more information on the ‘best treatment’ of surgical and trauma patients.

Ultimately, it should be in everyone’s interest to interpret the existing data on medical topics objectively and neutrally, without rushing to premature, far-reaching conclusions which could confuse physicians and even render future therapy with potentially life-saving drugs impossible.

Supplementary material
Supplementary material is available at British Journal of Anaesthesia online.

Declaration of interest
None declared.

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Evaluation of acoustic respiration rate monitoring after extubation in intensive care unit patients

Editor—The Anesthesia Patient Safety Foundation recommends both pulse oximetry (SpO₂) and respiration rate (RR) monitoring after extubation1 because in patients receiving supplemental oxygen, SpO₂ alone can be a late indicator of alveolar hypoventilation.2 We sought to compare the accuracy of acoustic RR (RRa, Rad-87, software version 7713, MasimoTM Corp., Irvine, CA, USA) measurement, a relatively new method of assessment and thoracic impedance RR measurement (RRI, PhilipsTM Intellivue MP2, Suresnes, France), the widely used method of assessment, with RR by capnography (Capno-streamTM 20, Oridon, Jerusalem, Israel) through a face mask (CapnomaskTM, Mediplus Ltd, Raleigh, NC, USA)3 used as reference method in intensive care unit (ICU) patients immediately after extubation.

After obtaining informed consent, patients 18 yr or older were enrolled in the study within 1 h after extubation. Patients with a neck or facial trauma preventing the application of a face mask, the acoustic sensor, or both and those requiring non-invasive ventilation or chest physiotherapy during recordings were excluded. RR was simultaneously recorded every second for 30–60 min by the three methods. Adjusted Bland and Altman analysis was used to calculate bias and limits of agreement for RRa or RRI compared with capnography.

Twenty-five patients [21 men; median (inter-quartile range) age: 61 (43–64) yr, BMI: 26.2 (23.9–29.6) kg m⁻², SAPS II score:5 41 (26–49)] were included. From the 69 347 triplet RR measurements collected, only 57 520 (83%) were usable due to removal of values corresponding to periods of calibration from the capnometer (n = 1034, 1.5%), detachment of RRa sensor (n = 3643, 5.2%), or the dislodgement of CapnomaskTM by the patient (n = 7150, 10.3%). Thus, RRa and capnography accounted for 30.8% and 69.2% of data loss, respectively. The median RR during recordings as measured by capnography was 19 (16–25) bpm.

Compared with capnography, bias was similar for acoustic monitoring and for impedance monitoring, but limits of...
agreement were narrower for acoustic monitoring (Fig. 1). Consequently, the proportion of RR values differing by more than 10% or 20% for more than 15 s compared with capnography were 4.4% and 1.7% for acoustic monitoring and 9.2% and 5.0% for impedance monitoring (P<0.0001 for both comparisons). The accuracy of RRa and impedance observed in this study is lower than that reported in extubated patients admitted in the post-anaesthesia care unit (respectively, +4.2 and ± 6.4 vs +1.4 and ± 4.1 bpm).² ³ RR values approximately two times higher on average than in previous studies may explain this finding. The accuracy of thoracic impedance is influenced by many factors such as patient motion and physiological movements of the chest wall that are independent of breathing, such as coughs or cries, situations frequently encountered in ICU patients.³ Factors that may interfere with the accuracy of the acoustic method are less well known. One study reported a decrease in accuracy in the presence of repetitive swallowing.⁵

Acoustic sensors were well tolerated, but repeated repositioning was required in six patients due to loss of

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**Fig 1** Bland and Altman graph with bias with limits of agreement for RR measured by capnography with Capnomask (RRcap no) vs non-invasive acoustic method (RRa) (A) or vs impedance (RRI) (B). Each circle represents a patient, and the diameter of the circle is proportional to the number of values per patient.
adhesive contact with the skin in heavily perspiring patients. The six episodes of detachment all occurred with the use of a flexible plastic version of the sensor. This problem seems to have been solved with the use of a new cloth sensor. Conversely, the Capnomask™ was removed on numerous occasions in three patients, which required the intervention of a healthcare provider to reposition it. These periods combined with those of recalibration of the capnograph resulted in the absence of RR measurement for nearly 12% of the duration of the recordings, which could jeopardize the routine use of this technique. These results support the use of RRA when accurate and continuous RR monitoring is desired.

Declaration of interest
D.F., M.P., and O.M. received lecture fees and travel expenses from Masimo™ Corp.

Funding
This study was funded by University Hospital of Poitiers. Masimo™ Corp. supplied the Radical-7 monitors and the sensors used for RRA measurements. The manufacturer had no input into the design or conduct of this study or in the decision to submit the manuscript for publication.

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Long-term activation of polymorph cannabinoid receptors does not affect receptor gene transcription

Editor—The role of cannabinoids in anaesthesia has received renewed interest with activation of the cannabinoid system capable of producing analgesia, anxiolysis, muscle relaxation, and immunomodulation.1 2 There have been major developments in cannabinoid receptor classification to possibly include the orphan G-protein-coupled receptor GPR55 alongside the classical CB1 and CB2,3 although this is highly controversial. Therapeutic activation is likely to be long term and there are no in vitro data after long-term exposure on expression of the genes encoding these receptors. We have therefore examined the effects of long-term treatment of human polymorphonuclear cells with the CB2 agonist L-5796564 and the GPR55 agonist L-α lyophosphatidylinositol (LPI)5 on mRNA encoding for CB1, CB2, and GPR55 receptors.

Human neutrophils isolated by density gradient separation from 12 consented, healthy volunteers, and HL60 cells (a neutrophil pre-cursor cell) were treated with DMSO (1.75%; control), LPI (10 μM), LPI (1 μM), or L-579656 (10 μM) at 37°C for 66 h. HL60 cells were differentiated with 120 mM dimethylformamide (DMF) for 72 h,6 and then immediately treated with LPI or L-579656.

mRNA was extracted (mirVANA™ System), cleaned to remove genomic DNA (Turbo DNA-free™ kit), then reverse transcribed using a high-capacity cDNA reverse transcription kit. cDNA samples were probed using TaqMan® probes for CB1, CB2, and GPR55. Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was used as the housekeeper gene and quantitative PCR was performed using the Step-one machine, with non-template controls.7 PCR data are presented as cycle thresholds (Ct) [mean (SEM)], where ΔCt is the difference between GAPDH and the gene of interest. Statistical analysis was by analysis of variance (ANOVA) followed by Dunnett’s post hoc testing when P<0.05 or paired t-test as appropriate.

Human neutrophils expressed CB2 and GPR55 receptor mRNA with ΔCt values of ~7.3 and ~10.6 (n=12), respectively. CB1 receptor mRNA was present at very low levels (Table 1). Relative to CB1, there was ~25- and ~2.5-fold more CB2 and GPR55 mRNA, respectively. Pretreatment with either L-579656 or LPI (1 or 10 μM) for 66 h did not affect the transcription of CB1, CB2, or GPR55 (Table 1). Pretreatment with LPI at 10 but not 1 μM significantly reduced GPR55 mRNA by ~1 cycle or ~2-fold.

HL60 cells expressed CB2 and GPR55 receptor mRNA with ΔCt values of 8.65 (0.25) and 16.63 (0.55), respectively (n=8). CB1 receptor mRNA was not detected (n=8). In view of the low expression of GPR55, we differentiated cells with DMF3 and observed an increase in the expression of GPR55 and CB2 by 73.88 (22.7) (n=6) and 7.31 (4.22) fold at 72 h (n=11). Subsequent treatment (n=3) with L-579656 and LPI (1 or 10 μM) was detrimental to cell survival.

In this study, we have shown that human neutrophils express the classical cannabinoid receptors along with the putative receptor GPR55 (rank order CB2>GPR55>CB1).