Neuromotor impairment was repetitively assessed by neurological severity score (NSS), rotarod test and open field test. 7dpi mice were euthanized and, after cryosectioning and Nissl-staining of the *in toto* removed brains, cerebral lesion was quantified by volumetry. Lung tissue was processed in paraffin sections and histologically analysed. qPCR analysis was performed for inflammatory marker genes in brain and lung tissues, complemented by plasma ELISA for LPS-binding protein (LBP). Statistics: Rout Outlier, Shapiro-Wilk, t-/Mann-Whitney-test, One-way-/Two-way-ANOVA, $p<0.05$.

Results and Discussion: Gas exchange area in lungs of LPS-treated animals was significantly reduced compared to vehicle groups, mainly caused by thickening of interalveolar tissue ($p<0.001$). Lung mRNA-expression of IL-6, TNF and TLR4 was increased in LPS groups ($p<0.05$) regardless of concomitant TBI. Mice of the CCI/LPS group lacked remission of neuromotor impairment compared to CCI/veh but the cerebral lesion volume remained unaffected. mRNA expression of IL-1, GFAP, TNF and TLR4 in the perilesional brain tissue was increased in CCI mice compared to sham but not aggravated by LPS exposition.

Conclusion(s): Repetitive nebulization of LPS leads to severe inflammatory response and histological damage in lung tissue. Although recovery from TBI was impaired in mice with LPS-exposition, histological brain damage and gene expression remained unaffected, suggesting potential auto-protective mechanisms in the brain which require further investigations.

Reference:

1. Matute-Bello G, Frevert CW, Martin TR. Animal models of acute lung injury. Am J Physiol Lung Cell Mol Physiol. 2008;295(3):L379-L399.

06AP03-10
Effects of antibiotic long-term treatment and intestinal dysbiosis on secondary brain damage after experimental traumatic brain injury

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Background and Goal of Study: Antibiotic therapies for various indications are common during the recovery process of patients suffering from traumatic brain injury (TBI). Disturbances of the intestinal microbiome can occur as a side effect and may affect the outcome of TBI (1). Here, we tested this hypothesis in a murine model of antibiotic-induced dysbiosis and TBI.

Materials and Methods: After approval of the responsible animal welfare committee (Landesuntersuchungsamt Rheinland-Pfalz, TVA G19-1-027) 80 male C57/BL6 mice were subjected to controlled cortical impact (CCI) or sham procedure, followed by combined treatment of amoxicillin/clavulanic acid, vancomycin and nystatin delivered via drinking water. Vehicle treatment served as a control (CCI/AB n=24, CCI/veh n=24; sham/AB n=16, sham/veh n=16). Neuromotor impairment was assessed repetitively by neurological severity score (NSS), rotarod test and open field test. Half of the population of each group was euthanized at either 5 days post injury (dpi) or 30dpi, with continuous antibiotic/vehicle treatment. Brains were processed by cryosectioning, Nissl-staining and cerebral lesion volumetry. Perilesional brain tissue was analysed by qPCR, Western Blot and immunohistochemistry. Faecal samples were analysed by MALDI-TOF pre-trauma and at 5dpi. Statistics: Grubb's outlier, Shapiro-Wilk, t-/Mann-Whitney-test, One-way-/Two-way-ANOVA, $p<0.05$)

Results and Discussion: Faecal samples revealed severe disruption of microbial colonization 5dpi in mice with antibiotic treatment compared to pretraumatic findings. Animals of CCI/AB group showed decreased neuromotor impairment until 5dpi compared to CCI/vehicle, while lesion volume remained unaffected. mRNA expression of IL-1, GFAP, Serpina3n and MHCII was reduced in perilesional brain tissue of antibiotic-treated mice at 30dpi compared to vehicle ($p<0.05$).

Conclusion (s): Combined antibiotic treatment leads to early severe disruption of the intestinal microbiome. Transiently improved neuromotor recovery after TBI was noted in antibiotic treated groups but histopathology was indistinguishable from vehicle treated TBI mice. However, gene expression analyses suggest mild anti-inflammatory effects of antibiotics therapy after TBI, which requires further studies to distinguish between microbial effects and possible cerebral off-target effects.

Reference:

Sharon G et al.: The Central Nervous System and the Gut Microbiome. Cell. 2016 Nov 3;167(4):915-932

06AP03-11
Incidence of BIS above 60 during propofol/remifentanil anesthesia for cervical spine surgery and possible awareness comparing standard versus deep neuromuscular blockade with sugammadex reversal

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Background and Goal of Study: In a randomized controlled trial[1] where 62 cervical spine surgery patients were subjected to BIS guided general anesthesia with TCI of Remifentanil and Propofol and to either Standard (n=32) or Deep Neuro-Muscular blockade (NMB) PTC<2 and reversal with Sugammadex, we showed that Deep NMB with Rocuronium infusion and Sugammadex reversal reduced both anesthetics requirements and halved time required to extubation. The present study is a sub-analysis of BIS data from that study, conducted to compare the incidence of BIS above 60 in both groups and to investigate the incidence of BIS>60 in relation to awareness. **Materials and Methods:** Patients received propofol/remifentanil TCI anesthesia. Rocuronium either by bolus and neostigmine reversal if TOF>90 or infusion until wound closure and sugammadex reversal. No benzodiazepines were used. Paracetamol and parecoxib were given at the end of surgery. Recorded BIS data (Rugloop™) was analyzed to extract every occurrence of BIS>60 lasting for at least 5 seconds. BIS readings were grouped according to BIS intervals (60 to 65; >65 to 70 and >70 to 75) and according to the duration (in seconds) of any continuous sequence of BIS>60 (0 to 30; 35 to 85; 90 to 145; 150 to 295 and >300 seconds). Patients were contacted by phone at home to assess for possible awareness using the Brice questionaire. Statistics used *Chi-square* independence test.

Results and Discussion: Results are presented in figure1. BIS was never above 75 for 5 seconds. Average procedure time (min) was 146 in the Standard vs 131 in the Deep NMB group. BIS above 60 occurred 1158 times, but in 939 (81%), for less than 30 seconds. There were no differences in the occurrence of BIS>60 or duration time of BIS>60 between groups. There was not a single report of awareness.

	BIS intervals						
	60-65		>65-70		>70-75		Total
Duration (secs)	Standard	Deep NMB	Standard	Deep NMB	Standard	Deep NMB	
0-30	283	532	39	72	6	7	939
35-85	47	65	16	36	3	5	172
90-145	6	10	6	11	2	2	37
150-295	2	1	2	3	0	0	8
>=300	0	0	1	0	1	0	2
Total	338	608	64	122	12	14	1158

Conclusions: BIS>60 for longer than 90 seconds occurred only 47 times, of which only 10 over 150 seconds. Periods of BIS above 60 shorter than 300 seconds and below 70 in patients receiving remifentanil/propofol did not result in awareness. These results suggest that Deep NMB blockade that reduced Propofol/Remifentanil requirements was not associated with higher incidence of BIS>60, nor awareness. Still, careful monitoring of anesthesia depth with alarms is mandatory when performing deep NMB.

Reference:

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06AP03-12
In vitro evaluation of the effects of intravenous anesthetics on glioblastoma cells with or without chemo- and radiotherapy

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Background and Goal of Study: Glioblastomas (GB) are the most aggressive and common primary brain tumors in adults. The evolution of this pathology is rapid and fatal (median survival less than 15 months). Therapeutic management combines surgery, radiotherapy (RT) and chemotherapy (CT). During tumor excision, patients are exposed to intravenous anesthetic agents.The objective of this work is to evaluate the influence of propofol and remifentanil on tumor cells treated or not with CT and RT.

Materials and Methods: GB cells lines (C6) were exposed to propofol (50 μg.ml^{-1}) and remifentanil (3.75 μg.ml^{-1}). Impact on cell survival was assessed by counting the number of Hoechst 33342 positive cells and by clonogenic assays. Effects of anesthetics on cell migration were studied by the wound healing test. Effect of propofol was also studied on GB cells lines GL261 and U251. Effects of anesthetics on the response to CT (temozolomide, 350 μM) or RT (4 Gy, 2Gy/min, X-RAD225 Cx irradiator) treatments were studied with clonogenic assays.

Results and Discussion: At 72 h post-exposure, propofol tends to reduce the number of C6 cells (p=0,34). Remifentanil does not modify cell survival. There is no effect of propofol or remifentanil on the migration of C6 cells. Cell survival measured 7 days after treatment by propofol is reduced in GL261 46 ± 4 % and in U251 58 ± 18 % (p<0.01) but not in C6. Propofol further decrease cell survival induced by CT alone. Remifentanil or propofol/remifentanil combination does not modify the response of C6 cells to CT. RT effects on C6 cell survival are potentiated by propofol (RT+propofol = 29 ± 10 % vs RT = 60 ± 19 % with 100% for Control, p<0.01) while no effect is observed with remifentanil. Propofol/remifentanil combined treatment reduced cell survival after RT (35 ±16% vs RT alone 61 ±14%, p<0.05). RT effects on survival of GL261 are potentiated by propofol (20±7% for RT+propofol vs 46±5% for RT, p<0.01). However, RT effects on survival of U251 are not modified by propofol (22±7% for RT+propofol vs 39±19% for RT, p=0.11).

Conclusion(s): This first work underlines that propofol reduces GB cell survival *in vitro*. Interestingly, this work demonstrates a radiosensitizing effect of propofol on C6 and GL261 cells. These results have to be confirmed *in vivo*.

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06AP04-01
The influence of vasopressor-induced arterial blood pressure elevation on muscle-recorded motor evoked potentials

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Background and Goal of Study: Muscle transcranial electrical stimulation motor evoked potentials (mTc-MEPs) are used to monitor the motor tracts during spinal surgery. The aim was to investigate the effects of noradrenaline (NE) induced mean arterial pressure (MAP) elevation on mTc-MEPs.

Materials and Methods: 25 patients undergoing spinal surgery were included in this prospective observational study. After induction, before incision, a NE infusion was used to increase the MAP from ±60mmHg to 100mmHg in 30 minutes. mTc-MEP amplitudes and area under the curves (AUC) were recorded from the tibialis anterior (TA) and abductor hallucis (AH) muscles every two minutes. Voltage thresholds were determined at MAPs of 60, 80 and 100mmHg. Mixed model analysis was used to adjust for the repeated mTc-MEP measurements.

Additional analyses were performed to adjust for propofol concentration, BIS, NE infusion rate and use of ephedrine. Moreover, the effects of increasing MAP on H-reflex and compound muscle action potential (CMAP) amplitudes were analysed.

Results and Discussion: A 10mmHg increase of the MAP was associated with a 14.4% increase (CI 11.4%, 17.9%; p<0.001) in amplitude and a 13.0% (CI 6.0%, 20.8%; p<0.001) increase in AUC. Increasing MAP from 60mmHg decreased the voltage thresholds by 2.27V (CI-7.29V, 2.74V; p=0.375) at a MAP of 80mmHg, and by 6.3V (CI -11.4V, -1.3V; p=0.016) at a MAP of 100mmHg. When adjusted for BIS and propofol concentration, we found a weaker association between MAP and mTc-MEP amplitude (p<0.001); and no association between MAP and AUC (p=0.070) and voltage threshold (p=0.621). Adjusting for NE and ephedrine increased the positive association between MAP and mTc-MEP amplitude. There was no association between MAP and H-reflex/CMAP amplitude (*Figure 1*).

Conclusions: MAP elevation is associated with higher mTc-MEP amplitudes, AUCs, and lower voltage thresholds. This might be due to increased cortical neuronal activity caused by either direct and/or