Introduction. Neurogenic stuttering is a disorder of neurologic origin in the rhythm of speech during which the patient knows exactly what he wants to say but is unable to because of an involuntary prolongation, cessation or repetition of a sound.

Aim. To assemble new insights regarding the epidemiology, pathophysiology, diagnosis, evaluation and treatment of neurogenic stuttering.

Development. A review of all PubMed and Scopus published articles between January 2000 and September 2016 was performed. Thirty-three publications were analyzed. Neurogenic stuttering is a rare entity whose epidemiological incidence is yet not fully established. It is correlated with several neurological diseases and with several possible localizations within the nervous system. Notwithstanding the recent advances in the understanding of the underlying mechanism, it is not yet possible to establish a single pathophysiological mechanism of neurogenic stuttering. The differential diagnosis is complex and requires the detailed knowledge of other language disorders. The treatment is currently based on specific speech language therapy strategies.

Conclusion. Neurogenic stuttering is a complex disorder which is not fully understood. Additional studies might help to better explain the underlying pathophysiological mechanism and to open doors to novel therapeutic methods.

The majority of the published articles consists in case reports or small case series [1,3,10]. However, its low incidence has been questioned, since it appears to occur more frequently in clinical practice settings [11-13]. Neurogenic stuttering seems to be more frequent in males, with reported incidences varying between 2:1 and 10:1 [6]. Strokes and traumatic brain injury are the most frequent reported causes [12]. The epidemiological data is sparse; additional studies are needed in order to provide more detailed information.

Pathophysiology

The underlying pathophysiologic mechanism is not yet fully understood. To this uncertainty contributes the fact that neurogenic stuttering can occur associated with multiple pathologies and multiple lesion sites.

In fact, neurogenic stuttering has already been reported in patients with stroke, traumatic brain injury, epilepsy, multiple sclerosis, Parkinson, corticobasal ganglionic degeneration, senile dementia, dialysis dementia, hypoxic ischemic encephalopathy, and pharmacological iatrogenesis [3,8,14-20]. The lesion site location is also heterogeneous. There are case reports of neurogenic stuttering in focal and diffuse lesions, unilateral and bilateral, cortical and subcortical lesions; the lesion site may be located in both hemispheres, brainstem and cerebellum [1,8,10,14,15,21-24].

Given the diversity of locations already described, it is possible that different lesion sites lead to a common final pathophysiological pathway; alternatively, it is possible that not yet identified small variations on stuttering characteristics may occur according to different locations.

Ludlow et al. compared the lesion sites of 10 patients with neurogenic stuttering after penetrating brain injury (from firearm projectile) with a group of patients also with penetrating brain injury but without neurogenic stuttering. They concluded that the striatum and the pale globe were significantly more affected in the neurogenic stuttering group [25].

More recently, Theys et al performed a study comparing 20 patients with post stroke stuttering with a group of 17 post stroke patients without stuttering. They identified nine left hemisphere areas with a significantly higher probability of being involved in neurogenic stuttering. The authors defend the existence of a left hemisphere circuit involving the inferior frontal cortex, superior temporal cortex, intraparietal cortex and basal ganglia with multiple interconnections between them. The disintegration of this circuit would cause stuttering [25]. Most of the included patients had a left cerebral media artery stroke, so it is not possible based on this study to perform conclusions about the involvement of other brain regions in the pathophysiology of neurogenic stuttering.

Studies performed in patients with developmental stuttering have identified the involvement of several structures: right frontal operculum, right frontal parafalcine region, right motor cortex e supplemental right motor cortex, right inferior temporal gyrus and right superior temporal gyrus, right cerebellar hemisphere, left cingulate gyrus, left temporal lobe, left rolandic operculum, left prefrontal cortex, left sensorimotor cortex, basal ganglia (ventrolateral nucleus of thalamus, mesothalamus and left caudate nucleus) and a disturbance in dopaminergic activity (hyperdopaminergic states and/or change in D1/D2 receptors proportion in striatum) [3,26-28].

We can speculate that the involvement of these mechanisms and structures might also be present in neurogenic stuttering after neurological damage of these same mechanisms and structures. However, the mechanism underlying developmental stut-
tering is far from fully understood and the studies with exclusive neurogenic stuttering populations remain scarce.

Differential diagnosis

Differential diagnosis with other stuttering types
Classically, some characteristics that might help distinguish neurogenic from other forms of stuttering are described:

- Disfluencies occur at a similar rate of occurrence in substantive and non-substantive words.
- Repetitions, prolongations and blocks occur in all word positions, as opposed to initial word position in developmental stuttering.
- There is consistency in stuttering behavior across different speech tasks (conversation, explanation, repetition and reading).
- The speaker may be annoyed, but does not appear overly anxious about the stuttering behavior.
- Secondary symptoms (facial grimacing, fist clenching, eye blinking or other involuntary movements) are rare.
- Absence of adaptation effect (there is no decreasing number of disfluencies across successive reading of the same passages).

These characteristics, first described by Canter and later reviewed by Helm-Estabrooks are frequently described in literature [1,2,8,12,13,15,29].

Lately these criteria have been questioned. Studies like van Borsel et al [11] demonstrated that it is not possible to distinguish developmental from neurogenic stuttering based only on these characteristics [2,8,13].

Currently, it is generally accepted that the presence of these criteria favors the diagnosis of neurogenic stuttering, however its presence is not necessary to establish the diagnosis [8,9,12,13,15,30].

The differential diagnosis between neurogenic stuttering and psychogenic stuttering is not always easy to make [13,31]. The phenomenological distinctive feature can also be applied, but in this case it is less useful [8,19,31]. The onset of a new neurological lesion might be accompanied by great psychological stress, therefore the precipitating events of both subtypes of stuttering might coexist [30].

Similarly to neurogenic stuttering, several speech characteristics were proposed as distinctive features of psychogenic stuttering (Deal’s Eight Features of Psychogenic Stuttering; Roth, Aronson & Davis’s Criteria for Psychogenic Stuttering; Baumgartner and Duffy’s Distinguishing Features) [8,15]. Once again, such discrimination does not seem to be possible based only on speech characteristics [15].

The feature that more consistently allows the differential diagnosis between psychogenic stuttering and other forms of stuttering is a fast and favorable treatment response in the former [15,19,31].

In addition to the already demanding differential diagnosis, there are also some case reports of stuttering malingering in order to obtain secondary gain or to prove innocence in court cases [19,29]. In these cases, the consistency across different speech tasks or different life circumstances and the type of response to facilitating speech strategies may be revealing of the correct diagnosis [29].

Differential diagnosis with other speech disorders

Sometimes, aphasia may present with disfluency which may resemble neurogenic stuttering.

Some of the disfluencies manifested with aphasia might be the result of successive self-correct attempts in the presence of phonemic paraphasias, something that may resemble stuttering-like repetitions [9,15]. Disfluency might as well be the result of the patient struggle in word retrieval due to decreased verbal production, something that might resemble the stuttering-like blocks [1,9].

Amnestic aphasia, Broca’s aphasia, conduction aphasia and Wernicke’s aphasia are the most common types of aphasia associated with stuttering-like disfluencies [15].

Under certain circumstances, apraxia of speech might also be easily confused with neurogenic stuttering. Apraxia of speech is an articulatory disorder, corresponding to a neurological impairment of the capacity to program the positioning and sequencing of muscle movements for the volitional production of phonemes [23].

Among the different possible characteristics of apraxia of speech, we are going to describe those that, due to their similarity, might hamper the differential diagnosis with neurogenic stuttering: speech/words initiation difficulty related to difficulty in articulating the intended sounds, articulatory prolongations, syllable segregation and sounds/syllables repetition caused by multiple ineffective attempts at verbal production [9,23].

The presence of articulatory errors, phoneme substitutions, exploratory movements of the mouth prior to vocalizations and frequent self-corrections
of apraxic errors favors the diagnosis of apraxia of speech [1,23]. Occasionally, dysprosody might be present. The difficulty in performing oromotor commands in the absence of muscle weakness or the absence of incoordination in reflex/automatic gestures allows the definitive diagnosis [23].

Palilalia is a complex speech disorder that can sometimes resemble neurogenic stuttering. It is usually associated with Parkinson's disease and other parkinsonian syndromes [9]. Palilalia is an involuntary repetition of semantically appropriated words or sentences, with an increasing rapidity and decreasing loudness (in contrast to stuttering, where repetitions occur at steady rate and only sounds/syllables are involved) [9,14,32]. It’s typical but not mandatory the presence of other characteristics, as stereotypic prosody or elevated voice pitch [32].

As we can observe, neurogenic stuttering diagnosis is complex and requires a deep knowledge of other language/speech disorders. It is not always easy to establish well defined boundaries between neurogenic stuttering and other language/speech disorders of neurological origin. Besides, the above mentioned entities are not mutually exclusive and might coexist with neurogenic stuttering, making the diagnosis even more difficult [19].

**Evaluation**

Stuttering should be analyzed in different speech tasks, including conversation, explanation, repetition and reading. The rhythm of speech, frequency, type (pause, blockage, prolongation, repetition) and the disfluencies duration should be sought. It is also necessary to identify the position of disfluencies in word and its relative occurrence in substantive and non substantive words [6,13,17,19,29]. It is also useful to register the presence of secondary symptoms [19]. The adaptation effect might also be calculated throughout successive readings of the same passage [12,13,17].

Audio or video recording may be used to facilitate the stuttering evaluation [6,13,33].

Some assessment instruments include: Stuttering Severity Instrument for Children and Adults (available in http://www.proedinc.com), the Overall Assessment of the Speaker’s Experience of Stuttering (OASES) the Modified Erickson Scale of Communication Attitudes (S-24), the Perceptions of Stuttering Inventory (PSI), the Self-Efficacy Scale for Adult Stutterers (SESAS), the Locus of Control, and the Tentative Assessment Procedure for Stuttering [1,17,19,20,29,31].

**Treatment**

**Non-pharmacological treatment**

The treatment methods traditionally used in developmental stuttering are also used in neurogenic stuttering. There is evidence of some beneficial effect of these strategies applied to neurogenic stuttering [9,12,24].

Speech therapy remains the mainstay of stuttering treatment. Multiple fluency enhancing strategies may be used, including: word facilitation, decreased speech rhythm, modifying/modeling fluency mechanisms, choral effect, metronome speech, non-automatic speech, change in vocal pitch, white noise, singing and vocal control techniques may all be used to improve speech fluency [24].

Among the different possible methods there is no consensus on the most effective. These methods can be used alone, sequentially or in combination.

There are also some devices that can enhance speech fluency, using modifying/modeling fluency mechanisms. The delayed auditory feedback (DAF) is a device that delays auditory feedback in order to decrease the rhythm of speech which in turn improves speech fluency [24,33]. In FAF (frequency altered auditory feedback), the frequency range of speaker’s speech is switched causing pitch distortion, this gives the feeling of someone replicating the speaker’s speech with a different voice [24]. In MAF (masking auditory feedback), an external noise is added in order to make the speaker’s voice no longer audible. Since the patient no longer has auditory feedback, he starts to control voice only by proprioception, which results in a disfluency decrease [24]. Studies on long term effects of these devices have not yet been published.

Studies about the aforementioned methods applicability on neurogenic subtype of stuttering are sparse and limited to few case reports. In all respects, neurogenic stuttering seems to be more resistant and present slower and less effective treatment response [2,19,33,34]. Despite this, great inter-individual variability in treatment response seems to take place in neurogenic stuttering.

There are case reports of improvement with the singing method [12,24], the choral effect [35], MAF [24] and DAF usage [2,33], or even with the adaptation effect usage [1]. There are also case reports of no improvement with adaptation effect usage [22, 24,34], no improvement with choral effect method [22,34], absence of improvement with DAF usage [34], FAF usage [22] or MAF usage [35]. There are also case reports ($n=4$) of an increase in disfluencies frequency with DAF and FAF usage [22,30,33,34].
It is possible that the great variability in treatment responses might be explained by different underlying pathophysiologic mechanisms, although more studies are needed before conclusions can be drawn.

**Pharmacological treatment**

Pharmacological treatment has no proven benefit, despite several drug treatments have already been reported.

Haloperidol is the most often referred drug has having potential beneficial effects on developmental stuttering treatment [26]. The underlying pathophysiological mechanism seems to involve the direct anti-dopaminergic effect of haloperidol. Haloperidol beneficial effect is not reproducible across different studies and the treatment is associated with significant adverse effects [26].

Other typical antipsychotic drugs (chlorpromazine, trifluoperazine, thioridazine), atypical antipsychotic (risperidone e olanzapine) and antiepileptic drugs (carbamazepine, sodium divalproate, levetiracetam) were also mentioned in some studies [26,36].

On the other hand, there are case reports of drug induced stuttering, including antipsychotic drugs (clozapine, olanzapine, risperidone), antiepileptic drugs (carbamazepine, gabapentine, topiramate, phenytoin, lamotrigine) serotonin reuptake inhibitors (sertraline, fluoxetine), tricyclic antidepressants, benzodiazepines, propranolol and theophyllin [9,15,26,36].

Particularly in neurogenic stuttering subtype, there are two case reports, one stating stuttering symptoms resolution with olanzapine administration for concomitant psychosis [26] and other claiming stuttering improvement with gabapentine usage [37]. Sechi et al have found beneficial effects with levetiracetam, in particular in reducing stuttering in five patients with partial epilepsy. Of these, two patients presented neurogenic stuttering and three patients presented developmental stuttering. Beneficial effects were found in all patients and were independent of levetiracetam effect on epilepsy control [36].

Neurogenic stuttering treatment is non-pharmacological. Despite several pharmacological trials, there is no evidence of additional benefit from the use of pharmacological treatment.

**Conclusion**

Neurogenic stuttering is a rare disorder whose epidemiological incidence is yet not fully established. It can be caused by several neurological disorders and several lesion locations. Despite recent advances, a single underlying pathophysiologic mechanism that fully explains neurogenic stuttering has still not been identified.

Neurogenic stuttering has its own characteristics, however, the differential diagnosis with psychogenic stuttering or developmental stuttering may be difficult to accomplish based only on speech characteristics. Other language/speech disorders of neurological origin may coexist, and sometimes it is hard to establish well defined boundaries between different entities.

Currently, there is no drug with proven efficacy in neurogenic stuttering treatment. Neurogenic stuttering treatment is based in the traditionally strategies used in developmental stuttering, namely a specific and individualized intervention by speech therapy.

Further studies with exclusively neurogenic stuttering patients, may help to better clarify the pathophysiologic mechanisms underlying this entity and open doors to new treatment possibilities.

**References**

Introducción. La tartamudez neurógena es un trastorno del ritmo de habla de origen neurológico en el cual el paciente sabe perfectamente lo que quiere decir, pero es incapaz de articularlo a causa de la prolongación, el cese o la repetición involuntaria de un sonido.

Objetivo. Reunir nuevos datos referentes a la epidemiología, la fisiopatología, el diagnóstico, la evaluación y el tratamiento de la tartamudez neurógena.

Desarrollo. Se llevó a cabo una revisión de todos los artículos publicados en PubMed y Scopus entre enero de 2000 y septiembre de 2016. Se examinaron 33 publicaciones. La tartamudez neurógena es una entidad poco frecuente cuya incidencia epidemiológica no se ha definido completamente. Aparece en el marco de diversas enfermedades neurológicas y ligada a distintos lugares del sistema nervioso. A pesar de los avances recientes en el conocimiento del mecanismo subyacente, aún no ha sido posible determinar un único mecanismo fisiopatológico de este trastorno. El diagnóstico diferencial es complejo y requiere un buen conocimiento de otros trastornos del lenguaje. El tratamiento se basa actualmente en terapias logopédicas específicas.

Conclusión. La tartamudez neurógena es un trastorno complejo que no se conoce con detalle. Nuevos estudios ayudarían a esclarecer los mecanismos fisiopatológicos que se ocultan tras ella y abrirían la puerta a nuevos métodos terapéuticos.