, L. Nan*1, X. G. Yang*1, Y. H. Feng*1, D. Y. Wang*1 and G. A. McLeod2
1 Department of Anesthesiology, The First Hospital of Jilin University, Changchun 130021, China. 2 Institute of Academic Anaesthesia, University of Dundee, Dundee, UK

The loss of resistance technique is routinely used to indicate Touhy needle placement during epidural block. Epidural pressure is one variable influencing loss of resistance and may change with pregnancy 1 and position.2 Therefore, the aim of this study was to compare epidural pressure in full-term pregnant and non-pregnant women during epidural block.3

Twenty full-term pregnant and 15 non-pregnant women were included in this study. Epidural block was performed in the left lateral position at the L2–3 interspace using a 16 G Touhy needle. Epidural pressure was measured on

![Fig 5 Bland–Altman plot showing mean at –0.93 g dl⁻¹ (2 SDs either side at –2.89 and 1.03 g dl⁻¹).](https://academic.oup.com/bja/article-abstract/108/4/709P/257090)

**Table 9 Mean (sd) epidural pressures (mm Hg) measured at four time points in full-term parturient (n=15) and non-pregnant women (n=20) during epidural block. *P<0.05**

<table>
<thead>
<tr>
<th></th>
<th>T0</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant</td>
<td>17.1 (2.0)</td>
<td>14.3 (0.6)</td>
<td>24.0 (1.0)</td>
<td>23.8 (1.2)</td>
</tr>
<tr>
<td>Non-pregnant</td>
<td>16.1 (3.1)</td>
<td>11.7 (1.0)*</td>
<td>20.5 (1.8)*</td>
<td>20.2 (1.7)*</td>
</tr>
</tbody>
</table>
four occasions: T0, Tuohy needle entering the epidural space; T1, 90 s after placement of the epidural catheter; T2, after returning to the supine position; and T3, after injection of local anaesthetics into the epidural space.

No differences in mean (SD) epidural pressure existed between groups at T0: 16.1 (3.1) vs 17.1 (2.0), P > 0.05. However, differences existed between groups at T1, T2, and T3 (Table 9). Epidural pressure increased in both groups after turning the patients into the supine position and after injection of local anaesthetics, but increased more in the pregnant group.

This study showed higher pressure in the epidural space in the full-term pregnant patient compared with the non-pregnant women.

References
2. Messih MNA. Anaesthesia 1981; 36: 775–82

Endogenous brain oscillations during sedation: initial results of a magnetoencephalography and functional magnetic resonance imaging study

N. Saxena*1, A. Diukova*2, M. Venzi*2, T. Gili*2, D. Huckle*1, S. Bell*1, R. G. Wise*2 and J. E. Hall1

1. Department of Anaesthetics, ICM and Pain Medicine, School of Medicine and 2. CUBRIC, School of Psychology, Cardiff University, Cardiff, UK

We investigated the modulation of endogenous brain activity during mild sedation using a multimodal approach: magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI). As the thalamus plays a pivotal role in sedation and anaesthesia,1 we focus on its role in brain oscillations measured electrophysiologically (MEG) and haemodynamically (fMRI).

Eight healthy male volunteers (age [mean (SD)]; 27.5 yr (7.2)) underwent (eyes-closed) 5 min resting-state whole-head MEG scans (CTF-275 channel gradiometer system). Five of these undertook 8 min of resting-state fMRI over 1 week later (3T GE HDx system). MEG and fMRI scans were performed both before and during mild sedation (TCI propofol to achieve OAA/S score 4). MEG analysis: power spectral density analysis was calculated for 1–80 Hz using Fourier transforms in Matlab. MRI analysis: images were acquired using a blood oxygen level-dependent weighted imaging sequence (TR=3 s, TE=35 ms, matrix=64 × 64, 50 slices). FMRI data were analysed using FSL (fmrib.ox.ac.uk/fsl). Images were corrected for movement, normalized to stereotaxic coordinates of MNI, and smoothed. Resting-state functional connectivity (fc): between the thalamus and the rest of the brain was evaluated by extracting individual subjects’ mean BOLD signal time series from the thalamus. Within-subject statistical comparisons of functional connectivity were performed at the group level between sedated and un-sedated conditions (Z-statistic images with cluster thresholding).

Increased power of the central delta, frontal alpha, central and frontal gamma, and central, frontal, and temporal beta rhythms was seen during sedation with MEG. Seeding in the thalamus revealed increased fMRI functional connectivity in a network involving both deep brain structures and cortical areas. Sedation (Fig. 6) increased the connectivity between the thalamus both with areas of the neocortex and with the rostral brainstem. There was increased connectivity between the precentral gyrus (primary motor cortex), postcentral gyrus (primary somatosensory cortex), and a network of cortical areas involved in the MEG-recordable oscillations.

Increases in functional connectivity seen with fc-fMRI may represent an increase in synchrony of thalamic and cortical neurones involved in the MEG-recordable oscillations.

References