

Value of Cushing reflex as warning sign for brain ischaemia during neuroendoscopy[†]

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Background. During an endoscopic neurosurgical procedure a sudden increase in intracranial pressure may occur at any time. We present a prospective study of haemodynamic changes during such procedures.

Methods. Physiological data were recorded during the whole operative procedure in 17 consecutive patients who underwent an endoscopic neurosurgical procedure under general anaesthesia. Monitoring included invasive blood pressure, intracranial pressure, electrocardiogram, end-expired carbon dioxide, pulse oximetry and heart rate. Pressure and ECG waveforms were recorded at 100 Hz and evaluated in a subsequent offline analysis.

Results. In almost every case, the occurrence of hypertension and tachycardia was clearly the result of an increase in intracranial pressure. Also, a Cushing reflex developed in almost every case where the cerebral perfusion pressure dropped below 15 mm Hg. The occurrence of bradycardia was not systematically associated with a low cerebral perfusion pressure.

Conclusion. In this study, we describe the haemodynamic effects of increased intracranial pressure during endoscopic neurosurgical procedures and their respective sequence of events at high temporal resolution. Although most clinicians rely on the occurrence of bradycardia to diagnose intracranial hypertension during endoscopic neurosurgical procedures, we show that a simultaneous onset of hypertension and tachycardia is a better indicator of impaired brain perfusion. Waiting for a persistent bradycardia to alert the surgeon during endoscopic neurosurgical procedures could allow severe bradycardia or even asystole to develop.

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Classically, the 'Cushing reflex' has been reported as the occurrence of hypertension, bradycardia and apnoea following intracranial hypertension.¹ Various animal pathophysiological studies, describing haemodynamic changes following sudden increases in intracranial pressure, refined Cushing's findings by showing an initial tachycardia associated with hypertension before the onset of bradycardia.² In a clinical context, observation of increased intracranial pressure resulting in haemodynamic instability was previously limited to a phenomenon following a time course of hours, days or months depending on the underlying pathology (e.g. subdural haematoma, tumours, hydrocephalus, etc.). At the time of clinical presentation, symptoms invariably already consisted of bradycardia and hypertension.

Since the introduction of neuroendoscopy³ in the treatment of cerebral pathology, the problem of early recognition of any sudden increase in intracranial pressure has become crucial. During this procedure, continuous rinsing of the ventricular cavities might cause a sudden increase in intracranial pressure. As a direct measurement of the intracranial pressure via the endoscope is not always accurate, the anaesthetist relies upon sudden haemodynamic changes to alert the surgeon. Many clinicians still use the occurrence of bradycardia and hypertension as an indication of acute intracranial hypertension.^{4–7} In a retrospective study, we showed that focusing only on these late symptoms might

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risk prolonged intracranial hypertension with a higher incidence of deleterious complications. Therefore we concluded that the occurrence of hypertension and tachycardia offers the most reliable warning sign of increased intracranial pressure during neuroendoscopy. This presumption was made on the basis of a review of animal studies² and clinical observations published early in the twentieth century.⁸

However, accurate simultaneous measurements of mean arterial blood pressure and intracranial pressure are essential to diagnose a decrease in the underlying cerebral perfusion pressure. As a precise description of the haemodynamic changes in relation to the intracranial pressure during neuroendoscopy is still lacking in the literature, the aim of this prospective observational study was to offer a high-resolution description of this phenomenon. Additionally, we aimed to determine the most suitable variables for early detection of brain ischaemia, together with possible strategies to keep the cerebral perfusion at a safe level.

Methods

After institutional ethics committee approval and written informed consent was obtained, haemodynamic data for consecutive patients between February 1, 2003 and February 1, 2004 who underwent neuroendoscopy for the treatment of obstructive hydrocephalus or tumour surgery under general anaesthesia were recorded throughout the operative procedure. Patient ages ranged from 1 month to 84 years.

The patients were not premedicated. Upon their arrival in the operating theatre the usual monitoring was applied: ECG, pulse oximetry and blood pressure by automated cuff. In children, if inhalation induction was indicated because of difficulty in obtaining intravenous access, sevoflurane was used to permit intravenous cannulation. After securing the intravenous access as quickly as possible, the sevoflurane was discontinued and the intravenous sequence instituted. In adults, anaesthesia was induced with propofol 1–2 mg kg⁻¹ and remifentanyl 0.1 µg kg⁻¹ min⁻¹, and the trachea was intubated (facilitated with cisatracurium 0.15 mg kg⁻¹ i.v.). Anaesthesia was maintained with propofol 6 mg kg⁻¹ h⁻¹, remifentanyl 0.1–0.2 µg kg⁻¹ min⁻¹ and cisatracurium 0.15 mg kg⁻¹ h⁻¹; the patients were ventilated with an oxygen–air mixture ($F_{I_{O_2}}$ 40%) to achieve an end-tidal CO₂ between 30 and 35 mm Hg. After induction, a 20-gauge 8-cm PE catheter (Laeder Cath, Laboratoires Pharmaceutiques, Vygon 95440, Ecouen, France) was inserted percutaneously into a radial artery, 1 cm proximal to the wrist. The catheter was connected via a 150-cm long (1.5 mm internal diameter) rigid pressure tubing, filled with saline, to a continuous-flush pressure-transducer system (Becton Dickinson Critical Care Systems, Singapore) to monitor beat-to-beat blood pressure. The heart rate was monitored continuously via the ECG. All patients remained in the supine position with the head flexed, so that the burr hole was located at the apex. Patients were kept

normothermic by a forced-air warming system. Once stable profiles of capnography and blood pressure were reached, ventilatory and drug delivery settings were kept unchanged. All vital signs were monitored using an S5-monitor (Datex-Ohmeda, Helsinki, Finland).

A rigid Caemaert endoscope (Wolf, Knittlingen, Germany) with an outer diameter of 6 mm was used. After positioning the patient and infiltrating with local anaesthetic, a burr hole was made at the classical point for endoscopic entry to the lateral ventricle and the standard neuroendoscopic introduction was performed.³ Once the endoscope was introduced into the ventricle or the cystic space,⁹ the mandrins of the two irrigation channels and the working channel were retracted, and the inlet and outlet irrigation tubes were connected. The outlet of the endoscope flushing system was connected by a 300-cm long pressure tube to a pressure transducer for continuous monitoring of the intracranial pressure.^{4,6} The level of the foramen of Monro was used as the zero reference point for both pressure transducers.

During the introduction of the endoscope the optical element was already inserted in the correct channel. We then began irrigation with Ringer lactate at body temperature. We made sure that the distal end of the outflow tube was fixed at the same level as the burr hole, so that there was no siphoning effect or raised intracranial pressure. At moderate flushing rates of the endoscope, the pressure value reliably represents the intracranial pressure at the bottom of the fourth ventricle, as long as no obstruction or increased resistance occurs inside the endoscope. The inflow of the rinsing fluid is managed by the surgeon. Using the same zero reference point for both transducers allows a precise determination of the cerebral perfusion pressure, independent of patient positioning. Both systems were calibrated against atmospheric pressure and both pressure transducers were connected to an S5-monitor (Datex-Ohmeda, Helsinki, Finland). All data from the monitor were recorded via Collect Software[®] (Datex-Ohmeda, Helsinki, Finland) for subsequent offline analysis. All variables were recorded numerically at 0.2 Hz. In addition, ECG, invasive arterial pressure and intracranial pressure waveforms were registered at 100 Hz.

In subsequent offline analysis, the data were transformed to an ASCII file and imported into Microsoft[®] Excel. The waveforms were analysed using invasive arterial pressure (Art) and intracranial pressure (ICP) signals. After importing the values into Microsoft[®] Excel, arterial and intracranial pressure waveforms, mean arterial pressure, mean intracranial pressure, mean cerebral perfusion pressure and heart rate were determined.

The cerebral perfusion pressure was calculated as the difference between mean arterial pressure and mean intracranial pressure. High-resolution waveforms at 100 Hz were visualized for detailed description of haemodynamic phenomena. In addition, trend curves were created at 1 Hz for whole-procedure evaluation of haemodynamic effects. The four algorithms are given in the Appendix.

All data were analysed for possible events: different classes of combined events were defined as shown in Table 2. For changes in cerebral perfusion pressure, we defined an event as a decrease in cerebral perfusion pressure lower than 50 mm Hg. Subsequent categories were defined as a cerebral perfusion pressure below 50, 40, 30, 20 and 15 mm Hg. For changes in heart rate and blood pressure, we defined brady/tachycardia and hypo/hypertension as a change of 20% from baseline lasting at least 3 s. The baseline values were defined as the mean values in the minutes during the procedure before an increase of the intracranial pressure occurred. Since the administration of remifentanyl was kept constant and tolerance¹⁰ for its analgesic and haemodynamic effects¹¹ may develop, rescaling the baseline values was sometimes necessary. A change in blood pressure or heart rate when the cerebral perfusion pressure was >50 mm Hg was defined as an isolated haemodynamic event.

A sensitivity/specificity analysis was performed based on decreases of the cerebral perfusion pressure below certain levels and the incidences of Cushing reflexes. In this assessment, we defined a Cushing reflex as a simultaneous occurrence of hypertension and tachycardia. The sensitivity of a Cushing reflex to detect a decrease in cerebral perfusion pressure below a certain value was determined as the ratio of the number of decreases in cerebral perfusion pressure coinciding with a Cushing reflex to the total number of decreases of cerebral perfusion pressure below the specified value. The specificity of a Cushing reflex in detecting a decrease in cerebral perfusion pressure was defined as the ratio of the number of Cushing reflexes associated with a decrease in cerebral perfusion pressure below a certain level to the total number of observed Cushing reflexes.

For statistical analysis of the data, non-parametric correlations were determined using SPSS 11.0 software (SPSS Inc., Chicago, IL, USA).

All patients awoke in the operating theatre and were directly transferred to the intensive care unit. For assessment of postoperative complications, intensive care files were evaluated for possible events. As described by Buxton and colleagues,¹² possible complications in neuroendoscopy are delay in waking, pneumoencephalus, pneumoventricle, convulsions, transient anisocoria, transient hemiparesis, haemorrhage, cerebral infarction, transient fever, meningism, infection, short-term memory loss, diabetes

insipidus, inappropriate antidiuretic hormone secretion, transient cerebrospinal leaks, chronic subdural haematomas, traumatic basilar aneurysm and hydrocephalus.

Results

The data recorded (total recording time 19.1 h covering 10.9 h of endoscopy) from 17 patients were analysed. The preoperative clinical characteristics of the patients are shown in Table 1. The end-tidal CO₂ concentration and body temperature stayed within target ranges in all patients.

Table 2 shows the incidence of haemodynamic changes for each patient in the seconds following a decrease in the cerebral perfusion pressure to a certain level, together with the type of procedure performed and the age of the patient. The incidences of haemodynamic changes with a normal cerebral perfusion pressure are also given (Isolated). Hypertension associated with tachycardia was prominently present when the cerebral perfusion pressure dropped below 15 mm Hg. At higher cerebral perfusion pressure levels, the changes were less prominent.

Figure 1 shows the relation between cerebral perfusion pressure and the relative changes in heart rate and mean arterial pressure. Figure 2 shows the relation between the intracranial pressure and the relative changes in heart rate and mean arterial pressure.

The sensitivity and specificity for the determination of decreased cerebral perfusion pressure by a Cushing reflex are shown in Table 3. Because multiple haemodynamic events occurred during tumour retraction in patient 14, haemodynamic changes may have been induced by direct stimulation of the brainstem. However, this was the only patient where severe bradycardia and hypertension were seen during a decreased cerebral perfusion pressure. Therefore the sensitivity analysis was performed using all patients and also with all patients except patient 14.

We have selected three patients for a detailed description. In the first (Fig. 3A) a sustained intracranial pressure of 50 mm Hg over 90 s induced no haemodynamic changes. This may be explained by the fact that the cerebral perfusion pressure was >35 mm Hg. At 2490 s, the intracranial pressure increased further, resulting in a decrease in the cerebral perfusion pressure and the occurrence of tachycardia and hypertension. After alerting the surgeon, the pressure was

Table 1 Preoperative clinical characteristics of the 17 patients studied. Intracranial HT refers to the possibility, on clinical grounds, for the patient to have pre-operative intracranial hypertension. Hb, haemoglobin; Hct, haematocrit

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Gender	M	F	M	F	F	M	M	F	F	M	M	M	M	M	M	M	M
Age	8	9	21	19	84	71	20	3 m	73	37	19	44	11	12	11	1 m	62
Weight (kg)	27	40	78	70	60	70	70	3.4	54	58	70	80	45	37	44	3.15	83
Hb (g dl ⁻¹)	12.2	12.4	16.1	12.1	11.8	13.7	14.0	8.6	11.4	14.4	14.0	12.7	14.9	13.3	13.4	9.7	12.6
Hct (%)	37.2	35.3	45.5	37.7	35.0	41.6	39.6	27.5	34.8	40.6	39.5	35.4	42.5	38.6	41.3	29.3	37.5
Glucose (g litre ⁻¹)	0.96	0.82	1.14	1.09	0.91	0.84	0.96	1.11	1.13	1.09	1.04	1.34	0.83	1.11	0.9	0.66	1.54
Intracranial HT	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes	No

Table 2 Procedure, age and incidence of hypertension (H), tachycardia (T), bradycardia (B) or Cushing reflex (H+T) in the seconds following a drop of the cerebral perfusion pressure for every patient. Isolated cases of haemodynamic change are also noted. In the last row, the sum of all the events in the respective category is shown. The procedures are: revision of a ventriculoperitoneal shunt (revision); diagnostic ventriculoscopy (ventr.scopy); pineal tumour resection (Tumour); third ventriculostomy (3VS); fenestration of a ventricular cyst (fenestr.); or biopsy of a pineal tumour (biopsy)

Patient	Age	Procedure	Isolated			40<CPP<50			30<CPP<40			20<CPP<30			15<CPP<20			CPP<15																			
			H	T	H+T	B	H+B	-	H	T	H+T	B	H+B	-	H	T	H+T	B	H+B	-	H	T	H+T	B	H+B												
1	8	Revision			3																																
2	9	Ventr.scopy			1			2																													
3	21	Tumour	1		18			9	4	2																											
4	19	3VS			6			1																													
5	84	3VS	1																																		
6	71	3VS	1		3			1																													
7	20	3VS	6	5	1			1																													
8	3 m	3VS			2																																
9	73	3VS			5			1																													
10	37	3VS			4			3	1																												
11	19	Tumour			1			1																													
12	44	Fenestr.	10																																		
13	11	3VS	1																																		
14	12	Tumour			7			8	1																												
15	11	Biopsy			8																																
16	1 m	3VS			1																																
17	62	Biopsy			1																																
SUM			20	8	6	4	1	48	0	0	0	0	24	8	2	0	0	0	1	21	8	0	3	2	2	3	5	0	3	2	4	0	0	0	14	0	1

released, leading to normalization of the intracranial pressure, heart rate and blood pressure within 120 s. Figure 3B shows a slower increase in intracranial pressure accompanied by a marginal increase in mean arterial pressure and an initial moderate decline of the heart rate. At 4285 s, a sudden additional increase in intracranial pressure is seen together with abrupt severe bradycardia. After 20 s, the heart rate recovers rapidly.

Figure 3C shows a Cushing reflex in a 3-month-old baby. The baseline cerebral perfusion pressure was 39 mm Hg since the normal mean arterial pressure is much lower in infants. In this patient, we see hypertensive adaptation at an intracranial pressure of 10 mm Hg and tachycardia at 34 mm Hg.

None of the patients suffered any of the postoperative complications described by Buxton and colleagues.¹²

Discussion

During neuroendoscopic procedures, early recognition of an excessive increase in intracranial pressure, jeopardizing brain perfusion, is of major importance for preserving cerebral homeostasis. Isolated or combined bradycardia and hypertension are commonly used during neuroendoscopy to alert the surgeon to increased intracranial pressure or mechanical stimulation of the floor of the third ventricle.⁵ Intracranial pressure or Doppler flow measurements have been used to evaluate cerebral perfusion.¹³ However, in a retrospective study, Van Aken and colleagues⁸ concluded that tachycardia occurred as frequently as bradycardia during neuroendoscopy. They hypothesized that the tachycardia coincided mostly with an increase in intracranial pressure caused by high-speed fluid irrigation or obstruction of the outflow tube. The observed tachycardia was nearly always accompanied by systemic hypertension. These signs might be seen as an atypical Cushing response. Unfortunately, intracranial pressure was not recorded in this study because a two-channel cystoscope, which did not allow measurement of the intracranial pressure, was used. The classic response, as described by Cushing¹⁴ in 1901, consists of apnoea, increased blood pressure and bradycardia. Therefore it might be interesting to perform a prospective evaluation of the adequacy of the occurrence of haemodynamic alterations for assessing the cerebral perfusion status during these procedures by simultaneously measuring heart rate and arterial and intracranial pressure.

We investigated the association between cerebral perfusion pressure and the occurrence of haemodynamic changes. We defined a haemodynamic change as a change of 20% from baseline for at least 3 s. Rescaling of the baseline values was sometimes necessary to eliminate slow haemodynamic changes caused by long-term anaesthesia, but this was only done after at least 2 min of haemodynamic stability and intracranial pressure levels <5 mm Hg. In our opinion, this was defensible and desirable since we were focusing mainly on the fast haemodynamic changes following

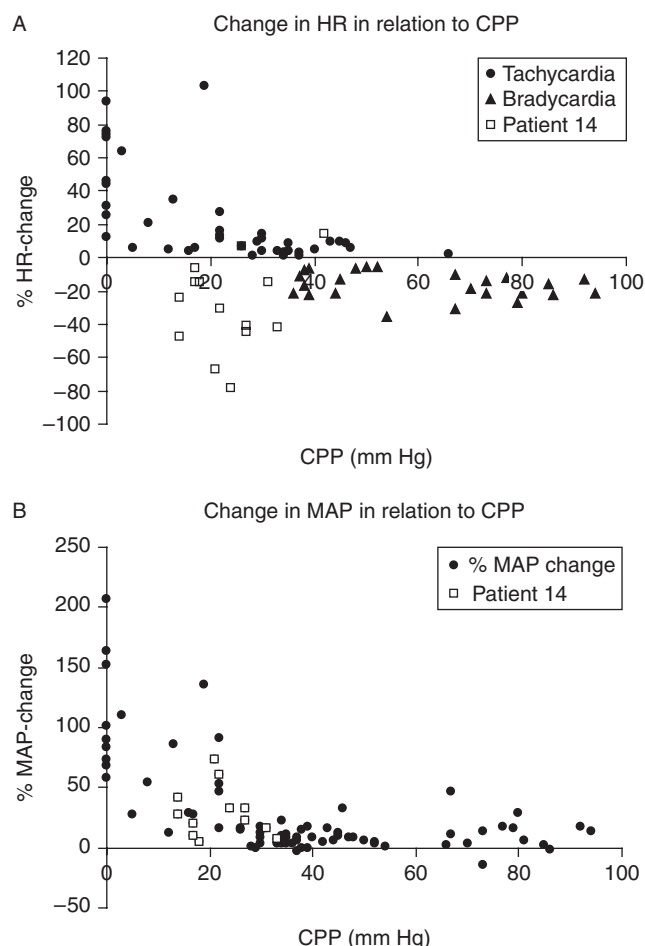


Fig 1 (A) Relative change of the heart rate during the neuroendoscopic procedures plotted against the lowest preceding cerebral perfusion pressure. (B) Relative change of the mean arterial pressure during the neuroendoscopic procedures plotted against the lowest preceding cerebral perfusion pressure. The events from patient 14 are shown by open squares; many of these haemodynamic events occurred during tumour retraction.

increased intracranial pressure and decreased cerebral perfusion pressure.

As shown in Table 2, a decrease in the cerebral perfusion pressure to <15 mm Hg always results in a Cushing reflex. Hypertension accompanied by tachycardia occurred in 14 of the 15 patients; a combination of hypertension and bradycardia was observed in the remaining case.

It only makes sense to use this detection technique if a high sensitivity/specificity level can be reached. Therefore a sensitivity and specificity analysis was performed as shown in Table 3. It can be seen that a simultaneous occurrence of hypertension and tachycardia, defined as a 20% increase in heart rate and mean arterial pressure, has a sensitivity of 93% for detecting a decrease in the cerebral perfusion pressure to <15 mm Hg. Furthermore, the single case where no tachycardia was observed was in patient 14 during tumour retraction, where we saw an abrupt bradycardia which may have prevented the emergence of tachycardia because of direct stimulation. A decrease in the cerebral perfusion pressure to

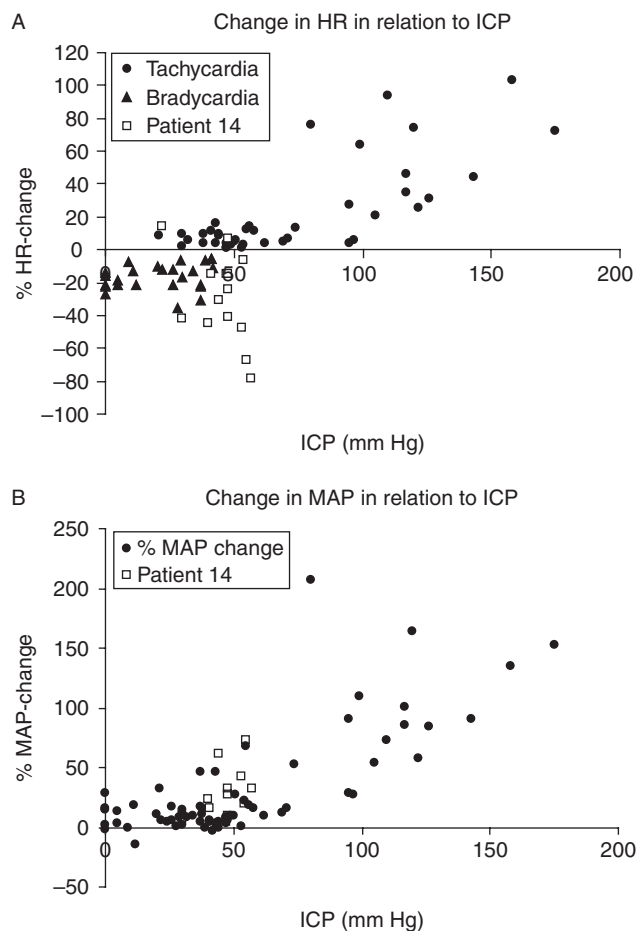


Fig 2 (A) Relative change of the heart rate during the neuroendoscopic procedures plotted against the lowest preceding intracranial pressure. (B) Relative change of the mean arterial pressure during the neuroendoscopic procedures plotted against the lowest preceding intracranial pressure. The events from patient 14 are shown by open squares; many of these haemodynamic events occurred during tumour retraction.

Table 3 The sensitivity and specificity of a simultaneous occurrence of hypertension and tachycardia, defined as a 20% increase in heart rate and mean arterial pressure, to detect a decreased cerebral perfusion pressure (CPP). Because we saw multiple episodes of bradycardia during tumour retraction in patient 14, the sensitivity and specificity is also shown with the events of this patient excluded from the analysis

CPP (mm Hg)	All patients		Patient 14 excluded	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
<15	93	54	100	54
<20	53	65	67	62
<30	29	77	39	73
<50	13	77	17	73

15–30 mm Hg often results in a Cushing reflex, but frequently causes hypertension without tachycardia or bradycardia. A decrease in the cerebral perfusion pressure to 30–40 mm Hg almost never results in a Cushing reflex. When we omit patient 14 from the analysis, the sensitivity of

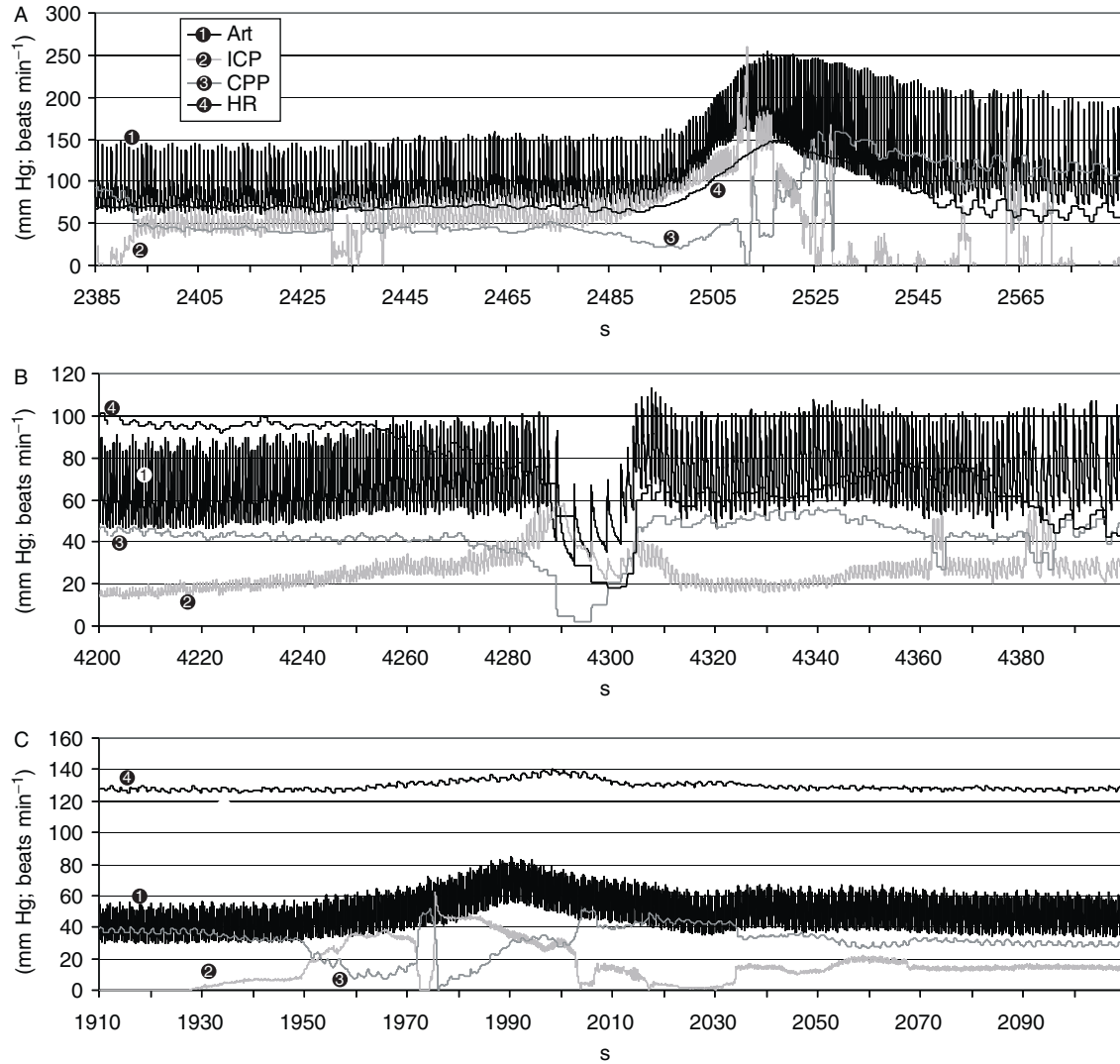


Fig 3 (A) After stable adaptive hypertension due to moderately increased intracranial pressure (ICP), a sudden increase in ICP results in a manifest Cushing reflex, which tends to normalize after ICP is lowered. (B) Occurrence of an acute bradycardia and hypertension following a drop in the cerebral perfusion pressure (CPP) to <30 mm Hg. (C) Occurrence of a Cushing reflex in a 3-month-old baby.

a Cushing reflex to detect a severely decreased cerebral perfusion pressure becomes even stronger. The occurrence of simultaneous hypertension and tachycardia during the endoscopic procedure has a specificity of 77% (20/26) in detecting a decrease of the cerebral perfusion pressure to <30 mm Hg.

A cerebral perfusion pressure <50 mm Hg does not always result in haemodynamic changes (Table 2). Moderate reduction of the cerebral perfusion pressure evokes an isolated adaptive hypertension within seconds caused by an unexplained mechanism. Remarkably, this often modest increase in blood pressure induces an increase in cerebral perfusion pressure. In all cases where the blood pressure increased following a moderate decrease in cerebral perfusion pressure, the rise in blood pressure was sufficient to normalize the cerebral perfusion pressure at a level between 35 and 50 mm Hg, as illustrated in Figure 3A. Since the adaptive

increase in the mean arterial pressure may result in a normalization of the cerebral perfusion pressure, such phenomena can be considered as a protective and effective action of the brain for preserving an adequate cerebral perfusion pressure despite an increased intracranial pressure. Beiner and colleagues¹⁵ proved that such an increase in the mean systemic arterial pressure restores the cerebral blood flow to approximately normal levels.

Tachycardia developed only when the increase in the intracranial pressure was too fast for adaptation, and consequently the cerebral perfusion pressure dropped below a threshold level. Within seconds of the cerebral perfusion pressure falling below a threshold (in most patients around 15 mm Hg), a prominent uncontrolled increase in mean arterial pressure and heart rate occurred, resulting in considerable overshoot of the cerebral perfusion pressure. However, when the cerebral perfusion pressure was restored

quickly (as a result of either the increased mean arterial pressure or the decreased intracranial pressure), normalization of the mean arterial pressure and heart rate is seen within minutes. Even in these instances, if an increased intracranial pressure demands an increased mean arterial pressure in order to preserve the cerebral perfusion pressure, the mean arterial pressure only normalizes up to the required value. Therefore one can state that exclusively measuring the intracranial pressure, without taking the mean arterial pressure into account, might result in misleading conclusions regarding cerebral perfusion. As observed in infants aged 1 and 3 months, an intracranial pressure generally considered tolerable may be unacceptably high in some instances of low mean arterial pressure. This is in agreement with previous observations by Fabregas and colleagues.^{6 13} These authors tried to solve the problem of early recognition of any increase in intracranial pressure by measuring the pressure inside the neuroendoscope. They observed a lack of systemic changes accompanying high-peak intracranial pressures, making it difficult to believe that these pressures really reflect the intracranial pressure.

These results might suggest that pharmacologically increasing the mean arterial pressure may enable higher intracranial pressure values to be tolerated, although this could also increase the risk of bleeding or other adverse effects. An optimal mean arterial pressure could be determined in consultation with the surgeon, based on the patient's risk factors and the type of procedure.

Direct stimulation of the floor of the third ventricle may induce both hypertension and hypotension, together with bradycardia or tachycardia.¹⁶ The underlying cause of bradycardia is different from tachycardia, as postulated by El-Dawlatly and colleagues.⁵ They specifically focused on the incidence of bradycardia during endoscopic third ventriculostomy. It was postulated that the bradycardia is the result of stimulation of the floor of the third ventricle by the endoscope⁴⁵ or is caused by distortion of the posterior hypothalamus.¹⁷ As can be seen in Table 2, the initial manifest bradycardia following a cerebral perfusion pressure drop was seen in only one patient, although it was seen many times in this patient. Thus this patient represents all episodes of bradycardia at cerebral perfusion pressure levels <50 mm Hg listed in Table 2. All these cases of isolated bradycardia coincided with manipulation of the tumour and may have been caused by direct mechanical stimulation; the increased intracranial pressure may have been coincidental and not the cause of the bradycardia, as suggested in Figure 1. The Cushing reflex was probably obscured by mechanical stimulation in an attempt to remove a pineal tumour. One of the severe bradycardic periods in this patient is illustrated in Figure 3B.

Our data suggest that, under stable anaesthetic conditions, severe haemodynamic changes that are not associated with tumour retraction are probably caused by compromised cerebral perfusion pressure. Furthermore, we almost exclusively observed tachycardia and hypertension, and

not bradycardia, in these patients. The anaesthetic used (total i.v. anaesthesia and remifentanyl) tends to give relatively slow heart rates, which may explain why relative bradycardia is seen less frequently, since the analysis is based on relative changes to baseline. Other general anaesthesia techniques might give different haemodynamic responses. Nevertheless, other causes of haemodynamic change must be considered during endoscopy. For instance, bradycardia might be caused by the pressor reflex (end of Fig. 3A) caused by iatrogenic hypertension during normal brain perfusion. In these cases, only a precise knowledge of the cerebral perfusion pressure values can permit us not to disturb the surgical procedure. Therefore it is crucial to correlate the observed haemodynamic instability with the intracranial pressure measured via the endoscope. As observed in traumatic brain injury in infants,¹⁸ open fontanelles and/or sutures do not preclude the development of intracranial hypertension. We recorded a clear Cushing reflex in infants aged 1 month and 3 months (Fig. 3C).

There is no consensus in the literature about safe intracranial pressure values during neuroendoscopic interventions.¹⁹ Our research suggests that a search for such a safe and convenient intracranial pressure value is doomed to fail, since the brain perfusion is regulated by the cerebral perfusion pressure. Our observations of the haemodynamic effects of the intracranial pressure and cerebral perfusion pressure show that no observable effects are seen with a cerebral perfusion pressure >40 mm Hg, independent of the intracranial pressure.

Because of ethical and medical considerations, we did not investigate the haemodynamic effect during long periods of decreased cerebral perfusion pressure. When an increased intracranial pressure coincided with a haemodynamic change, the surgeon was informed and the intracranial pressure was lowered immediately. As a result, we have not evaluated possible post-tachycardial bradycardia as classically described by Heymans.² Further animal experiments could be done to confirm this sequence of events during longer-lasting iatrogenic increases in intracranial pressure.

Meticulous assessment of the perfusion pressure is the only valid variable for assessment of brain perfusion, but one must always be aware of possible erroneously low intracranial pressure readings. For instance, in one patient, we noticed a sudden drop of the intracranial pressure and a disappearance of the cardiac pulsations on the intracranial pressure waveform. A few seconds later heart rate and blood pressure increased abruptly. This event occurred when a large amount of debris was floating in the rinsing fluid and was caused by an obstruction of the outflow. Shortly after retraction of the endoscope, the heart rate and blood pressure normalized. A continuous assessment of the irrigation pressure could be useful for early detection in such cases. Since outflow obstruction could be a cause of a sudden and potentially harmful rise in intracranial pressure, a safety system to detect such problems should be considered.

Our observations have important repercussions for the clinical plan in neuroendoscopic procedures, including those in small children. It is imperative to assess subtle cardiovascular changes, in particular hypertension coupled with tachycardia/bradycardia, as fast as possible in order to alert the surgeon. Our study shows that seeking and identifying a Cushing reflex, together with continuous monitoring of the arterial and intra-endoscopic pressure and the surgical manoeuvres is a reliable and valuable adjunct to the existing monitoring techniques to protect the patient undergoing a neuroendoscopic procedure.

Appendix. Algorithms for offline analysis of the pressure waveforms (Visual Basic programming in Microsoft® Excel)

Private Sub import_data_Click()

```

Const sampling_rate=100
Dim systolev(10): Dim systolet(10) 'systolevalue and
systoletime (going back 10 beats)
Dim diastolev(10): Dim diastolet(10) : diastolev(0)=500
Open 'C:/File1.asc' For Input As #1
Line Input #1, a$: Line Input #1, a$
Do While Not EOF(1)
    lijn=lijn+1
    Line Input #1, a$
    curve=1
    splitted=Split(a$, Chr$(9), -1)
    ECG=splitted(0)
    Art=splitted(1)
    ICP=splitted(2)
    If ICP<0 Then ICP=0

    second_counter=second_counter+0.01
    If Art>systolev(0) Then systolev(0)=Art: systolet(0)
    =lijn
    If Art<diastolev(0) Then diastolev(0)=Art:
    diastolet(0)=lijn
    If ICP>ICPS Then ICPS=ICP
    If ICP<ICPD Then ICPD=ICP
    If Art<systolev(0) And lijn-systolet(0)>40 And
    systolev(0)-diastolev(0)>30 Then
        For n=10 To 1 Step-1
            systolev(n)=systolev(n-1):systolet(n)=systolet(n-1)
            diastolev(n)=diastolev(n-1):diastolet(n)=diastolet
            (n-1)
        Next n
        systolev(0)=0: diastolev(0)=470
        ICP_systole=ICPS
        ICP_diastole=ICPD
        ICPS=0: ICPD=488
    End If
    If systolet(4)>0 Then HR=Int(100/(systolet(1)-
    systolet(4))*180)
    systole=systolev(0)
    Diastole=diastolev(0)
    Mean=Int((systolev(1)+2*diastolev(1))/3)

```

```

MIP=Int((ICP_systole+2*ICP_diastole)/3)
IPP=ICP_systole-ICP_diastole
CPP=Int(Mean-MIP)
If CPP<0 Then CPP=0
kolom=Int(lijn/40000)
rij=lijn-kolom*40000+1
Worksheets(2).Cells(rij, 8+kolom*8+1).Value=Art
Worksheets(2).Cells(rij, 8+kolom*8+2).Value=ICP
Worksheets(2).Cells(rij, 8+kolom*8+3).Value=Mean
Worksheets(2).Cells(rij, 8+kolom*8+4).Value=MIP
Worksheets(2).Cells(rij, 8+kolom*8+5).Value=CPP
Worksheets(2).Cells(rij, 8+kolom*8+6).Value=HR

rij=Int(lijn/100)+1
If systolet(4) > 0 Then
    Worksheets(3).Cells(rij, 3).Value=Mean
    Worksheets(3).Cells(rij, 4).Value=MIP
    Worksheets(3).Cells(rij, 5).Value=CPP
    Worksheets(3).Cells(rij, 6).Value=HR
    Worksheets(3).Cells(rij, 7).Value=Diastole
    Worksheets(3).Cells(rij, 8).Value=systole
    Worksheets(3).Cells(rij, 9).Value=ICP_diastole
    Worksheets(3).Cells(rij, 10).Value=ICP_systole
    Worksheets(3).Cells(rij, 11).Value=IPP
End If
Loop
Close #1
End Sub

```

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