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Avaliação da eficácia da estimulação
cerebral profunda no tratamento
cirúrgico da distonia cervical

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Área: Neurocirurgia

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Dr. Paulo José Campos Linhares Vieira**

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Evaluation of the efficacy of deep brain stimulation in the surgical treatment of cervical dystonia

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Evaluation of the efficacy of deep brain stimulation in the surgical treatment of cervical dystonia.

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SUMMARY

Objective: Deep brain stimulation (DBS) of the globus pallidus internus (GPI) is a promising therapeutic option for patients with medically refractory dystonia. We present the one year results of DBS of the GPI in four patients with cervical dystonia.

Materials and methods: Four patients with medically refractory cervical dystonia who underwent stereotactic pallidal DBS surgery between June 2010 and November 2011 were included in this retrospective study. Preoperative and postoperative evaluations at 3, 6 and 12 months after surgery were performed using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS).

Results: The four patients experienced sustained severity improvement by a mean of 74,25%, at 12 months follow-up. At one year follow-up, the disability benefit improved by 80,5% (mean). There were no stimulation-related side effects reported.

Conclusion: Pallidal DBS is a valid and promising surgical treatment for medically refractory focal dystonia, although an increased number of patients is necessary to confirm its sustained therapeutic value.

KEY-WORDS: Deep brain stimulation; Focal idiopathic dystonia; Cervical dystonia; Movement disorder; Globus pallidus; Botulinum toxins.

Evaluación de la eficacia de la estimulación cerebral profunda en el tratamiento quirúrgico de distonía cervical.

Resumen

Propósito: Estimulación cerebral profunda (ECP) del globo pálido interno es una terapéutica promisor para pacientes con distonía refractaria al tratamiento médico. Presentamos los resultados de la ECP a un año del globo pálido interno de cuatro pacientes con distonía cervical.

Materiales y métodos: Cuatro pacientes con distonía cervical refractaria al tratamiento médico que fueron sometidos a cirugía estereotáctica para ECP del globo pálido entre Junio 2010 y Noviembre 2011, fueron incluidos en este estudio retrospectivo. Evaluaciones pre y post-operatorias a los 3, 6 y 12 meses tras cirugía fueron realizadas utilizando la escala Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS).

Resultados: Los cuatro pacientes han gozado de una mejoría sustentada en la gravedad, con una media de 74,25% a los 12 meses de seguimiento. Al final de un año de seguimiento, la mejoría en la discapacidad fue de 80,5% (media). No han sido reportados efectos colaterales o secundarios relacionados con la estimulación.

Conclusiones: ECP del globo pálido es un tratamiento quirúrgico promisor para la distonía focal refractaria al tratamiento médico, aunque más pacientes sean necesarios para confirmar el valor terapéutico sostenido de la ECP.

PALABRAS-CLAVE: Estimulación cerebral profunda; Disonía focal idiopática; Disonía cervical; Trastornos del movimiento; Globo pálido; Toxinas botulínicas.

Abbreviations: DBS=Deep brain stimulation; TWSTRS=Toronto Western Spasmodic Torticollis Rating Scale; MRI = Magnetic resonance imaging.

INTRODUCTION

Dystonia is a chronic disease that has a major impact in life quality ¹⁻³. It represents one of the most painful and disabling movement disorders consisting of repetitive, sustained and involuntary contractions of both agonist and antagonist muscles, that leads to abnormal postures, twisting and patterned movements ¹⁻⁴.

Dystonia also manifests during voluntary movements through the activation of additional muscles, usually not requested for the purposed movement ¹⁻².

Several systems have been purposed to classify dystonia, according to aetiology (primary and secondary), age of onset (early-onset and adult-onset), and affected muscles groups (focal, segmented, multifocal, hemidystonia and generalized) ^{2,4,5-7}.

Focal dystonia can be further subdivide according to the affected area of the body ⁵⁻⁶. Cervical dystonia is the most frequent type of focal dystonia and affects neck muscles ⁸. Other focal dystonias are blepharospasm, oromandibular dystonia, spasmodic dysphonia, limb dystonia, truncal dystonia and abdominal wall dystonia ⁵⁻⁶.

Primary (or idiopathic) dystonia occurs alone, without other neurological features or brain abnormalities, although brainstem changes have been reported ⁵⁻⁶. They tend to be hereditary, especially if they are generalized. We can further subdivide

primary dystonias into pure dystonias, dystonias plus syndromes and paroxysmal dystonias ⁵⁻⁶.

Most primary dystonias are sporadic cases, although some genetic mutations have been identified, such as the DYT1 (TOR1A), DYT6 (THAP1), GCH1, DYT11 (SGCE), among others ^{4-5, 22-23}.

Secondary dystonias results from injuries to the CNS, such as a trauma, stroke, metabolic or oncologic disorder. Other signs and symptoms, neurological or not, can manifest. In this subgroup, neuropathological abnormalities are frequently found on MRI ⁵⁻⁶. Usually they are associated with degenerative or destructive lesions that affect the basal ganglia, the cerebellum or the cerebellar outflow pathways ⁵. Parkinson disease is probably the most common cause of secondary dystonia, due to the associated degenerative lesions in basal ganglia and brainstem ⁵.

A specific type of secondary dystonia is tardive dystonia that follows the use of dopamine antagonists ⁶.

Despite being a common movement disorder, uncertainties about dystonia pathology remain since the number of human dystonia cases that have been studied for neuropathological mechanisms is reduced ⁵.

Although gene mutations and other causes have already been identified, little is known about the pathophysiology of dystonic disorders. It is believed that all dystonias implicate a final neurological pathway of diminished thalamocortical output, allowing for simultaneous activation of opposing muscles ⁴.

Aberrant discharge patterns in the Globus pallidus were identified in neurophysiologic studies in dystonic patients, confirming the role of this structure in the pathology of dystonia ⁶.

Firing rates abnormalities in Globus Pallidus, specially in Pars interna, suggests a preponderant role of this structure in the pathology of dystonia which is confirmed by symptomatic improvements after pallidotomy.

The occurrence of lesions in the Putamen and Globus pallidus is frequently found in secondary dystonia ⁵⁻⁶, a finding that supports the involvement of basal ganglia in the pathophysiology of primary dystonia ⁵⁻⁶.

This evidence confirms the role of Basal Ganglia in dystonic disorders.

Some animal studies and human imaging also suggest an involvement of cerebellar structures and cerebellar outflow pathways ⁵⁻⁶. Functional imaging studies in dystonic patients consistently showed overactivity of cerebellar structures, presumably related with abnormalities in glutamate signaling ^{7:23}.

Studies in patients with secondary cervical dystonia reported cerebellar lesions or involvement of cerebellar pathways ⁵, which sustain evidence for the role of this structure in dystonia pathophysiology. This evidence may suggest the existence of more extensive pathways between basal ganglia and cerebellum, than previously thought ⁵.

Although it is not usually associated with diminished cognitive abilities or life span, there are rare complications that one must be aware of such as hyperthermia, rhabdomyolysis, myoglobinuria, respiratory failure and dystonic storm or status dystonicus.

Medical treatment

So far there is no cure for dystonia and available treatments are symptoms directed ⁹.

Botulin-toxin EMG-guided chemodenervation is the gold standard therapy for cervical idiopathic dystonia ⁶⁻¹¹. Both botulinum toxin A and B are approved for cervical dystonia treatment ¹¹⁻¹². The development of antibodies against botulinum-toxin may

diminish the efficacy of this treatment, although is a less common situation with new botulinum toxin products ⁶.

Trihexyphenidyl, benzodiazepines, tetrabenazine, cyclobenzaprine, carbamazepine and oral baclofen are also approved for the treatment of cervical dystonia.

Despite these options, with the exception of dopa-responsive dystonia, pharmacological treatment is usual unsatisfactory, with patients experience little or no relief of symptoms at all ⁵⁻⁶.

With medical failure it is time to consider neurosurgical options. The first-line surgical option is deep brain stimulation of the internal segment of the globus pallidus but several procedures are available for dystonic patients, as peripheral denervation ¹⁰. For instance, cervical dystonia could be treated with peripheral denervation and myectomy of neck muscles ^{6,8,12}.

The implantation of an intrathecal baclofen pump is another option but usually reserved for patients with generalized dystonia with associated spasticity ⁶.

Neurosurgical techniques, such as pallidotomy and thalamotomy, concern permanent lesioning of basal ganglia, are being replaced for DBS. The irreversibility and non-adjustable characteristic are some disadvantages of these ablative surgeries. Permanent cognitive adverse effects, as well as speech and swallowing impairments, are frequent findings after lesioning of basal ganglia ^{6,11}.

DBS surgery is a more valid and safe option for cervical idiopathic dystonia, with several advantages over ablative procedures ^{6-7,13}.

DBS

Among the available surgical options, pallidal DBS is currently the most effective treatment for medically refractory dystonia, having replaced pallidotomy and thalamotomy that were associated with neurologic disabling side effects ^{6,13-14}.

Although DBS mimics lesioning procedures, it is reversible and neurostimulation variables are adaptable ^{12,15}.

The precise mechanism by which pallidal stimulation modulates dystonia is unknown. It is believed that DBS changes both neuronal discharge as well as axonal propagation, functionally modifying the aberrant motor pathways, leading to a normalized motor response ⁶.

Some evidence points to the maintenance of DBS benefit even after suspension of pallidal stimulation. One patient with cervical dystonia, treated with DBS for 5 years, showed sustained improvement for 6 months after discontinuation of pallidal stimulation. There is a similar report for a patient with cranial dystonia. This evidence suggests that in focal dystonia DBS may permanently correct the abnormal motor pathways ⁶.

Despite a large number of successful reports, the criteria for chronic DBS remain empirical. The variability of response to pallidal stimulation reflects the lack of recognition regarding patient selection and clinical outcome predictors. To this moment, no possible predictive factors have been established, but data points to lower preoperative severity score, younger age at surgery, positive DYT1 mutation, shorter duration of disease and the lack of skeletal deformities as possible predictive factors ^{9,11,13}.

It is important to perform the surgery before the occurrence of definitive orthopedic abnormalities that will limit the functional benefit achieved with the DBS surgery ^{6,16}.

The experience of the surgical team, precise lead placement and correct device programming all contribute to achieve good outcomes ¹¹.

Concerning children, DBS has been performed safely, and with positive outcomes, in an increasing number of pediatric patients. Pallidal stimulation is appropriate for a developing brain and should therefore be considered a safe therapeutic option for children presenting with severe, medically refractory dystonia ¹⁵.

It is widely accepted that DBS is an effective option to treat focal and generalized primary dystonia. However, remains unclear whether pallidal stimulation is also effective in the treatment of secondary dystonias ¹¹.

Positive outcomes have also been reported in the treatment of severe tardive dystonia, myoclonus-dystonia and status dystonicus. Due to the severity of status dystonicus, a life-threatening condition that must be solved prompt, DBS is an acute therapeutic option ¹¹.

In DBS surgery, the device is usually implanted in two stages. In the first one, the quadripolar lead containing the electrodes is implanted stereotactically into the Globus pallidus internus. This can be performed with the patient awake, which allows for a more precise location of the lead, although it may not be possible with children or patients with severe dystonic postures ^{11,17}.

In the second stage, the pulse generator is implanted in the chest wall and the extension cable is implanted connecting the lead to the pulse generator. These two stages could be done in the same operative time.

Regarding the stimulus provided by the DBS device, four parameters can be adjusted: amplitude, pulse width, frequency and choice of the active contacts.

Optimal settings in the treatment of dystonia are unknown. Some studies report positive outcomes with wide pulses (210-400 μ sec) and high frequencies (130 Hz or

higher), and others have found good results with lower settings (60-80 Hz; 210 μ sec), as well as a less frequent need to replace the battery ¹¹.

Regarded as a promising surgical option in cervical dystonia, more data is needed to improve and predict outcomes ^{6,13}.

The only contraindications to DBS surgery may be severe psychiatric disease, cognitive disability or other psychosocial circumstances that would impair the necessary close follow-up for programming and maintenance of the device ^{6,11}.

As previously mentioned for pharmacological treatment, DBS is a symptomatic treatment, not a treatment aimed at etiologic mechanisms, although these remain the ultimate objective towards the cure of dystonia.

The objective of this study is to evaluate the efficacy of pallidal DBS in the treatment of medically refractory cervical dystonia.

MATERIALS AND METHODS

We obtained institutional ethics committee review and approval for this study.

The study took place at Neurosurgery Department of Centro Hospitalar de S.João, in Porto, Portugal, between July 2010 and March 2013.

Four patients were consecutively recruited. Inclusion criteria were clinically diagnosed cervical dystonia, pharmacological treatment failure, having been submitted to DBS surgery for focal idiopathic dystonia, between June 2010 and November 2011, no secondary cause for dystonia, no other changes besides dystonia on neurological examination, normal findings on cerebral magnetic resonance imaging (MRI), absence of cognitive and psychiatric disturbances.

All patients had injections of botulinum toxin (both toxin A and B) into the affected muscles. The four experienced primary failure or diminished response and insufficient relief from botulinum toxin over time.

One patient had early onset dystonia (<28 years) and hand tremor.

Table 1 summarizes the demographic characteristics of the patients in our study.

By the time of DBS surgery, the mean age of patients was 46,25 years (SD +- 11,47). The mean age at the onset of disease was 38,5 years (SD+- 15,61), and the mean duration of symptoms before surgery was 7,75 years (SD+-5,12).

Drugs for treatment of dystonia at the time of surgery included trihexyphenidyl, baclofen, benzodiazepines, antidepressants, analgesics and physiotherapy.

To evaluate patients clinical response the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) was applied at baseline (preoperatively) and at 3, 6 and 12 months of follow-up. The TWSTRS subscales of severity and disability were applied. Patients were filmed and evaluated by the same physician.

The same surgical team carried out DBS surgery in all four patients, at Centro Hospitalar de S.João. The preliminary target for electrodes implantation was defined by stereotactic CT fused with a volumetric MRI.

Postoperative CT fusion with pre-operative MRI allowed assessment of electrodes correct location.

Although stimulation settings are not an issue on this study, setting at the last follow-up are specified in table 2.

No	Sex	Age at	Age at onset	Duration of	Medical
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		surgery	of dystonia	disease	therapy
1	F	45	40	5	DZP, CZP, BAC, GBP
2	F	58	56	2	APZ, THP, BPP
3	M	31	18	13	DZP, THP
4	F	51	40	11	VFX, DZP, MRP, Physiotherapy

Table 1. Demographic features of patients in this study. DZP, Diazepam; CZP, Clonazepam; BAC, Baclofen; GBP, Gabapentin; APZ, Alprazolam; THP, Trihexyphenidyl; BPP, Bupropion; VFX, Venlafaxine; MRP, Morphine sulfate.

No	Gpi	Frequency (Hz)	Pulse width (µs)	Mean amplitude (V)	Impedance
1	Left	130	120	4,0	1200
	Right	130	120	4,2	1203
2	Left	130	90	3,6	1100
	Right	130	60	3,4	1200
3	Left	130	60	3,2	1133
	Right	130	60	3	972
4	Left	130	60	3,8	1101
	Right	130	60	3,6	1121

Table 2. Stimulation settings

RESULTS

Results are presented as Mean (+- Standard deviation).

Percent of benefit was calculated with the formula $[(TWSTRS \text{ score at baseline} - TWSTRS \text{ score postoperatively}) / TWSTRS \text{ score at baseline}] \times 100$.

Data shown concern TWSTRS severity subscale (Table 3) and disability subscale (Table 4).

Both severity and disability scores were significantly reduced in all patients since the beginning of follow-up.

Three months after surgery, the mean improvement in severity was 71,75%. Patients experienced an 81,5% improvement in disability scores, at 3 months follow up.

At 6 months follow-up, both severity and disability scores were slightly higher, with correspondent lower severity and disability improvements: 70% and 76,5%, respectively.

However, at 12 months follow-up, both severity and disability scores improved. The four patients experienced sustained severity improvement by a mean of 80,5%, at 12 months follow-up. At one year follow-up, the disability benefit improved by 74,25% (mean).

No	TWSTRS baseline	TWSTRS at 3 months	Severity benefit at 3 months (%)	TWSTRS at 6 months	Severity benefit at 6 months (%)	TWSTRS at 12 months	Severity benefit at 12 months (%)
1	19	7	63%	10	47%	10	47%
2	22	6	73%	6	73%	4	82%
3	24	5	79%	3	88%	1	96%
4	25	7	72%	7	72%	7	72%
Mean	22,5 (2,65)	6,25 (0,96)	71,75% (6,6)	6,5 (2,89)	70% (16,99)	5,5 (3,87)	74,25% (20,66)

Table 3. TWSTRS severity subscores

No	TWSTRS baseline	TWSTRS at 3 months	Disability benefit at 3 months (%)	TWSTRS at 6 months	Disability benefit at 6 months (%)	TWSTRS at 12 months	Disability benefit at 12 months (%)
1	14	5	64%	6	57%	6	57%
2	19	2	89%	3	84%	0	100%
3	12	0	100%	1	92%	1	92%
4	15	4	73%	4	73%	4	73%
Mean	15 (2,94)	2,75 (4,92)	81,5% (16,09)	3,5 (2,08)	76,5% (15,15)	2,75 (2,75)	80,5% (19,33)

Table 4. TWSTRS disability subscores

DISCUSSION

Until de late 1990s, regarding cervical dystonia treatment, DBS was considered a third-line option, after botulinum toxin injections and surgical peripheral denervation of the affected muscles.

Since the introduction of DBS by Krauss and coworkers the confirmation of sustained benefit in dystonia treatment was observed in several studies ^{18,21,24-27}. Loss of benefit from DBS after one year is rare ⁶ so DBS is now a valid and safe first-line treatment for cervical dystonia ⁸.

DBS surgery has a low rate of complications. These can be intraoperative hemorrhage or ischemia, perioperative infection, requiring device removal, and displacement or fracture of the extension cable. Sometimes, lead fracture can occur, more frequently than in Parkinson's or tremor's patients, due to vigorous dystonic movements. In the rare case of inadequate response, lead repositioning may be necessary ^{6,12}.

So far, concerning cognitive and neuropsychiatric effects, no adverse outcomes were described ^{6,12}.

There were no perioperative complications in all four surgeries.

Our study shows that patients with cervical dystonia with previous medical failure including botulinum toxin injections may achieve sustained improvement after pallidal stimulation. Like in other studies gradual increase in benefit occurs and may take several months to reach the maximum benefit ^{8,10}, although it may not be true for all patients ¹⁰.

A limitation of our study is the small number of patients, which doesn't allow us to assert new conclusions. However all patients had cervical dystonia, creating a homogeneous group of patients.

Despite the reduced number of participants, outcomes at 12 month follow-up were similar to that published by other groups^{8,18-19}. Loher *et al* found a mean severity improvement of 55% and a 66,8% disability benefit (mean), at one year follow-up⁸. Ostrem *et al* found a severity improvement of 43,5%, and a disability benefit of 70,8%⁶. Krauss *et al* found a mean improvement of 63% in both severity and disability, with a longer follow-up (20 months)²¹. In our group of patients we found mean improvements in severity and disability scores of 64,5% and 78,5%, respectively. Another study, Kiss *et al*, found smaller improvements: 43% benefit in severity scores and 24% improvement in disability⁵.

One strength of our study is the fact that the same surgical team performed the DBS surgery in all four patients, and outcomes were evaluated by the same physician at the same hospital facilities.

The application of a known validated scale, the TWSTRS, to assess severity and disability scores at baseline, as well as clinical outcomes after DBS surgery allows us to trust on our results^{11,20}.

We couldn't find any relationship between duration of disease and improvement achieved. In our patients, those with a longer duration of disease (patients no 3 and 4) had high improvement scores, both in severity (96% and 72% respectively) and disability (92% and 73% respectively).

Due to the variability of scores as time passes by, it would be helpful to evaluate patients for a longer time, in order to understand when improvements are stable.

In our study we didn't evaluate the stimulation settings so no prognosis factors were identified. However, one patient needed to adjust stimulation settings (from GPi left: 3,2V/60µs/130Hz, impedance 1278; GPi right: 2,5V/60µs/130Hz, impedance 700, to GPi left: 3,2V/60µs/130Hz, impedance 1133; GPi right: 3V/60µs/130Hz, impedance

972), which suggests us an important role of this variables in cervical dystonia treatment with DBS.

CONCLUSION

This study demonstrated that pallidal stimulation allows for a sustained decreased in the severity of cervical dystonia. DBS also results in frank improvements in disability resulting from this movement disorder, and the rate of complications is considerably small.

Therefore, pallidal DBS must be considered a safe, valid and successful surgical therapeutic option for cervical dystonia.

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manifestados.

Neurocirugía

Revista de la Sociedad Española de Neurocirugía

INSTRUCCIONES PARA LOS AUTORES

Julio de 2012

CONSIDERACIONES GENERALES

Neurocirugía (www.elsevier.es/neurocirugia) de periodicidad bimestral considerará para su publicación trabajos científicos originales de contenido clínico y experimental relacionados con la neurocirugía y otras ciencias neurológicas afines, así como artículos solicitados de expertos, casos clínicos, artículos de opinión y cualquier otra información de interés para los neurocirujanos. *Neurocirugía* acepta trabajos tanto en castellano como en inglés.

La revista está indexada en *Science Citation Index Expanded*, *Journal of Citation Reports*, *Scopus* y *Science Direct*.

Todos los manuscritos se someten a una valoración efectuada por revisores expertos (*peer review*), ajenos al Comité de Redacción de la revista y realizada de forma anónima.

Los manuscritos deben elaborarse siguiendo los requisitos de uniformidad para manuscritos presentados para la publicación en revistas biomédicas, elaborados por el Comité Internacional de Directores de Revistas Médicas, disponibles en <http://www.icmje.org>, y ajustarse a las siguientes instrucciones para los autores.

ENVÍO DE MANUSCRITOS

Los manuscritos deben remitirse por vía electrónica a través del *Elsevier Editorial System* (EES) en la dirección <http://ees.elsevier.com/neurocirugia>, donde se encuentra la información necesaria para realizar el envío. La utilización de este recurso permite seguir el estado del manuscrito a través la página web.

El manuscrito se debe acompañar de una carta de presentación (véase más adelante) redactada en la sección **Enter Comments** del EES. A través de esta plataforma, además de cargar la carta, los autores deberán declarar si el trabajo ha tenido algún tipo de financiación, si tienen algún conflicto de intereses, el cumplimiento de las responsabilidades éticas y transferir todos los derechos sobre el artículo.

El texto del manuscrito (salvo la primera página o página del título), el resumen/*abstract*, las palabras clave/*key words*, las referencias, las tablas, las leyendas y los pies

de figuras se incluirán en un único fichero, y cada una de las figuras en ficheros separados. Estos documentos se grabarán en la sección **Attach Files**.

Consulte las instrucciones generales de uso del EES en su tutorial para autores:

<http://epsupport.elsevier.com/al/12/1/article.aspx?aid=1562&bt=4>

CARTA DE PRESENTACIÓN

Todos los manuscritos deben ir acompañados necesariamente de una carta de presentación (véase el apartado "*Obligaciones del autor*") que se incluirá en la sección **Attach Files** del EES, en la que, además de incluir el título del trabajo, se indique:

- 1) La sección de la revista en la que se desea publicar el trabajo.
- 2) La declaración de que el trabajo es original y no se encuentra en proceso de evaluación por ninguna otra revista científica.
- 3) La explicación, en un párrafo como máximo, de cuál es la aportación original y la relevancia del trabajo en el área de la revista.
- 4) La declaración de que los autores han tenido en cuenta las "Responsabilidades éticas" incluidas en estas normas y, entre ellas: a) que los procedimientos seguidos en la investigación se han realizado conforme a las normas éticas del comité de experimentación humana o animal responsable (institucional o regional) y de acuerdo con la Asociación Médica Mundial y la Declaración de Helsinki; b) que garantizan el derecho de sus pacientes a la privacidad y confidencialidad conforme a lo descrito en el apartado correspondiente de esas normas y que en el artículo se ha evitado cualquier tipo de dato identificativo en texto o imágenes y, en cualquier caso, c) que están en posesión del consentimiento informado de los pacientes para la participación en el estudio y la publicación de los resultados en formato de libre acceso en Internet en la revista *Neurocirugía* y que así lo han declarado en el EES.
- 5) La declaración de cualquier beca (técnica o económica) de una institución.
- 6) La confirmación de que los autores firmantes cumplen los requisitos de autoría (es opcional declarar el grado de participación) conforme a lo recogido en el apartado de "Autoría" de estas normas y conforme con lo han declarado en el EES.

- 7) En el supuesto de que parte del artículo hubiera sido previamente publicado en otra revista (publicación redundante o duplicada), se deberán especificar aquí los detalles y declarar que se está en posesión de los permisos de publicación necesarios por parte del autor y el editor de la misma (véase también el apartado “Garantías y cesión de derechos de propiedad intelectual”).
- 8) La declaración en este punto por cada uno de los autores de la existencia o no de conflicto de intereses y la confirmación de su declaración en la sección **Additional Information** del EES.
- 9) Deberá hacerse constar si el trabajo o parte del mismo ha sido presentado en la Reunión Anual de la SENEC o en otras reuniones o congresos.

Los autores podrán proponer a personas que consideren cualificadas para realizar la revisión crítica del manuscrito. Los revisores sugeridos no deben haber sido colaboradores o coautores en los tres años anteriores ni deben haber contribuido con una crítica sustancial del manuscrito. Pueden hacer sus sugerencias a través del EES, en la sección **Suggest Reviewers**.

SECCIONES

Originales. Trabajos empíricos relacionados con cualquier aspecto de la investigación en el campo de la neurocirugía que tengan forma de trabajo científico, con los siguientes apartados: resumen, introducción, material y métodos, resultados y discusión. La extensión del texto será ilimitada, incluyendo un resumen estructurado, palabras clave y referencias bibliográficas. Además del texto, se admitirán figuras y tablas. El número de autores recomendado es de 6, aunque se permitirá un máximo de 8.

Para la elaboración de ensayos clínicos controlados deberá seguirse la normativa CONSORT (JAMA.1996;276:637-9). Disponible en: <http://www.consort-statement.org/> y para el metaanálisis la normativa QUOROM (<http://www.consort-statement.org/QUOROM.pdf>). Los manuscritos que presenten resultados de estudios sobre validez de pruebas diagnósticas deberán incluir el diagrama de flujo STARD (<http://www.consort-statement.org/stardstatement.htm>).

Casos clínicos. Casos que supongan una aportación importante al conocimiento de la fisiopatología, etiología u otros aspectos de un proceso clínico. La extensión máxima del texto será de 1.500 palabras, 5 DIN-A4, incluyendo un resumen sin estructurar de 150 palabras y un máximo de 15 referencias bibliográficas. La estructura de estos trabajos será la misma que la de los originales (introducción, métodos, resultados y discusión), Resumen, Introducción, Caso o Casos Clínicos, Discusión, y Conclusiones y podrá incluirse hasta un máximo de 3 tablas y/o figuras. El número de autores recomendado es de 4, aunque se permitirá un máximo de 6.

Revisiones. Este tipo de manuscritos será encargado específicamente por el Comité Editorial. Los autores que espontáneamente deseen colaborar en esta sección deberán consultar previamente a los editores de la revista. Serán trabajos de revisión sobre temas relevantes y de actuali-

dad en neurocirugía con la siguiente estructura: Resumen, Introducción, Desarrollo y Conclusiones. La extensión máxima del texto será de 16 DIN-A4, en cuya extensión se incluirá un resumen y un *abstract* de 150 palabras si no está, y las palabras clave correspondientes. También se incluirán 50 referencias bibliográficas como máximo. Es aconsejable que el número de firmantes no sea superior a 3. Además del texto, se admitirán hasta 4 figuras o tablas.

Artículos de opinión. Esta sección tiene como objetivo publicar temas relevantes y de actualidad en neurocirugía que contengan componentes novedosos para la especialidad. No es necesario que el texto se estructure formalmente, pero deberá guardar la lógica narrativa (introducción, desarrollo de la experiencia y conclusiones). La extensión máxima del texto será de 10 DIN-A4, en cuya extensión se incluirá un resumen y un *abstract* de 150 palabras sin estructurar o de 250 si está estructurado) y las palabras clave correspondientes. También se incluirán 15 referencias bibliográficas como máximo. Además del texto se admitirán hasta 2 figuras o tablas.

Cartas al director. Harán referencia a trabajos publicados en la revista y aportarán opiniones, observaciones o experiencias que por sus características puedan ser resumidas en un texto breve. La extensión máxima será de 2 DIN-A4 de texto, sin resumen, incluyendo un máximo de 5 referencias bibliográficas. El número máximo de autores será 4. Se admitirá 1 figura o 1 tabla.

Otras secciones. La revista incluye otras secciones (Editoriales y Artículos especiales, entre otras) cuyos artículos encarga el Comité Editorial. Los autores que espontáneamente deseen colaborar en alguna de estas secciones deberán consultar previamente a los editores asociados de la revista.

PRESENTACIÓN GENERAL DEL MANUSCRITO

Los manuscritos, que podrán estar escritos en español o en portugués, tendrán el formato de papel tamaño DIN-A4 a doble espacio con un tipo de letra de 11 caracteres por pulgada. Las páginas deben estar numeradas correlativamente. Las abreviaturas se introducirán tras el término completo al que representa en el primer uso que se haga de ellas en el artículo a excepción del título. Las unidades de medida se expresarán preferentemente en unidades del sistema internacional. Las cifras decimales se separarán de las unidades mediante una coma y los millares se indicarán mediante un punto.

1. Página del título

Constará de la siguiente información:

- El título del artículo (en castellano y en inglés para el *abstract*) debe describir adecuadamente el contenido del trabajo. Será breve, claro e informativo y sin acrónimos.
- El nombre y el primer apellido de los autores (o los dos apellidos unidos mediante guión). Se recomienda que los autores definan su “apellido bibliográfico” mediante el uso de un solo apellido o, en su defecto, los dos apelli-

dos unidos mediante un guión, para evitar confusiones en las bases de datos bibliográficas.

- En el nombre del (los) departamento(s) y la(s) institución(es) a los que el trabajo debe ser atribuido no se incluirá el cargo académico o profesional.
- Se incluirá el nombre completo, número de teléfono, correo electrónico y la dirección postal completa del autor al que se dirige la correspondencia, que será el responsable de la corrección de las pruebas.

La primera página debe presentarse en un archivo separado del resto del manuscrito.

2. Resumen y palabras clave (2ª página)

Es el apartado que sirve de presentación del trabajo en bases de datos, tanto nacionales como internacionales; por eso es de vital importancia su redacción. Debe realizarse en español y en inglés. Será de 150 palabras y sin estructurar en el caso de las “Revisiones” y las “Revisiones breves” con Introducción, Desarrollo y Conclusiones. El de los “Originales” será de 250 palabras y estructurado en los siguientes apartados: *Objetivo*, señalando el propósito fundamental de la investigación; *Material y método*, la manera de llevarla a cabo: explicando el diseño del estudio, los criterios de valoración de las pruebas diagnósticas y la dirección temporal (retrospectivo o prospectivo). Se mencionará el procedimiento de selección de los pacientes, los criterios de entrada, y el número de los pacientes que comienzan y terminan el estudio; *Resultados*, hará constar los resultados más relevantes y significativos del estudio, así como su valoración estadística; *Conclusiones*, se mencionarán las que se sustentan directamente en los datos junto con su aplicabilidad clínica. Habrá que otorgar el mismo énfasis a los hallazgos positivos y a los negativos con similar interés científico.

Al final del resumen deben figurar 6 palabras clave de acuerdo con las incluidas en el *Medical Subject Headings (MeSH)* del *Index Medicus/MEDLINE*, disponible en inglés en: <http://www.nlm.nih.gov/mesh/meshhome.html> y traducirlas al castellano.

A continuación del resumen y palabras clave se redactará el *title*, el *abstract* y se añadirán las *key words*. El *abstract* debe ser una traducción completa y correcta del resumen al inglés.

3. El texto (3ª página y siguientes)

En la redacción del texto se recomienda la forma impersonal. Conviene dividir claramente los trabajos en apartados, siendo de desear que el esquema general sea el siguiente:

- 1) *Introducción*. Será breve y debe proporcionar sólo la explicación necesaria para que el lector pueda comprender el texto que sigue a continuación. Se deben citar sólo aquellas referencias estrictamente necesarias según criterios de actualidad y relevancia en relación con los objetivos del estudio. No debe contener tablas ni figuras. Debe incluir un último párrafo en el que se exponga de forma clara el o los objetivos del trabajo.
- 2) *Material y métodos*. Se referirá el centro donde se ha realizado la investigación, el período o duración, las características de los pacientes y el criterio de selección y las

técnicas utilizadas, describiendo con precisión cómo se llevó a cabo el estudio, el tipo de diseño utilizado, los criterios de inclusión y exclusión, las pautas de tratamiento, el análisis estadístico, etc., proporcionando los detalles suficientes para que la experiencia pueda repetirse sobre la base de la información aportada. Cuando sea aplicable, deben describirse brevemente las normas éticas seguidas por los investigadores tanto en estudios observacionales como experimentales o cuasi experimentales. Los estudios en seres humanos deben contar con la aprobación expresa del comité local de ética y de ensayos clínicos, y así debe figurar en el manuscrito (véanse “Responsabilidades éticas”). Se debe exponer concisamente el tipo de diseño y, en referencia a los métodos estadísticos empleados, describir con detalle aquellos que no sean habituales en la investigación en neurocirugía. En las revisiones, en el apartado de fuentes, se describirá dónde y cómo se ha realizado la búsqueda de la información.

- 3) Los resultados deben ser concisos y claros, e incluirán el mínimo necesario de tablas y figuras, de acuerdo con el tipo de trabajo. Se presentarán de tal modo que no exista duplicación y repetición innecesaria de información en el texto y en las figuras y tablas.
- 4) *Discusión*. Los autores tienen que exponer sus propias opiniones sobre el tema. Destacan aquí: a) el significado y la aplicación práctica de los resultados; b) las consideraciones sobre una posible inconsistencia de la metodología y las razones por las que pueden ser válidos los resultados y sus limitaciones, relacionándolas con otros estudios importantes; c) la relación con publicaciones similares y la comparación entre las áreas de acuerdo y desacuerdo, y d) las indicaciones y las directrices para futuras investigaciones.

4. Información incorporada por la editorial

En este punto la editorial añadirá la información relativa a las “*Obligaciones del autor*” declaradas en el EES en relación a las “*Responsabilidades Éticas*”, en concreto lo relativo a: a) la protección de personas y animales; b) la confidencialidad, y c) el derecho a la privacidad y el consentimiento informado; la financiación; el grado de participación de los autores (opcional) y las declaraciones de cada uno de ellos en relación con la existencia o no de un conflicto de intereses.

5. Agradecimientos

Sólo se expresarán a aquellas personas que hayan contribuido claramente a hacer posible el trabajo, pero que no puedan ser reconocidos como autores. Todas las personas mencionadas específicamente en “*Agradecimientos*” deben conocer y aprobar su inclusión en dicho apartado. La ayuda técnica debe ser expresada en un párrafo distinto al dedicado a reconocer las ayudas económicas y materiales procedentes de instituciones, que deben reconocerse en “*Financiación*” y dan lugar a un potencial conflicto de intereses.

6. Bibliografía

Los nombres de las revistas deben abreviarse de acuerdo con el estilo usado en el *Index Medicus*: consultar la «List

of Journals Indexed» que se incluye todos los años en el número de enero del Index Medicus.

Las referencias bibliográficas se identificarán en el texto mediante llamada en números arábigos en superíndice y numeración consecutiva, según su orden de aparición en el texto, tablas y figuras. En los casos que la cita se coloque junto a un signo de puntuación, la cita precederá al signo (por ejemplo, a diferencia de trabajos previos⁶⁻⁹, los resultados muestran...).

Se evitará en lo posible la inclusión como referencias bibliográficas de libros de texto y de actas de reuniones.

En lo posible se evitará el uso de frases imprecisas como referencias bibliográficas; no pueden emplearse como tales «observaciones no publicadas» ni «comunicación personal», pero sí pueden citarse entre paréntesis dentro del texto.

Las abreviaciones de las revistas se ajustarán a las que utiliza el *Index Medicus* de la *US National Library of Medicine*, disponibles en: <http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi>

Las citas bibliográficas deben comprobarse comparándolas con los documentos originales, indicando la página inicial y la página final, señalando sólo los dígitos que difieran de la página inicial (por ejemplo, 34-9 y no 34-39; 136-41 y no 136-141). La exactitud y veracidad de las referencias bibliográficas es de la máxima importancia y debe ser garantizada por los autores. Las citas tendrán el formato propuesto por el Grupo de Vancouver. A continuación se dan unos ejemplos de citas correctas para diferentes tipos de documentos (para formatos no incluidos en esta relación pueden consultarse más ejemplos en la página web: <http://www.icmje.org>).

Artículo de revista

Apellido e iniciales del nombre separados por comas. Se citarán todos los autores si son 6 o menos de 6, colocando solamente una coma entre ellos, y un punto tras el último autor; si son 7 o más, relacionar sólo los 6 primeros y se añadirá la expresión et al. A continuación se incluye el título del trabajo en el idioma original y un punto al final, abreviatura del nombre de la revista, seguido también de punto, año de publicación seguido de punto y coma, número de volumen, tras el que se pondrán dos puntos, y la primera y última página del trabajo separadas por un guión.

Artículo de revista estándar con menos de 6 autores

Castle M, Barrena C, Samprón N, Arrese I. Remote cerebellar haemorrhage after lumbar arthrodesis: case report and literature review. *Neurocirugía (Astur)*. 2011;22:574-8.

Artículo de revista estándar con más de 6 autores

Álvarez-Salgado JA, Ruiz-Ginés JA, Fuentes-Ventura CD, Gonzales-Sejas AG, Belinchón de Diego JM, González-Llanos Fernández de Mesa F, et al. Intracranial tuberculoma simulating a malignant tumor: case report and literature review. *Neurocirugía (Astur)*. 2011;22:600-4.

Artículo en prensa

Barrow DL, Tindall GT. Visual loss following transephenoidal surgery. *Neurosurgery*. En prensa 2011.

El autor es una organización

Grupo de Estudios de Enfermedades Cerebrovasculares de la SEN. Enfermedad carótida de origen aterotrombótico: hacia un consenso en la prevención. *Neurología*. 2004;19:193-212.

Individuo y organización, ambos son autores

Vallancien G, Emberton M, Harving N, Van Moorselaar RJ, Alf-One Study Group. Sexual dysfunction in 1274 European men suffering from lower urinary tract symptoms. *J Urol*. 2003;169:2257-61.

Sin autor

The entry of NEUROCIROGIA in the Index Medicus/MEDLINE database. *Neurocirugía (Astur)*. 2002;13:4-5.

Suplemento de un volumen

Magni F, Rossoni G, Berti F. BN-52021 protects Guinea pigs from heart anaphylaxis. *Pharmacol Res Comoun*. 1988;20 Suppl 5:75-8.

Suplemento de un número

Pou A. Enfermedades de las neuronas motoras. Estado actual. *Neurología*. 1996;11 Suppl 5:1S-6S.

Parte de un volumen

Abend SM, Kulish N. The psychoanalytic method from an epistemological viewpoint. *Int J Psychoanal*. 2002;83 (Pt 2):491-5.

Parte de un número

Ahrar K, Madoff DC, Gupta S, Wallace MJ, Price RE, Wright KC. Development of a large animal model for lung tumors. *J Vasc Interv Radiol*. 2002;13(9 Pt 1):923-8.

Número sin volumen

Baumeister AA. Origins and control of stereotyped movements. *Monogr Am Assoc Ment Defic*. 1978;(3):352-84.

Sin volumen ni número

Outreach: bringing HIV-positive individuals into care. *HRSA Careaction*. 2002 Jun:1-6.

Libro

Autores como editores

Diener HC, Wilkinson M, editores. *Drug-induced headache*. Nueva York: Springer-Verlag; 1988.

Autor(es) personal(es) (no editores)

Jennett B, Teasdale G. *Management of Head Injuries*. Philadelphia; FA Davis Company; 1981.

Autores y editores distintos

Breedlove GK, Schorfheide AM. Adolescent pregnancy. 2ª ed. En: Wiczorek RR, editor. *White Plains: March of Dimes Education Services*; 2001.

Organización como autor

Royal Adelaide Hospital; University of Adelaide, Department of Clinical Nursing. *Compendium of nursing research and practice development, 1999-2000*. Adelaide: Adelaide University; 2001.

Capítulo de libro

Rhoton AL. Microsurgical anatomy of the third ventricular region. En: Apuzzo MLJ, editor. Surgery of the third ventricle. Baltimore; Williams & Wilkins; 1987. p. 92-166.

Actas de reuniones

Vivian VL, editor. Child abuse and neglect: a medical community response. Actas de First AMA National Conference on Child abuse and neglect; 1984, marzo 30-31; Chicago, American Medical Association, 1985.

Tesis

Gómez López PA. Hemorragia subaracnoidea aneurismática: Análisis de los factores que influyen en la aparición de isquemia cerebral y en la evolución final [tesis]. Madrid: Facultad de Medicina. Universidad Autónoma; 1991.

Documentos en formato electrónico

Artículo estándar en formato electrónico

Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis. [revista electrónica] 1995;1 [consultado 5 Jun 1996]: Disponible en: <http://www.cdc.gov/ncidod/EID/eid.htm>

CD-ROM:

Anderson SC, Poulsen KB. Anderson's electronic atlas of haematology [CD-ROM]. Filadelfia: Lippincott Williams & Wilkins; 2002.

Sitio en internet (página)

Cancer-Pain.org [página en internet]. Nueva York: Association of Cancer Online Resources, Inc.; c2000-01 [actualizada 16 May 2002; citada 9 Jul 2002]. Disponible en: <http://www.cancer-pain.org/>

Otros materiales publicados

Libro de resúmenes de congreso (Conference proceedings)

Harnden P, Joffe JK, Jones WG, editores. Germ cell tumours V. Proceedings of the 5th Germ Cell Tumour Conference; 13-15 septiembre 2001; Leeds, UK. Nueva York: Springer; 2002.

7. Tablas

Se presentarán en hojas aparte dentro del archivo de texto e incluirán: a) numeración de la tabla con números arábigos, y b) el título correspondiente. Se presentará una sola tabla por hoja y se procurará que sean claras y que su comprensión sea posible sin hacer referencias al texto. Las siglas y abreviaturas se acompañarán siempre de una nota explicativa al pie. Si una tabla ocupa más de una página, se repetirán los encabezamientos en la hoja siguiente. La revista admitirá tablas que ocupen hasta un máximo de una página impresa. A pie de tabla se hará constar el grado de significación estadística, si no se hubiera incluido en el texto de la tabla.

8. Figuras

Se considerarán figuras las fotografías, gráficos de datos y esquemas. Cada figura irá en un archivo aparte. Se identificarán con números arábigos que coincidan con su orden

de aparición en el texto. Es muy importante que las imágenes sean de calidad inmejorable para poder obtener así buenas reproducciones; se presentarán de manera que los cuerpos opacos (huesos, sustancias de contraste) aparezcan en blanco. El Comité de Redacción de la Revista se reserva el derecho de rechazar, previa información a los autores, las figuras que no reúnan la calidad necesaria para conseguir una buena reproducción. Las fotografías se enviarán preferiblemente en formato JPG o TIFF, con una resolución de 300 puntos por pulgada (dpi). Las fotografías se publicarán en blanco y negro en la versión impresa de la revista mientras que se mantendrá el color en la versión electrónica.

Si se reproducen fotografías o datos de pacientes, éstos no deben ser identificativos del sujeto. En todos los casos, los autores deben haber obtenido el consentimiento informado escrito del paciente que autorice su publicación, reproducción y divulgación en soporte papel y en Internet en la Revista.

Las gráficas y esquemas se realizarán cuidando que el formato de las mismas sea de 9 × 12 cm o un múltiplo. La resolución de gráficas y esquemas será de 500 puntos por pulgada (dpi), mientras que para los casos en los que se combinen en una misma figura gráficos y fotografías se recomienda una resolución de 1000 dpi.

Asimismo, los autores son responsables de obtener los oportunos permisos para reproducir en la Revista material (texto, tablas o figuras) publicado previamente. Estos permisos deben solicitarse tanto al autor como a la editorial que ha publicado dicho material.

Los pies de las figuras se prepararán a doble espacio en páginas separadas. Deberán contener información suficiente para poder interpretar los datos presentados sin necesidad de recurrir al texto. Cuando se usen símbolos, flechas, números o letras para identificar parte de las ilustraciones, deberán explicarse claramente en la leyenda con notas explicativas a pie de figura mediante llamadas en forma de letras minúsculas en superíndice y en orden alfabético (a, b...). En las reproducciones histológicas se especificará la tinción empleada y el aumento.

OBLIGACIONES DEL AUTOR

1. Responsabilidades éticas

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Neurocirugía

Revista de la Sociedad Española de Neurocirugía

INSTRUCTIONS FOR AUTHORS

February 2012

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Originals. Empirical studies associated with any aspect of research in the field of Neurosurgery that is in the form of a scientific article, with the following sections: abstract, introduction, Material and methods, Results, and Discussion. The length of the text will be unlimited, including a structured abstract, key words and literature references. Besides the text, Figures and Tables will be accepted. It is recommended that the number of authors does not exceed 6, although a maximum of 8 will be allowed.

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Clinical cases. Cases that make an important contribution to the knowledge of the pathophysiology, aetiology or other aspects of a clinical process. The maximum length of the text will be 1,500 words on 5 DIN-A4, including an unstructured abstract of 150 words and a maximum of 15 literature references. The structure of these articles will be the same as Originals (Introduction, material and methods, Results, and Discussion). Abstract, Introduction, Clinical Case or Cases, Discussion, and Conclusion, and may include up to a maximum of 3 Tables and/ or Figures. The recommended number of authors is 4, although a maximum of 6 will be allowed.

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articles on relevant and current topics in Neurosurgery with the following structure: Abstract, Introduction, Development and Conclusions. The maximum length of text will be 16 DIN-A4 pages, in this length the abstract/*resumen* of 150 words, if it is unstructured, (in English and Spanish) will be included, as well as the corresponding key words. Up to a maximum of 50 literature references will also be included. It is advisable that the number of signing authors does not exceed 3. Besides the text, up to 4 Figures or Tables will be accepted.

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There must be 6 key words at the end of the abstract in accordance with those included in the Medical Subject Headings (MeSH) of *Index Medicus*/MEDLINE, available in English at: <http://www.nlm.nih.gov/mesh/meshhome.html> and translate them into Spanish.

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5. Acknowledgements

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The names of the Journals must be abbreviated in accordance with the style used in Index Medicus, consult the "List of Journals Indexed" which is included every year in the January edition of Index Medicus.

The literature references must be identified in the text using Arabic numerals in superscript and numbered consecutively, in the order that they appear in the text, Tables and Figures). Where the quote is placed next to a punctuation sign, this number will precede the sign (e.g., unlike in previous works⁶⁻⁹, the results show...).

Wherever possible avoid including text books and meeting minutes as literature references.

Avoid the use of vague phrases as literature references; those such as "unpublished observations" or "personal communication" may not be used, but they may be quoted between inverted commas within the text.

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The literature references must be checked by comparing them with the original documents, indicating the initial and final page, indication only the digits that differ from the initial page (for example, 34-9 and not 34-39); 136-41 and not 136-141). The accuracy and veracity of the literature references are of utmost importance and must be guaranteed by the authors. The references will be in the format proposed by the Vancouver Group. Some examples of correct references are shown below for the different types of documents (for formats not included in this list, consult more examples on the web page: <http://www.icmje.org>).

Journal Article

Surname and initials separated by commas. List all the authors if there are 6 or less than 6, placing only a coma between them, and a full stop after the last author; if there are 7 or more, list the first 6 and add the expression "et al". The title of the article is then included (in the original language) followed by a full stop, abbreviation of the journal name, also followed by a full stop, year of publication followed by a semi-colon, volume number, after which is placed a colon, then the first and last page of the reference separated by a hyphen.

Standard journal article with less than 6 authors

Castle M, Barrena C, Samprón N, Arrese I. Remote cerebellar haemorrhage after lumbar arthrodesis: case report and literature review. *Neurocirugía (Astur)*. 2011;22:574-8.

Standard journal article with more than 6 authors

Álvarez-Salgado JA, Ruiz-Ginés JA, Fuentes-Ventura CD, Gonzales-Sejas AG, Belinchón de Diego JM, González-Llanos Fernández de Mesa F, et al. Intracranial tuberculoma simulating a malignant tumor: case report and literature review. *Neurocirugía (Astur)*. 2011;22:600-4.

Article In press

Barrow DL, Tindall GT. Visual loss following transsphenoidal surgery. *Neurosurgery*. In press 2011.

The author is an organisation

Grupo de Estudios de Enfermedades Cerebrovasculares de la SEN. Enfermedad carotida de origen aterotrombotico: hacia un consenso en la prevencion. *Neurología*. 2004;19:193-212.

Individual and Organisation, both are authors

Vallancien G, Emberton M, Harving N, Van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1274 European men suffering from lower urinary tract symptoms. *J Urol*. 2003;169:2257-61.

No author

The entry of NEUROCIRUGIA in the Index Medicus/MEDLINE database. *Neurocirugía (Astur)*. 2002;13:4-5.

Supplement of a volume

Magni F, Rossoni G, Berti F. BN-52021 protects Guinea pigs from heart anaphylaxis. *Pharmacol Res Comoun*. 1988;20 Suppl 5:75-8.

Issue supplement

Pou A. Enfermedades de las neuronas motoras. Estado actual. *Neurología*. 1996;11 Suppl 5:1S-6S.

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Abend SM, Kulish N. The psychoanalytic method from an epistemological viewpoint. *Int J Psychoanal*. 2002;83 (Pt 2):491-5.

Part of a number

Ahrar K, Madoff DC, Gupta S, Wallace MJ, Price RE, Wright KC. Development of a large animal model for lung tumors. *J Vasc Interv Radiol*. 2002;13(9 Pt 1):923-8.

Number without a volume

Baumeister AA. Origins and control of stereotyped movements. *Monogr Am Assoc Ment Defic*. 1978;(3):352-84.

No volume or number

Outreach: bringing HIV-positive individuals into care. *HRSA Careaction*. 2002 Jun:1-6.

Book

Authors as Editors

Diener HC, Wilkinson M, Editors. *Drug-induced headache*. New York: Springer-Verlag; 1988.

Personal author(s) (no editors)

Jennett B, Teasdale G. *Management of Head Injuries*. Philadelphia; FA Davis Company; 1981.

Different Authors and Editors

Breedlove GK, Schorfheide AM. Adolescent pregnancy. 2nd ed. In: Wiczorek RR, Editor. *White Plains: March of Dimes Education Services*; 2001.

Organisation as Author

Royal Adelaide Hospital; University of Adelaide, Department of Clinical Nursing. *Compendium of nursing research and practice development, 1999-2000*. Adelaide: Adelaide University; 2001.

Book chapter

Rhoton AL. Microsurgical anatomy of the third ventricular region. In: Apuzzo MLJ, Editor. Surgery of the third ventricle. Baltimore; Williams & Wilkins; 1987. pp. 92-166.

Meeting Minutes

Vivian VL, Editor. Child abuse and neglect: a medical community response. Minutes of the First AMA National Conference on Child abuse and neglect; 1984, March 30-31; Chicago, American Medical Association, 1985.

Thesis

Gómez López PA. Hemorragia subaracnoidea aneurismática: Análisis de los factores que influyen en la aparición de isquemia cerebral y en la evolución final [tesis]. Madrid: Facultad de Medicina. Universidad Autónoma; 1991.

Documents in electronic format

Standard article in electronic format

Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis. [electronic journal] 1995;1 [consulted 05-06-1996]; Available at: <http://www.cdc.gov/ncidod/EID/eid.htm>

CD-ROM

Anderson SC, Poulsen KB. Anderson's electronic atlas of haematology [CD-ROM]. Philadelphia: Lippincott Williams & Wilkins; 2002.

Internet site (page)

Cancer-Pain.org [internet page] New York: Association of Cancer Online Resources, Inc.; c2000-01 [updated 16 May 2002; quoted 9 July 2002] Available at: <http://www.cancer-pain.org/>

Other published material

Conference Proceedings

Harnden P, Joffe JK, Jones WG, Editors. Germ cell tumours V. Proceedings of the 5th Germ Cell Tumour Conference; 13-15 September 2001; Leeds, UK. New York: Springer; 2002.

7. Tables

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