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Kim et al. from the University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea, therefore developed and validated a radiomics model using multiparametric MRI to differentiate pseudoprogression from early tumor progression in patients with glioblastoma.

The model was developed from the enlarging contrast-enhancing portions of 61 glioblastomas within

3 months after standard treatment with 6472 radiomic features being obtained from contrast-enhanced T1-weighted imaging, fluid attenuated inversion recovery imaging, and apparent diffusion coefficient (ADC), and cerebral blood volume (CBV) maps. Imaging features were selected using a least absolute shrinkage and selection operator (LASSO) logistic regression model with 10-fold cross-validation. Diagnostic performance for pseudoprogression was compared with that for single parameters (mean and minimum ADC and mean and maximum CBV) and single imaging radiomics models using the area under the receiver-operating-characteristics curve (AUC). The model was validated with an external cohort (n = 34) imaged on a different scanner and an internal prospective registry data (n = 23).

Twelve significant radiomic features (3 from conventional, 2 from diffusion and 7 from perfusion MRI) were selected for model construction. The multiparametric radiomics model (AUC 0.90) showed significantly better performance than any single ADC or CBV parameter (AUC 0.57-0.79, P<.05), and better than single radiomics model using conventional MRI (AUC 0.76, P =.012), ADC (AUC 0.78, P =.014), or CBV (AUC 0.80, P=.43). The multiparametric radiomics showed higher performance in the external validation (AUC 0.85) and internal validation (AUC 0.96) than any single approach, thus demonstrating robustness.

Incorporating diffusion- and perfusion weighted imaging into a radiomics model improved diagnostic performance for identifying pseudoprogression and showed robustness in a multicenter setting [1)].

Kolenda H, Ludwig HC. Professor Emeritus Evangelos Markakis. J Neurol Surg A Cent Eur Neurosurg. 2018 Sep;79(5):357. doi: 10.1055/s-0038-1668094. Epub 2018 Aug 7. PubMed PMID: 30086578.

Spergel from the Department of Neurosurgery, Yale University School of Medicine, New Haven, CT, USA. reviewed the neuropeptides that have been shown to act directly and that may also act indirectly, on GnRH neurons, the reproduction-related processes with which the neuropeptides may be associated or the physiological information they may convey, as well as their cognate receptors, signaling pathways and roles in the modulation of GnRH neuronal firing, [Ca2+]i, GnRH secretion and reproduction. The review focuses on recent research in mice, which offer the most tractable experimental system for studying mammalian GnRH neurons [2)].

The objective of Barr et al., from the University of British Columbia, Vancouver, Canada, was to determine whether the British Columbia experience implementing a province-wide prevention program reduced Abusive head trauma (AHT) hospitalization rates. A 3-dose primary, universal education program (the Period of PURPLE Crying) was implemented through maternal and public health units and assessed by retrospective-prospective surveillance. With parents of all newborn infants born between January 2009 and December 2016 (n = 354,477), nurses discussed crying and shaking while delivering a booklet and DVD during maternity admission (dose 1). Public health nurses reinforced Talking Points by telephone and/or home visits post-discharge (dose 2) and community education was instituted annually (dose 3). During admission, program delivery occurred for 90% of mothers. Fathers were present 74.4% of the time. By 2-4 months, 70.9% of mothers and 50.5% of fathers watched the DVD and/or read the booklet. AHT admissions decreased for <12-month-olds from 10.6 (95% CI: 8.3-13.5) to 7.1 (95% CI: 4.8-10.5) or, for <24-month-olds, from 6.7 (95% CI: 5.4-8.3) to 4.4 (95% CI: 3.1-6.2) cases per 100,000 person-years. Relative risk of admission was 0.67

(95% CI: 0.42-1.07, P = 0.090) and 0.65 (95% CI: 0.43-0.99, P = 0.048) respectively.

Barr et al., concluded that the intervention was associated with a 35% reduction in infant AHT admissions that was significant for <24-month-olds. The results are encouraging that, despite a low initial incidence and economic recession, reductions in AHT may be achievable with a system-wide implementation of a comprehensive parental education prevention program [3].

The pathophysiology of pain in symptomatic thoracic disc herniation (TDH) patients remains poorly understood. Mere mechanical compression of the spinal cord and/or the exiting nerve root by a prolapsed disc cannot explain the pathogenesis of pain in all cases. Previous studies report a direct correlation between the levels of proinflammatory cytokines in disc biopsy and the severity of leg pain in patients with lumbar disc herniations.

Using ELISA and high-performance liquid chromatography (HPLC), Andrade et al., from Cologne, Würzburg, Germany. Maastricht, The Netherlands, determined inflammatory cytokine levels (TNF-α, IL-1β and IL-10) and aminoacid levels (glutamate, aspartate, GABA, glycine and arginine) in CSF samples from ten thoracic disc herniation (TDH) patients and ten control subjects who did not suffer an inflammatory disease nor pain related to spinal cord compression, and subsequently correlated these levels with preoperative pain scores. Differences between both groups were evaluated by a Whitney-U-test. In order to estimate the correlation between cytokine or amino acid expression and pain scores, data were analyzed using linear regression analysis.

No inflammatory cytokines were found in CSF samples from control subjects, whereas TNF-α, IL-1β and IL-10 were detectable by ELISA in all CSF samples from TDH patients. TNF-α and IL-10, but not IL-1β levels moderately correlated with preoperative pain scores. Elevated TNF-αlevels positively correlated with high pain scores; elevated IL-10 levels negatively correlated with high pain scores. Amino acids were detectable in all samples from both groups. There were no significant differences between the groups in any of the amino acids measured with HPLC.

Increased proinflammatory cytokine expression is associated with elevated pain scores in symptomatic TDH patients. On the other hand, there is no conclusive correlation between the intensity of pain and the local or systemic presence of amino acids associated with pain transmission [4].

Finger et al., from the Neurosurgery Department of Cristo Redentor Hospital, Porto Alegre, Brazil, report a case of spontaneous posterior fossa subdural hematoma treated with anticoagulant therapy that made good recovery after surgical treatment [5].

Bernat et al., from the Department of Neurosurgery Toronto Western Hospital, La Pitié-Salpêtrière hospital, Paris, France. King Faisal Specialist Hospital and Research Center, Riyadh, Ain Shams University, Cairo, Egypt, performed a retrospective analysis of patients submitted to endoscopic endonasal approach or transcranial approach for anterior skull base meningiomas (ASBM) resection from May 2006 to January 2016 Clinical, radiological and pathology data were retrieved for analysis. Tumor size, location, surgical technique, extent of resection and tumour grade were assessed. The two groups were compared to identify predictors and differences regarding tumor recurrence.

Fifty-two patients (17 Olfactory Groove meningioma & 35 Tuberculum sellae meningioma) were included; 26 (6 Olfactory Groove meningioma & 20 Tuberculum sellae meningioma) underwent endoscopic endonasal approach and 26 (13 Olfactory Groove meningioma & 13 Tuberculum sellae meningioma) transcranial approach, with a mean follow up of 41 months. GTR was achieved in 38 (73%) patients (18 (69%) in endoscopic endonasal approach and 20 (77%) in transcranial approach). Eight (15 %) patients presented with recurrence (5 (19 %) in endoscopic endonasal approach group; 3(11.5%) in transcranial approach group without statistical difference (p= 0.69). Among the recurrences, GTR had been achieved in 1 case of each group. In group endoscopic endonasal approach, one patient underwent transcranial approach for a recurrent tumor and another patient was referred for radiosurgery.

This study has shown an overall similar recurrence rate of Anterior skull base meningioma regardless the technique used. However analysis of larger series with longer follow-up is necessary to clearly define the indications and to fully validate the efficacy of endoscopic endonasal approach [6].

Ali et al., from the Department of Neurosurgery, Vanderbilt University Medical Center, Nashville, TN, USA report a novel institutional experience with performing cSCS trials with patients placed in an upright sitting position. This allows easy access to the cervical epidural space and has the added benefit of unobstructed access to the airway.

They retrospectively reviewed data for patients who had undergone cervical spinal cord stimulation trial procedures in an upright, sitting position.

Demographic information including age, gender, preoperative diagnosis, progression to permanent implant after a successful trial and operative time in minutes was collected.

A detailed description of the technique for implantation of cervical spinal cord stimulator trial leads in an upright sitting position is described. A total of 29 patients were implanted; 16 (55%) were female. Mean operative time was 78 minutes from incision to closing. The majority of patients (25/29; 86%) had successful trials and proceeded to permanent implant. No complications occurred and the procedure was well tolerated by all patients.

Cervical spinal cord stimulation trials performed in an upright, sitting position allows for easy epidural access and an unobstructed airway with reasonable set up time [7].

Hoogmoed et al., from the Department of Neurosurgery, Academic Medical Center, Amsterdam, The Netherlands, investigated which disease-related characteristics, present at admission, could identify patients with chance of good outcome.

146 consecutive WFNS grade V SAH patients (2002 - 2013) were included. Demographic and disease-related characteristics were compared between patients with a good outcome (Glasgow outcome scale (GOS) 4 & 5) and a poor outcome (GOS 1-3). Subgroups were made of patients with aneurysm treatment according to outcome; 1) good outcome, 2) poor outcome, with optimal general treatment, 3) poor outcome, general treatment discontinued.

34 of the 146 patients had a good outcome (36% of all treated patients); 16 (47%) of these presented with a GCS score of 3, versus 65 (58%) of patients with a poor outcome (p = 0.33). Eleven (33%) patients in the good outcome group presented with pupillary abnormalities; four (12%) even had

bilaterally fixed and dilated pupils, versus 49 (46%) in patients with a poor outcome ($p < 0.01$). In 51 patients the aneurysm was not treated; all died.

Over a third of all treated WFNS grade V SAH patients had a good outcome. All patients, in whom the aneurysm was not treated, died. Reliable identification of patients who will reach good outcome, on the basis of symptoms on admission, seems impossible, as these symptoms are not discriminating enough [8].

Pijpker et al., Department of Neurosurgery, Groningen, The Netherlands, present a case of severe congenital kyphoscoliosis in a young girl who suffers from skeletal dysplasia. A closing wedge extended Pedicle Subtraction Osteotomy was 3D virtual planned using medical computer design software. After the optimal 3D-wedge was planned, individualized osteotomy guiding templates were designed, for translation of the planned PSO towards the surgical procedure. During surgery the PSO was carried out by use of the osteotomy templates. A successful correction of the kyphoscoliosis was realized.

The kyphosis was successfully reduced using wedge shaped extended PSO, based on the pre-operative 3D virtual planning, assisted by 3D printed individualized osteotomy guiding templates. Besides direct translation of the planned PSO towards surgery, the 3D planning also facilitated detailed preoperative evaluation, more insight in the case-specific anatomy, and accurate planning of the required correction [9].

Sidhu et al., presented a case of a 65-year-old man who presented with right-sided body weakness. He had a past medical history of uncontrolled diabetes mellitus, hypertension, and obstructive sleep apnea requiring use of a nasal continuous positive airway pressure device during sleep.

They performed a computed tomography brain scan, which revealed a left-sided acute on chronic subdural hematoma. Due to his multiple comorbidities, they decided to perform the surgical procedure under electroacupuncture anesthesia. The aim of this case report is to describe a craniotomy performed under electroacupuncture on an elderly patient with multiple comorbidities who was awake during the procedure and in whom this procedure, if it had been performed under general anesthesia, would have carried high risk [10].

Liang Low H. Comment on “Electroacupuncture-assisted craniotomy on an awake patient”. J Acupunct Meridian Stud. 2018 Aug 1. pii: S2005-2901(18)30051-7. doi: 10.1016/j.jams.2018.07.004. [Epub ahead of print] PubMed PMID: 30076994.

Overdrainage and frequent reprogramming are common issues with programmable valves after ventriculoperitoneal shunt surgery for idiopathic normal pressure hydrocephalus (iNPH). Flow regulated valves may address these limitations, but data on their efficacy are sparse.

Wetzel et al., from the Center for Neurosurgery, University Hospital of Cologne, Germany, present a single-center experience with flow-regulated valves focusing on overdrainage and efficiency.

Thirty-two patients with iNPH treated with the Integra® NPH Low Flow Valve were prospectively enrolled. Clinical evaluation was performed at baseline, postoperatively as well as 3 and 6 months

after surgery. The outcome was assessed by employing the iNPH grading scale and the Mini Mental State Examination (MMSE). Overdrainage was assessed clinically and radiologically by computed tomography.

The mean patient age was 71 years. All patients presented with gait disorder, 29 had cognitive disorder and 25 had urinary incontinence. The mean duration of symptoms was 22.9 months. At 3-month follow-up, 25/31 patients (80.6%) improved on the total iNPH score by at least 5 points ($p < 0.001$). The mean MMSE score increased from 24.5 to 26.1 points ($p = 0.013$). After 6 months, the improvement rates of the iNPH (82.1%) and the MMSE scores (26.8 points) were stable. The rate of clinically significant overdrainage was 3.2%. One patient presented with subdural hygromas that necessitated evacuation. In the remaining patients, clinical and radiological signs of overdrainage were absent.

The use of the Integra® NPH Low Flow Valve leads to a good neurological outcome and has low overdrainage rates without the need for reprogramming. These results are encouraging and justify further investigation of this valve [11].

Harary et al., from the Department of Neurosurgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA, conducted a systematic review of the literature to identify cases reporting on management of distant MCC brain metastases (BM). A pooled survival analysis was performed on the institutional and literature cases to assess predictors of OS.

Forty cases were included for analysis, describing operative [14] and non-operative [26] management. Median time to central nervous system involvement was 17.0-mos (interquartile range 10.5-26.5), and most patients had a single BM (62.5%). Management of intracranial disease included radiotherapy (82.5%), systemic therapy (59.5%) and surgical resection (35%). Operative management was associated with a lower intracranial disease burden (DB), but similar DB. Both neurosurgery (hazard ratio [HR] 0.18, 95% confidence interval [CI]: 0.06-0.54, p = 0.002), having RT (HR 0.37, 95% CI: 0.14:0.93, p = 0.04) and having a single BM (extensive intracranial DB: HR 2.51, 95% CI: 1.12-5.6, p = 0.03) conferred an OS benefit on risk-unadjusted analysis. Only, neurosurgical resection was an independent predictor of OS (HR 0.12, 95% CI: 0.03-0.49, p = 0.003), controlling for age, DB and radiotherapy.

Resection of MCC BM may confer a survival benefit given appropriate patient selection. Prospective investigation of multimodal management of neurometastatic MCC is warranted, especially given the promise of new immunotherapy agents in treating MCC [12].

Wu et al. reported previously that bone marrow mesenchymal stem cell (MSC)-derived neural network scaffold not only survived in the injury/graft site of spinal cord but also served as a “neuronal relay” that was capable of improving the limb motor function in a complete spinal cord injury (SCI) rat model. It remained to be explored whether such a strategy was effective for repairing the large spinal cord tissue loss as well as restoring motor function in larger animals.

They have therefore extended in this study to construct a canine MSC-derived neural network tissue in vitro with the aim to evaluate its efficacy in treating adult beagle dog subjected to a complete transection of the spinal cord. The results showed that after co-culturing with neurotropin-3 overexpressing Schwann cells in a gelatin sponge scaffold for 14 days, TrkC overexpressing MSCs differentiated into neuron-like cells. In the latter, some cells appeared to make contacts with each

other through synapse-like structures with trans-synaptic electrical activities. Remarkably, the SCI canines receiving the transplantation of the MSC-derived neural network tissue demonstrated a gradual restoration of paralyzed limb motor function, along with improved electrophysiological presentation when compared with the control group. Magnetic resonance imaging and diffusion tensor imaging showed that the canines receiving the MSC-derived neural network tissue exhibited robust nerve tract regeneration in the injury/graft site. Histological analysis showed that some of the MSC-derived neuron-like cells had survived in the injury/graft site up to 6.5 months. Implantation of MSC-derived neural network tissue significantly improved the microenvironment of the injury/graft site. It is noteworthy that a variable number of them had integrated with the regenerating corticospinal tract nerve fibers and 5-HT nerve fibers through formation of synapse-like contacts. The results suggest that the transplanted MSC-derived neural network tissue may serve as a structural and functional “neuronal relay” to restore the paralyzed limb motor function in the canine with complete SCI [13)].

A 66 year old man fell backwards from the first rung of a ladder sustaining a cervical transverse process fracture of C6 vertebral body and a new diagnosis of ankylosing spondylitis. He was taken for surgical fixation, however his oesophagus was discovered entrapped within the fracture at the time of surgery. Despite the severity of the injury, with surgical reduction, fixation and oesophageal exclusion this patient made a full recovery.

This case demonstrates the severity of injury after minor trauma in the context of ankylosing spondylitis, the capacity for full recovery in oesophageal perforations in spinal trauma, and that clinical suspicion of such injuries allows early diagnosis, treatment and reduced complications [14)].

An initial in silico data mining in a published ependymoma (EPN) patient series (GSE21687) revealed upregulation of EMT-Transcription factors (EMT-TFs) in tumor samples. Further, quantitative real-time polymerase chain reaction (q-RT-PCR) based gene expression analysis of EMT-TFs in 96 EPNs showed significant up-regulation of SNAI1, SNAI2, ZEB1, and TWIST1 as compared to normal brain, associated with upregulation of CDH2/N-Cadherin and downregulation of CDH1/E-Cadherin. Although this was observed in varying degrees in all clinico-pathological-molecular subgroups of EPNs, it was most evident in supratentorial Ependymoma RELA fusion positive and in posterior fossa ependymomas. Immunohistochemistry performed in 60 of the above cases corroborated with gene expression patterns and immunopositivity for Snail, Slug, Zeb1, and Twist1 was observed in 80%, 80%, 81%, and 63% of all EPNs. Immunopositivity for N-Cadherin and E-Cadherin was observed in 76.6% and 2% cases respectively. Univariate Cox regression analysis showed that low expression of CDH1/E-Cadherin (P=.002) and high expression levels of CDH2/N-Cadherin (P<.001), SNAI1/Snail (P=.023), SNAI2/Slug (P<.001) and ZEB1 (P<.001) to be associated with shorter progression free survival.

Malgulwar et al., from the All India Institute of Medical Sciences, New Delhi report for the first time the existence of EMT- like phenotype in EPNs. These factors could represent new prognostic and therapeutic targets in EPN [15)].

A study of Fenske et al.,from the University of Leipzig,Würzburg,Munich, Lübeck Basel St. Gallen, Bern, Lucerne, Aarau, Belo Horizonte and the Department of Neurosurgery, University Hospital Hamburg-Eppendorf, compared the indirect water-deprivation test with direct detection of plasma

copeptin, a precursor-derived surrogate of arginine vasopressin.

From 2013 to 2017, they recruited 156 patients with hypotonic polyuria at 11 medical centers to undergo both water-deprivation and hypertonic saline infusion tests. In the latter test, plasma copeptin was measured when the plasma sodium level had increased to at least 150 mmol per liter after infusion of hypertonic saline. The primary outcome was the overall diagnostic accuracy of each test as compared with the final reference diagnosis, which was determined on the basis of medical history, test results, and treatment response, with copeptin levels masked.

A total of 144 patients underwent both tests. The final diagnosis was primary polydipsia in 82 patients (57%), central diabetes insipidus in 59 (41%), and nephrogenic diabetes insipidus in 3 (2%). Overall, among the 141 patients included in the analysis, the indirect water-deprivation test determined the correct diagnosis in 108 patients (diagnostic accuracy, 76.6%; 95% confidence interval [CI], 68.9 to 83.2), and the hypertonic saline infusion test (with a copeptin cutoff level of >4.9 pmol per liter) determined the correct diagnosis in 136 patients (96.5%; 95% CI, 92.1 to 98.6; P<0.001). The indirect water-deprivation test correctly distinguished primary polydipsia from partial central diabetes insipidus in 77 of 105 patients (73.3%; 95% CI, 63.9 to 81.2), and the hypertonic saline infusion test distinguished between the two conditions in 99 of 104 patients (95.2%; 95% CI, 89.4 to 98.1; adjusted P<0.001). One serious adverse event (desmopressin-induced hyponatremia that resulted in hospitalization) occurred during the water-deprivation test.

The direct measurement of hypertonic saline-stimulated plasma copeptin had greater diagnostic accuracy than the water-deprivation test in patients with hypotonic polyuria. (Funded by the Swiss National Foundation and others; ClinicalTrials.gov number, NCT01940614 .) [16].

Systemic coexpression analysis of glioma could be beneficial for the identification and development of new prognostic and predictive markers in the clinical management.

Shi et al., from Hangzhou, Department of Neurosurgery, Changhai Hospital, Second Military Medical University, Shanghai. Department of Neurosurgery, Huai'an Second People's Hospital, The Affiliated Huai'an Hospital of Xuzhou Medical University, Huai'an, China, extracted data sets from the Gene Expression Omnibus data set by using “glioma” as the keyword. Then, a coexpression module was constructed with the help of Weighted Gene Coexpression Network Analysis software. Besides, Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses were performed on the genes in these modules. As a result, the critical modules and target genes were identified. Eight coexpression modules were constructed using the 4,000 genes with a high expression value of the total 141 glioma samples. The result of the analysis of the interaction among these modules showed that there was a high scale independence degree among them. The GO and KEGG enrichment analyses showed that there was a significant difference in the enriched terms and degree among these eight modules, and module 5 was identified as the most important module. Besides, the pathways it was enriched in, hsa04510: Focal adhesion and hsa04610: Complement and coagulation cascades, were determined as the most important pathways. In summary, module 5 and the pathways it was enriched in, hsa04510: Focal adhesion and has 04610: Complement and coagulation cascades, have the potential to serve as glioma biomarkers [17].

The age-standardized incidence of stroke has decreased globally but, for reasons unknown, conflicting results have been observed regarding trend in incidence of major stroke subtypes in young adults.

Stroke hospitalizations of young people declined in Finland, except for men 35-44 years of age for whom IS hospitalizations increased. Declining length of stay (LOS) and in-hospital mortality of IS patients suggests admission of less severe cases, improved care or both [18].

Kwon et al., from the Department of Neurosurgery, Korea University Guro Hospital South Korea introduced in 2018 a technique and results of retro-pleural/ peritoneal “lateral pediculectomy” for the decompression of Thoracolumbar spine fractures and reconstruction using expandable titanium cage, and circumferential fixation at a single stage.

18 patients who had single unstable, burst Thoracolumbar spine fracture were treated by this technique between January 2014 and December 2016 (T12: 9 cases, L1: 7 cases, L2: 2 cases). They were reviewed retrospectively in terms of radiologic (CT scan and X-ray), clinical outcomes and complications. The results were compared with another cohort of Thoracolumbar spine fractures treated by posterior only surgery.

There was no radiologic complications implying pseudoarthrosis or instrument failure on the postoperative 6 months CT scan. There was also no neurologic deterioration or infections during the same period. 2 patients (11.%) of iatrogenic and 1 patient of trauma related injury of the dura were secured without any delayed complications. 3 patients (16.7%) of transient weakness in left hip flexion immediately after operation were observed and recovered within 2 weeks in all cases. 6 patients (33.3%) complained of dysesthesia and/or hypoesthesia on incision site.

The present technique suggests “lateral pediclectomy” as a distinct anatomic landmark and surgical tactics to access and remove bony fragment effectively and safely. This provides a more straightforward assess to the burst fragment and helps the surgeon to make better intra-operative decompression strategies. Moreover, this circumferential instrumentation with anterior support and fusion revealed better restoration of the thoracolumbar spine alignment compared to posterior only surgery, with acceptable complications rates [19].

Ishida et al., from the Department of Neurosurgery, Johns Hopkins Hospital and Department of Neurosurgery, Kumagaya General Hospital Japan, describe a unique surgical strategy of performing hippocampal transection (HT) plus tumor resection for CRTLE to solve the question of how to balance postoperative seizure outcomes and neuropsychological outcomes.

From 2005 to 2016, seven cases of HT plus tumor resection have been performed for the patients with CRTLE. They routinely perform intraoperative electrocorticography just before and after the resection of the tumor with hemosiderin rim. In cases with residual spikes from hippocampus after the resection, they add HT, considering laterality of the lesion, preoperative memory functions and MRI abnormalities in hippocampi. Patient information, including follow-up periods, seizure outcomes, and preoperative and postoperative (12 months postoperatively) Wechsler Memory Scale-Revised (WMS-R), has been collected.

In the mean follow-up of 62.7 months [range 20-119], the postoperative seizure outcome is as follows: Engel class I in six cases (85.7%) and II in one case (14.3%). Perioperative changes in WMS-R score were as follows: 93.5 preoperatively versus 99.5 postoperatively (P=0.408) in verbal memory and 90.7 versus 98.0 (P=0.351) in delayed recall. Overall, no patient presented with more than 25% decline in any of the WMS-R indices postoperatively.

Postoperative seizure outcomes are acceptable in this study with favorable postoperative memory outcomes. Although it did not reach the statistical significance, memory functions were rather improved postoperatively. In patients with CRTLE, additional HT is a reasonable treatment option [20].

Understanding the costs of microsurgical or radiosurgical intracranial meningioma treatment may offer direction in reducing healthcare costs and establishing cost-effective algorithms.

Abou-Al-Shaar et al., from the Department of Neurosurgery, Clinical Neurosciences Center, University of Utah, Salt Lake City, used the Value-Driven Outcome (VDO) database, which identifies cost drivers and tracks changes over time, to evaluate cost drivers for management of intracranial meningioma.

A single-center, retrospective cohort of patients undergoing microsurgical or radiosurgical treatment of intracranial meningiomas from July 2011 to April 2017 was analyzed. Patient and tumor characteristics, subcategory costs, and potential cost drivers were analyzed within each treatment modality.

Of 268 intracranial meningiomas treated, 198 were managed microsurgically and 70 with stereotactic radiosurgery (SRS). Facility costs were the largest contributor to total costs for microsurgery (59.7%), whereas imaging costs were the largest contributor to SRS total costs (98.2%). Patients with tumors in non-skull base locations had larger tumors (3.7±1.9 vs. 2.7±1.2 cm, p=0.0001) and were more likely to undergo microsurgery (81.7% vs. 55.2%) than patients with skull base tumors. Univariable analysis suggested that ASA Score, length of stay, discharge disposition, and maximal tumor size impacted cost during microsurgery (p=0.001) but only LOS (p=0.0001) and maximal tumor size (p=0.01) were drivers of total costs on multivariate analysis. For radiosurgery, age significantly affected cost in univariable (p=0.001) and multivariate analysis (p=0.003).

Implementing protocols to reduce facility utilization and imaging would mitigate total costs and improve resource utilization, while maintaining high-quality patient care. Additional cost effectiveness studies evaluating patients with true therapeutic equipoise will provide further guidance in these efforts [21].

Arabi H, Ghazi M, Zyani M, Akhaddar A, Niamane R. The Back Book translated to Arabic. Ann Phys Rehabil Med. 2018 Jul 28. pii: S1877-0657(18)31431-3. doi: 10.1016/j.rehab.2018.07.004. [Epub ahead of print] PubMed PMID: 30063980.

The objective of a systematic literature review was to evaluate if intraoperative neurophysiological monitoring (IONM) can prevent neurological injury during spinal operative surgical procedures.

IONM seems to have presumable positive effects in identifying neurological deficits. However, the role of IONM in the decrease of new neurological deficits remains unclear.

Using the Preferred Reporting Items for Systematic Reviews and MetaAnalyses (PRISMA) guidelines for systematic reviews and Meta-analysis, Daniel et al., from São Paulo, Brazil, reviewed clinical comparative study who evaluate the rate of new neurological events in patients who had a spinal surgery with and without IONM. Studies were then classified according to their level of evidence. Methodological quality was assessed according to methodological index for non-randomized studies

instrument.

Six studies were evaluated comparing neurological events with and without IONM use by the random effects model. There was a great statistical heterogeneity. The pooled odds ratio (OR) was 0.72 {0.71; 1.79}, P=0.4584. A specific analysis was done for two studies reporting the results of IONM for spinal surgery of intramedullary lesions. The OR was 0.1993 (0.0384; 1.0350), P=0.0550.

IONM did not result into fewer neurological events with the obtained evidence of the included studies. For intramedullary lesions, there was a trend to fewer neurological events in patients who underwent surgery with IONM. Further prospective randomized studies are necessary to clarify the indications of IONM in spinal surgery [22].

Patient recall of information about procedures, including risks and benefits and potential outcomes, is often insufficient.

Bethune et al., from University of Toronto, sought to determine whether a multimedia patient educational tool enhances the informed consent discussion for elective neurosurgical procedures by increasing patient knowledge of the procedure.

Adult patients from a single neurosurgical site eligible for 4 neurosurgical procedures (lumbar spine or cervical spine decompression for degenerative disease, craniotomy for brain tumor or trigeminal neuralgia treatment) were offered enrolment. Patients were randomly assigned to either the control arm (standard consent discussion) or the intervention arm (review of an e-book containing information tailored to their disease/injury plus standard consent discussion). Participants completed a 14-item questionnaire before and after the consent discussion.

Questionnaires were completed by 38 participants, 18 in the control group and 20 in the intervention group. The mean age was 62.2 (standard deviation [SD] 13.6) years and did not differ significantly between the 2 groups. The mean baseline questionnaire scores were similar for the control and intervention groups (20.4 [SD 7.3] v. 20.6 [SD 6.7]). However, the mean scores on the follow-up questionnaire were significantly different between the 2 groups (20.2 [SD 4.0] v. 23.2 [SD 4.9], p = 0.02). There was no change in the scores on the 2 questionnaires in the control group, whereas, in the intervention group, the mean score was significantly higher after the intervention (p = 0.03).

The use of an electronic booklet appears to improve patients' knowledge of their surgical procedure. The use of multimedia booklets in clinical practice could help standardize and optimize the consent process, ensuring that patients receive the relevant information to make a truly informed decision [23].

Findlay et al., from London and Edinburgh, researched for cervical total disc replacement versus anterior cervical discectomy and fusion.

Databases including Medline, Embase, and Scopus were searched. Inclusion criteria involved prospective randomized control trials (RCTs) reporting the surgical treatment of patients with symptomatic degenerative cervical disc disease. Two independent investigators extracted the data. The strength of evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) criteria. The primary outcome measures were overall and neurological success, and these were included in the meta-analysis. Standardized patient-reported outcomes, including the incidence of further surgery and adjacent segment disease, were

summarized and discussed.

A total of 22 papers published from 14 randomized control trials (RCTs) were included, representing 3160 patients with follow-up of up to ten years. Meta-analysis indicated that TDR is superior to ACDF at two years and between four and seven years. In the short-term, patients who underwent TDR had better patient-reported outcomes than those who underwent ACDF, but at two years this was typically not significant. Results between four and seven years showed significant differences in Neck Disability Index (NDI), 36-Item Short-Form Health Survey (SF-36) physical component scores, dysphagia, and satisfaction, all favouring TDR. Most trials found significantly less adjacent segment disease after TDR at both two years (short-term) and between four and seven years (medium- to long-term).

TDR is as effective as ACDF and superior for some outcomes. Disc replacement reduces the risk of adjacent segment disease. Continued uncertainty remains about degeneration of the prosthesis. Long-term surveillance of patients who undergo TDR may allow its routine use [24)].

Lefevre et al., from the Groupe Hospitalier Pitié-Salpêtrière, Paris, France published a retrospective multicenter study, reporting the clinical manifestations, radiological characteristics, histopathological features, treatment strategies and long-term outcomes of patients who have been treated for a Pituicytoma at various institutions in Paris, France over the past 10 years. In addition, they compared the results to the world literature in order to identify similarities concerning the radiographic diagnosis and the treatment strategies of these tumors.

Eight patients were operated on in four different hospitals. Misdiagnosis was constant before surgery, pituitary neuroendocrine tumor or craniopharyngioma being suspected. During surgery (transsphenoidal approach: six cases, transcranial approach: two cases) unusual tumors were noted, with important bleeding in most cases. Complete resection could be obtained in five patients. Pathological diagnosis was confirmed in all cases. During the follow up two recurrences occurred. One was subsequently treated with radiotherapy, the other underwent a second surgery.

Recent updates concerning the histological diagnosis of pituicytomas should be generalized to our practice in order to provide a better understanding of this rare pathology and its natural course [25)].

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Wilkinson et al., from the Department of Neurosurgery, University of Michigan, Ann Arbor, performed a retrospective analysis of all patients with autosomal dominant polycystic kidney disease (ADPKD) and IAs at a single center from 2000 to 2016.

Forty-five patients with ADPKD harboring 71 aneurysms were identified, including 11 patients with subarachnoid hemorrhage (SAH). Of 22 aneurysms managed with observation, none ruptured in 136 yr of clinical follow-up. Thirty-five aneurysms were treated with open surgery and 14 with an endovascular approach. Among treated aneurysms, poor neurologic outcome (modified Rankin scale >2) was seen only in patients presenting with SAH (17% SAH vs 0% elective, P = .06). Acute kidney injury (AKI) was also significantly associated with SAH presentation (22% SAH vs 0% elective, P = .05). Neither procedural complications nor AKI were associated with treatment modality. Among 175 yr of radiographic follow-up in patients with known IAs, 8 de novo aneurysms were found, including 3 that were treated. Of 11 patients with SAH, 7 ruptured in the setting of previously known ADPKD, including 2 with prior angiographic screening and 5 without screening.

Poor outcomes occurred only with ruptured presentation but were equivalent between treatment modalities. Screening is performed only selectively, and 64% (7 of 11) of patients presenting with SAH had previously known ADPKD [26].

Single-stage spine shortening osteotomy without treating spinal cord malformations may have potential advantages for the treatment of severe congenital scoliosis (CS) with Type I Split Cord Malformation (SSCM); however, the study of this technique was limited.

To evaluate the safety and efficacy of a single-stage spine shortening osteotomy in the treatment of severe CS associated with type I SSCM. Huang et al., published a retrospective study designed to compare 2 case series including 12 severe congenital scoliosis (CS) patients with type I SSCM and 26 patients with type A cord function (without spinal cord malformations, evoked potential abnormalities, and neurological dysfunctions preoperatively) treated with a single-stage spine-shortening posterior vertebral column resection (PVCR). Patient demographic, clinical, operative, and radiographic data were obtained and compared between groups.

The surgical procedure was successfully performed in both groups, and the patients were observed for an average of 44.9 mo (range 25-78 mo) after the initial surgery. The radiographic parameters, intraoperative data, and new neurological deficits showed no difference, while deformity angular ratio (SSCM group: control group = 16.6 ± 3.6: 20.1 ± 3.9, P = .01) and corrective rate (SSCM group: control group = 50%: 58%, P = .046) of the main curve were statistically different between groups. All of the new neurological deficits were recovered within 1 yr.

The single-stage spine-shortening posterior vertebral column resection (PVCR) with moderate correction could be applied to the treatment of CS associated with type I SSCM. This strategy can achieve safe spinal deformity correction while obviate the neurological complications brought by the detethering procedures, which merits further clinical investigation [27].

In a study from Rasulić et al. published in 2018 of surgically treated civilian traumatic brachial plexus injury in Serbia, there were seven different etiological factors. The road traffic accidents were the most common-41 (60.3%), while the motorcycle accidents were the most dominant subtype (53.7%) of all road traffic accidents, and also representing 32.4% of all causes of trauma. Supraclavicular elements of the brachial plexus were injured in more than 80% of patients. A total of 49 (72.1%) patients from the study had one or more associated injuries. The most common associated injuries were bone fractures, cerebral contusions, and vascular injury [28].

Golpayegani et al., from the Department of Neurosurgery, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Department of Neurosurgery, Children's Hospital Medical Center, Tehran University of Medical Sciences, Tehran, Iran, reported in 2018 the first congenital case of huge bilateral temporal horn entrapment. A six-month-old boy was admitted with progressive intracranial hypertension who was managed with bilateral ventricular catheters and Y tube connected to one peritoneal catheter [29)].

Sato et al., from Fukushima, Japan, Essen, Germany, published in 2018 a novel high-resolution intraoperative imaging system using laser light source for simultaneously visualizing both visible light and near infrared (NIR) fluorescence images of indocyanine green videoangiography (ICG-VA).

They used a novel system for 14 cerebrovascular cases. The operative field was illuminated via an surgical microscope using a novel laser light source with four bands at 464 (blue), 532 (green), 640 (red), and 785 nm (NIR region). The observed light from the operative field was split using a beam splitter cube into visible (420- 660 nm) and NIR fluorescence emission light (832-900 nm). Images from the color video and NIR fluorescence emission windows were merged for visualization on a monitor screen simultaneously. Laser light was compared with xenon light, and both setups were tested for cerebrovascular surgery.

Laser light has numerous advantages over xenon light. The present setup clearly visualized the color operative field with enhanced blood flow. Complete clipping or incomplete clipping with neck remnant or remnant flow into an aneurysm was confirmed in aneurysm surgeries. Feeding artery and draining veins were easily distinguished in case of arteriovenous malformation.

Using the present setup, they can observe the color operative field and enhanced blood flow using ICG in real-time. This setup could facilitate cerebrovascular surgery [30)].

A study of Çavdar et al., from Istanbul, Turkey, in 2018 aims to define the cortical and subcortical and brain stem connections of the cerebellum via the superior cerebellar peduncle (SCP) and middle cerebellar peduncle (MCP) using biotinylated dextran amine (BDA) and FluoroGold (FG) tracer in Wistar rats. 14 male rats received 20-50-nl pressure injections of either FG or BDA tracer into the SCP and MCP. Following 7-10 days of survival period, the animals were processed according to the related protocol for two tracers. Labelled cells and axons were documented using light and fluorescence microscope. The SCP connects cerebellum to the insular and infralimbic cortices whereas, MCP addition to the insular cortex, it also connects cerebellum to the rhinal cortex, primary sensory cortex, piriform cortex and auditory cortex. Both SCP and MCP connected the cerebellum to the ventral, lateral, posterior and central, thalamic nuclei. Additionally, SCP also connects parafasicular thalamic nucleus to the cerebellum. The SCP connects cerebellum to basal ganglia (ventral pallidum and clastrum) and limbic structures (amygdala nuclei and bed nucleus of stria terminalis), however, the MCP have no connections with basal ganglia or limbic structures. Both the SCP and MCP densely connects cerebellum to various brainstem structures. Attaining the knowledge of the connections of the SCP and MCP is important for the diagnosis of lesions in the MCP and SCP and would deepen current understanding of the neural circuit of various diseases or lesions involving the SCP and MCP [31)].

Shimada et al., from the Department of Neurosurgery, Minamisoma Municipal General Hospital, Japan. compared in 2018 hospital mortality in patients who sheltered-in-place (non-evacuees) after the incident with the baseline preincident mortality and articulated postincident circumstances of the hospital while sheltering-in-place.

They considered all 484 patients admitted to Takano Hospital (located 22 km South of the Fukushima Daiichi nuclear power plant) from 1 January 2008 to 31 December 2016.

Significant differences in mortality rates between preincident baseline and three postincident groups (evacuees, non-evacuees (our major interest) and new admittees) were tested using the Bayesian survival analysis with Weibull multivariate regression and survival probability using the Kaplan-Meier product limit method. All the analyses were separately performed by the internal and psychiatry department.

After adjusting for covariates, non-evacuees in the internal department had a significantly higher mortality risk with an HR of 1.57 (95% credible intervals 1.11 to 2.18) than the baseline preincident. Of them, most deaths occurred within the first 100 days of the incident. No significant increase in mortality risk was identified in evacuees and new admittees postincident in the department, which were adjusted for covariates. In contrast, for the psychiatry department, statistical difference in mortality risk was not identified in any groups.

The mortality risk of sheltering-in-place in a harsh environment might be comparable to those in an unplanned evacuation. If sheltering-in-place with sufficient resources is not guaranteed, evacuation could be a reasonable option, which might save more lives of vulnerable people if performed in a well-planned manner with satisfactory arrangements for appropriate transportation and places to safely evacuate [32].

Synaptic plasticity, induced by the close temporal association of two neural signals, supports associative forms of learning. However, the millisecond timescales for association often do not match the much longer delays for behaviorally relevant signals that supervise learning. In particular, information about the behavioral outcome of neural activity can be delayed, leading to a problem of temporal credit assignment. Recent studies suggest that synaptic plasticity can have temporal rules that not only accommodate the delays relevant to the circuit, but also be precisely tuned to the behavior the circuit supports. These discoveries highlight the diversity of plasticity rules, whose temporal requirements may depend on circuit delays and the contingencies of behavior [33].

The risk of hip dislocation increases with the severity and extent of cerebral palsy (CP), exceeding 70% in the most severe cases. Hip dislocation causes pain in up to 30% of cases, carries a risk of orthopaedic and cutaneous complications, and hinders patient installation and nursing care. These adverse outcomes warrant routine screening, which has been proven effective in lessening the frequency and severity of hip displacement. Preventive techniques including physical therapy, orthoses, and treatments to alleviate spasticity are strongly recommended in every case. The beneficial effects of treating spasticity, if needed via neurosurgical procedures, have been convincingly established. Orthopaedic surgery is required when prevention fails. Soft-tissue release is designed to correct the asymmetry in the forces applied by the muscles. Femoral osteotomy creates

the possibility for spontaneous correction of secondary acetabular dysplasia. Progress has been made in standardising the use of multilevel surgery involving the soft tissues, femur, and pelvis, which is often effective in correcting the morphological abnormalities and stabilising the joint. When hip pain or alterations are severe, hip resection or total hip arthroplasty are highly effective in alleviating the pain and improving patient comfort. The spastic hip is a complex condition in which currently available screening protocols and treatment strategies have been proven effective in benefitting patient outcomes [34].

Emerging evidence implicates sphingosine-1-phosphate (S1P) signaling in the pathobiology of glioblastoma and angiogenesis, but its role in glioblastoma-endothelial crosstalk remains largely unknown. In a study of Hadi et al., in 2018 from the Department of Medical Biotechnology and Translational Medicine, Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico Milan, Laboratory of General Physiology, Department of Biology and Biotechnology “Lazzaro Spallanzani”, University of Pavia, Italy, sought to determine whether the crosstalk between glioblastoma cells and brain endothelial cells regulates sphingosine-1-phosphate signaling in the tumor microenvironment. Using human glioblastoma and brain endothelial cell lines, as well as primary brain endothelial cells derived from human glioblastoma, they report that glioblastoma-co-culture promotes the expression, activity, and plasma membrane enrichment of sphingosine kinase 2 in brain endothelial cells, leading to increased cellular level of sphingosine-1-phosphate, and significant potentiation of its secretion. In turn, extracellular sphingosine-1-phosphate stimulates glioblastoma cell proliferation, and brain endothelial cells migration and angiogenesis. They also showed that, after co-culture, glioblastoma cells exhibit enhanced expression of S1P1 and S1P3, the sphingosine-1-phosphate receptors that are of paramount importance for cell growth and invasivity. Collectively, the results envision glioblastoma-endothelial crosstalk as a multi-compartmental strategy to enforce pro-tumoral sphingosine-1-phosphate signaling in the glioblastoma microenvironment [35].

Using a bioinformatic approach, Wu et al., from the Department of Gastroenterology, The First Affiliated hospital of Wenzhou Medical University, Wenzhou. Department of Neurosurgery, Nanjing Medical University Affiliated Changzhou NO.2 People's Hospital. Department of Chemoradiation Oncology, The First Affiliated hospital of Wenzhou Medical University, China, identified a microRNA, miR-1273 g-3p, that is predicted to target the 3' untranslated region (UTR) of MAGEA3/6. Analyzing miR-1273 g-3p expression in human colon cancer tissues, they found a reduction in miR-1273 g-3p expression correlating with increased MAGEA3/6 expression and AMPKα1 downregulation. Expression of miR-1273 g in HT-29 cells and primary human colon cancer cells down-regulated MAGEA3/6, leading to AMPKα1 upregulation, inhibition of proliferation and cell apoptosis. The anti-CRC activity of miR-1273 g was blocked by AMPKα1 knockout. MAGEA3/6 shRNA silencing mimicked and abolished miR-1273 g-induced actions in HT-29 cells. In vivo, miR-1273 g- or MAGEA3/6 shRNA-expressing HT-29 tumors grew significantly slower than control tumors.

They propose a novel MicroRNA-based mechanism, whereby miR-1273 g represses MAGEA3/6 expression in human CRC cells and tissues, which may provide a novel cancer-specific therapeutic [36].

The aim of a study of Dou et al., was to observe the influence of combined zinc and folic acid administration on depression and to explore its mechanism of action. Male Sprague Dawley rats were randomly divided into five groups: control, model, paroxetine (P), zinc + folic acid (ZnY), and

zinc + folic acid + paroxetine (ZnYP) groups. Rat models of depression were established by chronic mild unpredictable stress for three weeks. These rats were then treated with different interventions for four weeks and the sucrose preference test was then performed to observe changes in rats' behavior. An HPLC-electrochemical method was used to detect the levels of 5-hydroxytryptamine (5-HT), dopamine (DA) and norepinephrine (NE) in the frontal cortex. qRT-PCR was employed to detect the mRNA levels of Tropomyosin receptor kinase B (Trk B) and N-methyl-D-aspartate acid (NMDA) in the frontal cortex; Western blotting was used to detect the protein levels of brain derived neurotrophic factor (BDNF) in the frontal cortex. The results showed that compared with the model group, sucrose consumption, 5-HT, NE and DA levels were significantly increased in the ZnY group ($P < 0.05$). Also the mRNA levels of Trk B and NMDA were significantly increased in the ZnY group compared with the model group ($P < 0.001$). No significant up-regulation of BDNF was observed in the ZnY group.

They conclude that combined administration of zinc and folic acid can improve the symptoms of depression-model rats, and its mechanism is related to increased levels of 5-HT, DA and NE in the brain, and to the up-regulation of Trk B and NMDA [37)].

Prabhala et al., from the Department of Neuroscience and Experimental Therapeutics, Department of Pathology and Laboratory Medicine, Department of Neurosurgery, Department of Neuroscience and Experimental Therapeutics, Albany Medical College, Acoustic Med Systems, Savoy United States, was to assess the effects of external focused ultrasound on sensory thresholds utilizing a common peroneal nerve injury (CPNI) rat model. CPNI was induced by ligating the common peroneal nerve (CPN) of the left hind paw. Neuropathic phenotype was confirmed using the Von Frey Fibers (VFF) with a 50% mechanical detection threshold below 4.0. The Place Escape Avoidance Paradigm (PEAP) was employed as a behavioral correlate. External FUS treatment was applied to the left L4,5 DRG at 8 W for 3-minutes. There were two treatment groups; one received a single FUS treatment, while the other received two. Control groups consisted of one sham CPNI group that received FUS treatment and a CPNI group that received sham FUS treatment. Behavioral tests were conducted pre-CPNI surgery, 1-week post-surgery, and for 1-week post-FUS treatment(s). CPNI surgery resulted in lower VFF mechanical thresholds in the left hind paw compared to baseline ($p < 0.0001$) and increased proportion of time spent on bright side compared to baseline values on PEAP ($p = 0.0473$), indicating neuropathic state. FUS treatment increased VFF thresholds after 24-hours ($p < 0.0001$), 48-hours ($p = 0.0079$), and 72-hours ($p = 0.0164$). VFF returned to baseline values from day 4-7. Following a second FUS treatment on day 8, increased mechanical thresholds were similarly observed after 24-hours ($p = 0.0021$), 48-hours ($p < 0.0001$), and 72-hours ($p = 0.0256$). Control group analysis showed (1) CPNI rats experienced no change in mechanical thresholds following sham FUS treatment and (2) Sham CPNI rats receiving FUS did not experience significantly different mechanical thresholds compared to baseline and post-CPNI values. Post-FUS histological analysis demonstrated healthy ganglion cells without chromatolysis.

The results demonstrate changes in VFF and PEAP in rats who underwent CPNI. Single and multiple doses of external FUS increase mechanical thresholds without inducing histological damage. Based on this results, they demonstrated the potential of FUS to serve as a non-pharmacological and non-ablative neuromodulatory approach for the treatment of allodynia and neuropathic pain [38)].

Intrasciatic nerve injection of the Ricinus communis agglutinin (RCA or ricin) causes motor neuron disease with functional deficits, such as those that occur in amyotrophic lateral sclerosis (ALS).

The objective of a study of Liang et al., from Johns Hopkins Hospital, Baltimore, was to develop a new comprehensive platform for quantitative evaluation of motor neuron (MN) loss, muscular atrophy and behavioral deficits using different ricin injection regimens.

Fluorogold (FG)-guided stereology of MNs, in vivo magnetic resonance imaging (MRI) of muscular atrophy, and CatWalk behavioral testing were used to evaluate the outcome of rats treated with different ricin regimens (RCA60 0.5 µg, RCA60 3 µg, and RCA120 6 µg) as animal models of MN degeneration.

FG-guided stereological counting of MNs enabled identification, dissection and robust quantification of ricin-induced MN loss. The RCA60 0.5 µg and RCA120 6 µg regimens were found to be best suited as preclinical MN depletion models, with a low mortality and a reproducible MN loss, accompanied by muscle atrophy and functional deficits evaluated by MRI and the CatWalk method, respectively.

1) Fluorogold neuronal tracing provides a robust and straightforward means for quantifying MN loss in the spinal cord; 2) MRI is well-suited to non-invasively assess muscle atrophy; and 3) The CatWalk method is more flexible than rotarod test for studying motor deficits.

Intrasciatic injection of RCA60 or RCA120 induces nerve injury and muscle atrophy, which can be properly evaluated by a comprehensive platform using FG-guided quantitative 3D topographic histological analysis, MRI and the CatWalk behavioral test [39].

Results in fifty-three spontaneous hypertensive rats, suggest that even at therapeutic plasma concentrations, rivaroxaban may increase the risk of hemorrhagic transformation (HT) after thrombolysis in some conditions, such as hypertension and/or a prolonged ischemic period.

Izuma et al., from the Department of Neurosurgery, Yamaguchi University School of Medicine, Ube, Japan, performed transient middle cerebral artery occlusion for 270 minutes. Placebo, 10 mg/kg or 20 mg/kg rivaroxaban were administered via a stomach tube 180 minutes after induction of ischemia, and rtPA (10 mg/kg) was administered just before reperfusion. Ninety minutes after rivaroxaban administration we measured the rivaroxaban plasma concentration and prothrombin time (PT). HT volume was assessed by hemoglobin spectrophotometry. Additionally, infarct volume, IgG leakage volume, and neurological outcome were assessed.

Rivaroxaban plasma concentration and PT increased in a dose dependent manner but were lower than human peak levels after a once-daily dose of 20 mg rivaroxaban. HT volume increased after treatment with 20 mg/kg rivaroxaban compared with placebo treated controls or those treated with 10 mg/kg rivaroxaban (26.5 ± 5.4, 26.8 ± 8.7, and 41.4 ± 12.6 µL in placebo, 10 mg/kg, and 20 mg/kg treated groups, respectively; $P < .05$). [40].

There is contradictory evidence in the literature on the role of nitric oxide in the pathophysiology of traumatic brain injury (TBI). These contradictory perspectives are likely due to different Nitric oxide synthase (NOS) isoforms - endothelial (eNOS), inducible (iNOS) and neuronal (nNOS) which are expressed in the central nervous system. Of these, the role of nNOS in acute injury remains less clear.

A study of Madan et al., from the Baylor College of Medicine, Houston, aimed to employ a genetic approach by overexpressing arginase isoforms specifically in neurons using a Thy-1 promoter to manipulate cell autonomous NO production in the context of TBI. The hypothesis was that increased

arginase would divert arginine from pathological NO production.

They generated 2 mouse lines that overexpress arginase I (a cytoplasmic enzyme) or arginase II (a mitochondrial enzyme) in neurons of FVB mice.

They found that two-weeks after induction of controlled cortical injury, overexpressing arginase I but not arginase II in neurons significantly reduced contusion size and contusion index compared to wild-type (WT) mice. This study establishes enhanced neuronal arginase levels as a strategy to affect the course of TBI and provides support for the potential role of neuronal NO production in this condition [41].

While dopamine agonists are a primary method of therapeutic treatment for Lactotroph adenoma, the rate of resistance to these drugs continues to increase each year. During previous long-term clinical investigations, Hu et al., from Department of Neurosurgery and Pituitary Tumor Center, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China, found that partial resistant prolactinomas exhibited significantly more fibrosis than did sensitive adenomas, suggesting a role of fibrosis in their drug resistance. Furthermore, resistant adenomas with extensive fibrosis mainly express type I and type III collagens. Since TGF-β1 is the key factor in the initiation and development of tissue fibrosis, including in the pituitary, in this study, they aimed to determine whether TGF-β1 mediated fibrosis in prolactinomas and whether fibrosis was related to prolactinoma drug resistance. Using immunochemistry and western blotting, they found that the TGF-β1/Smad3 signaling pathway-related proteins were elevated in resistant prolactinoma specimens with high degrees of fibrosis compared to levels in sensitive samples, suggesting that this pathway may play a role in prolactinoma fibrosis. In vitro, TGF-β1 stimulation promoted collagen expression in normal HS27 fibroblasts. Furthermore, the sensitivity of rat prolactinoma MMQ cells to bromocriptine decreased when they were co-cultured with HS27 cells treated with TGF-β1. The TGF-β1/Smad3 signaling-specific inhibitor SB431542 counteracted these effects, indicating that TGF-β1/Smad3-mediated fibrosis was involved in the drug-resistant mechanisms of prolactinomas. These results indicate that SB431542 may serve as a promising novel treatment for preventing fibrosis and further improving the drug resistance of prolactinomas [42].

In a randomised, placebo-controlled, double-blind, multicentre trial, Katzenschlager et al., enrolled patients at 23 European hospitals who had been diagnosed with Parkinson's disease more than 3 years previously and had motor fluctuations not adequately controlled by medical treatment. Patients were randomly assigned (1:1) with a computer-generated randomisation code, stratified by site, to receive 3-8 mg/h apomorphine or placebo saline infusion during waking hours (16 h a day [range 14-18 was acceptable]) for 12 weeks. The flow rate of the study drug and other oral medications could be adjusted during the first 4 weeks on the basis of individual efficacy and tolerability, after which patients entered an 8-week maintenance period. The primary endpoint was the absolute change in daily off time based on patient's diaries, and was assessed in the full analysis set, which was defined as all patients who received at least one dose of allocated study drug and had efficacy data available at any timepoint post-baseline. Safety was assessed in all patients who received at least one dose of apomorphine or placebo. All study participants and investigators were masked to treatment assignment. Both the 12-week double-blind phase and the 52-week open-label phase of this study are now complete; this paper reports results for the double-blind phase only. This study is registered with ClinicalTrials.gov (NCT02006121).

Between March 3, 2014, and March 1, 2016, 128 patients were screened for eligibility and 107 were randomly assigned, of whom 106 were included in the full analysis set (n=53 in both groups). Apomorphine infusion (mean final dose 4·68 mg/h [SD 1·50]) significantly reduced off time compared with placebo (-2·47 h per day [SD 3·70] in the apomorphine group vs -0·58 h per day [2·80] in the placebo group; difference -1·89 h per day, 95% CI -3·16 to -0·62; p=0·0025). Apomorphine was well tolerated without any unexpected safety signals. Six patients in the apomorphine group withdrew from the study because of treatment-related adverse events.

Apomorphine infusion results in a clinically meaningful reduction in off time in patients with Parkinson's disease with persistent motor fluctuations despite optimised oral or transdermal therapy [43].

The primary aim of a study of Ehrmann-Müller et al., from the University of Wuerzburg, Germany, was to assess the audiological abilities before and after cochlear implants (CI) provision in children with cochlear nerve hypoplasia or aplasia. Additionally, they aimed to determine if audiological outcomes differed in children with aplasia from those with hypoplasia. Such data should be helpful in determining if CI provision is appropriate for such children.

This retrospective study presents 7 children who were diagnosed with cochlear nerve aplasia or hypoplasia and received a CI. The pre- and postoperative audiological performance and the hearing and speech development of the children were examined.

4 children were unilateral CI users and 3 were bilateral CI users. Hearing reactions could be detected in all children. Already at first fitting, prompt responses and reactions to songs were observed. The aided thresholds in free field in children with hypoplasia were between 30 and 60 dB. Even in children with aplasia, the results in free field with CI averaged between 30 and 70 dB. Therefore the aided thresholds in children with hypoplasia and in children with aplasia of the CN are similar. It could be demonstrated that hearing reactions improve with the long term use of the implant. Improvement in general development could be observed in all children despite the very heterogeneous conditions and the accompanying handicaps.

The results of this study support the hypothesis that children with radiologically-defined CN hypoplasia or aplasia and detectable responses to electrical or acoustical stimuli can improve their sound detection thresholds and their awareness of sound when provided with a CI [44].

The purpose of a retrospective study of Lesueur et al., from Caen, France, was to elucidate if hypofractionated stereotactic radiotherapy (HFSRT) impacts local control of brain metastases from radioresistant tumors such as melanoma and renal cancer, in comparison with radiosurgery (SRS).

Between 2012 and 2016, 193 metastases, smaller than 3 cm, from patients suffering from radioresistant primaries (melanoma and renal cancer) were treated with HFSRT or SRS. The primary outcome was local progression free survival (LPFS) at 6, 12 and 18 months. Overall survival (OS) and cerebral progression free survival (CPFS) were secondary outcomes, and were evaluated per patient. Objective response rate and radionecrosis incidence were also reported. The statistical analysis included a supplementary propensity score analysis to deal with bias induced by non-randomized data.

After a median follow-up of 7.4 months, LPFS rates at 6, 12 and 18 months for the whole population

were 83, 74 and 70%, respectively. With respect to fractionation, LPFS rates at 6, 12 and 18 months were 89, 79 and 73% for the SRS group and 80, 72 and 68% for the HFSRT group. The fractionation schedule was not statistically associated with LPFS (HR = 1.39, CI95% [0.65-2.96], p = 0.38). Time from planning MRI to first irradiation session longer than 14 days was associated with a poorer local control rate. Over this time, LPFS at 12 months was reduced from 86 to 70% (p = 0.009). Radionecrosis occurred in 7.1% for HFSRT treated metastases to 9.6% to SRS treated metastases, without any difference according to fractionation (p = 0.55). The median OS was 9.6 months. Six, 12 and 18 months CPFS rates were 54, 24 and 17%, respectively.

Fractionation does not decrease LPFS. Even for small radioresistant brain metastases (< 3 cm), HFSRT, with 3 or 6 fractions, leads to an excellent local control rate of 72% at 1 year with a rate of 7.1% of radionecrosis. HFSRT is a safe and efficient alternative treatment to SRS [45].

Zhang et al., from the Department of Neurosurgery, Yale University School of Medicine, New Haven, United States tested a chimeric virus in which the Vesicular stomatitis virus (VSV) glycoprotein is replaced with the Chikungunya polyprotein E3-E2-6K-E1 (VSVΔG-CHIKV). Control mice with brain tumors survived a mean of 40 days after tumor implant. VSVΔG-CHIKV selectively infected and eliminated the tumor, and extended survival substantially in all tumor-bearing mice to over 100 days. VSVΔG-CHIKV also targeted intracranial primary patient derived melanoma xenografts. Virus injected into one melanoma spread to other melanomas within the same brain with little detectable infection of normal cells. Intravenous VSVΔG-CHIKV infected tumor cells but not normal tissue. In immunocompetent mice, VSVΔG-CHIKV selectively infected mouse melanoma cells within the brain. These data suggest VSVΔG-CHIKV can target and destroy brain tumors in multiple animal models without the neurotropism associated with the wild type VSV glycoprotein [46].

Altinoz et al., from the Neuroacademy Research Group, Department of Neurosurgery Memorial Hospital, Department of Medical Biochemistry, Acibadem University; Department of Neurology, Kizilay Hospital, Bakirkoy, Istanbul, Turkey; Department of Psychiatry, Maastricht University, Holland, Netherlands.Department of Neurosurgery, Department of Neuroimmunology, Neurological Institute, McGill University, Montreal Canada, were the first to show that medroxyprogesterone acetate (MPA) reduces rat C6 glioma growth in vitro. Now they aimed to determine the effects of MPA on human brain cancers (particularly glioblastoma) in vitro and C6 glioma in vivo.

They evaluated the effects of MPA on: i) monolayer growth of human U87 and U251 glioblastoma, ii) 3D-spheroid growth and invasion of C6 rat glioma and human U251 glioma, iii) interactions with PI3-Kinase inhibitors and coxsackie-adenovirus receptor (CAR) in modifying 3D-spheroid invasion of glioma.

MPA at low doses (3.25-13 µM) insignificantly stimulated and at high doses (above 52 µM) strongly suppressed the growth of human U87 and U251 cells in vitro. MPA also binds to glucocorticoid receptors similar to dexamethasone (Dex) and unexpectedly, PI3-Kinase inhibitors at low doses suppressed anti-invasive efficacies of MPA and Dex. MPA exerted higher invasion-inhibitory effects on CAR-expressing human glioma cells. Lastly, MPA suppressed growth of C6 glioma implanted into rat brain.

Progesterone analogues deserve to be studied in future experimental models of high grade glial brain tumors [47].

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