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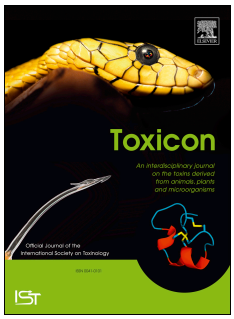


# DOES A DIAGNOSTIC NERVE BLOCK PREDICT THE OUTCOME OF BOTULINUM TOXIN TREATMENT? A NARRATIVE REVIEW

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# DOES A DIAGNOSTIC NERVE BLOCK PREDICT THE OUTCOME OF BOTULINUM TOXIN TREATMENT? A NARRATIVE REVIEW

**Running title:** Does DNB predicts BoNT outcome

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**Conflict of interest:** Thierry Deltombe has served as investigator, speaker and advisor for Abbvie, Ipsen and Merz. Anthony Ward has previously served as investigator, speaker and advisor for Abbvie, Ipsen and Merz.

## ABSTRACT

Botulinum toxin type A is a first line choice in the treatment of spastic muscle overactivity. However, targeting the muscles involved in the deformity with the appropriate dose as well as choosing the goal to achieve and predicting the expected results can be challenging. Diagnostic nerve block with anaesthetics rapidly and temporarily suppresses overactivity of the selected muscle allowing clinicians to identify the involved muscles and the potential improvement of botulinum toxin injections. This narrative review summarizes the predictive value of the diagnostic nerve block before botulinum toxin injections. In the case of a stiff knee gait, rectus femoris blockade seems to predict knee flexion and gait speed improvement, which is subsequently obtained after rectus femoris botulinum toxin injections, but underestimates improvements in balance. In the case of spastic equinovarus foot, tibial nerve block provides a greater reduction in spasticity. Diagnostic nerve block assessment prior to botulinum toxin type A injections leads to an increase in the number of injected muscles, in the dose per muscle and in the overall cumulative dose. Finally, diagnostic nerve block may help to increase the goal achievement rate. Further well conducted studies are necessary.


**Key Words:** Muscle Spasticity, Nerve block, Botulinum neurotoxin a, neurologic gait disorders, neuromuscular agents, predictive value of tests

## 1) Introduction

Lesions of the central nervous system (CNS) involving the corticospinal pathways may lead to the deforming spastic paresis syndrome with a neurological and a muscle component (Baude et al., 2019). It has several etiologies of the brain (stroke, multiple sclerosis, trauma, etc.) and spinal (traumatic, inflammatory, etc.) origin. The deforming spastic paresis syndrome includes a quantitative lack of voluntary motor command leading to a stretch-sensitive weakness (paresis), a soft tissue rearrangement with loss of muscle extensibility leading to muscle shortening (deforming) and muscle overactivity (spastic). This spastic muscle overactivity (SMO) mainly includes spasticity (a velocity dependent increase in muscle tone), spastic dystonia (muscle activity at rest with spasticity) and spastic co-contraction (inappropriate antagonist activation during agonist voluntary contraction) (Baude et al., 2019). SMO can negatively affect function (gait, transfers), interfere with positioning, cause pain and discomfort and increase carer burden (Verduzco-Gutierrez et al., 2024). Spastic co-contraction seems mostly correlated to functional limitations (Chalard et al., 2019). Notably, a muscle or a muscle group, such as triceps surae may present the associated three components at the same time.

The treatment of the deforming spastic paresis syndrome is multimodal and includes neuro-rehabilitation techniques as well as a medical and surgical strategy as part of an interdisciplinary rehabilitation approach (Reebye et al., 2024). A patient-centric approach is essential in order to determine the patient's goal and related treatment (Jacinto et al., 2023; Ward, 2012). The deforming component (contracture) can be treated by stretching, taping, splinting, casting and/or

muscle or tendon lengthening. The SMO can be treated by oral medications, electro-neuromuscular and transcutaneous nerve stimulations, extracorporeal shock-wave therapy, botulinum toxin type A (BoNT-A) injections, phenol or alcohol nerve block, intra-thecal baclofen therapy and/or selective neurotomy. Lastly the paretic component (paresis) is treated by strengthening, exercise training, orthosis and/or functional electrical stimulation (Deltombe et al., 2017; Khan et al., 2019; Verduzco-Gutierrez et al., 2024). However, the treatment(s) will also vary according to the etiology (i.e. cortical or spinal), the pattern (i.e. clenched fist or equinovarus), the extent of the disabling syndrome (localized or generalized), the level of spasticity and the expected goal (i.e. comfort or function). In clinical practice, one of the main difficulties is to determine the respective responsibility of the three components of the deforming spastic paresis syndrome in the patient's complaints and limitations. As an example, in the case of a spastic clenched fist, the main contributor is usually the finger flexor SMO, while in the case of an equinus in the swing phase of gait, the main contributor is the ankle dorsiflexor muscles' weakness. Therefore, such determination is crucial as the goal and the treatment(s) will vary accordingly.

## 2) **Botulinum toxin type A in muscle overactivity**

BoNT-A, as a part of a multimodal approach, is the first line treatment of the focal and multifocal SMO. In published meta-analyses, there is strong Level A evidence of the effectiveness of BoNT-A to decrease muscle overactivity (Andringa 2019 et al). When injected in the upper limb, BoNT-A improves comfort and reduces spasticity-related pain and caregiver burden. while repeated injections improve active movements and perceived function (Andringa et al., 2019; Gracies et al., 2018). When injected in the lower limbs, BoNT-A improves gait speed especially after repeated injections (Esquenazi et al., 2021; Varvarousis et al., 2021).

However, treatment with BoNT-A injections does not always achieve the patient's expected goals. Several reasons may explain this. The selection of a SMART (specific, measurable, achievable, realistic and time-based) goal is mandatory. If an unrealistic goal (e.g.. unimanual function in case of clenched first without any finger extensors' activation) is chosen, it will not be achieved. An appropriate BoNT-A injection guidance technique using ultrasound and electrical stimulation or EMG should be used to target the selected muscle(s) (Asimakidou & Sidiropoulos, 2023). As BoNT-A has a dose-dependent effect, BoNT-A injected dose may be insufficient as to effectively reduce the SMO, especially in mutifocal spasticity patterns involving large muscles, where the maximal BoNT-A dose limits the safe dose per muscle (O'Dell et al, 2018) ). Lastly, the muscles involved in the deformity may vary between patients. As an example, soleus and/or gastrocnemii muscle overactivity may vary in their contribution to an equinus deformity. In complex cases, it is essential to determine the muscle(s) implicated in

contributing to the deformity, which will necessitate BoNT-A injection. In contrast, muscle(s) not involved should be spared.

### 3) Diagnostic nerve block as an assessment tool

Diagnostic nerve blocks with anaesthetic (DNB) help to determine which of the different muscles' overactivity is responsible for the deformity. DNB consists of injecting a small dose (usually 1 to 3 ml) of a local anaesthetic (usually Lidocaine 2%) onto a nerve innervating a spastic muscle in order to decrease muscle overactivity rapidly and temporarily. DNB is recognised as a cornerstone in the management of the spastic equinovarus foot (Deltombe et al., 2017; Salga et al., 2023). Moreover, guidelines have been published concerning their usage in the field of rehabilitation (Yelnik et al., 2019).

DNB may target a large sensori-motor nerve, such as musculocutaneous, median, ulnar, obturator, femoral, sciatic and/or tibial nerve. For example, in the case of a tibial nerve diagnostic blockade, suppressing the spasticity of all the innervated muscles, which would include soleus, gastrocnemii, tibialis posterior, flexor digitorum muscles), it would be impossible to identify which of the muscle(s)) is responsible for the deformity. It would only allow the injector to differentiate SMO from contracture and, by suppressing the co-contraction of the targeted muscles, to assess the antagonist muscle strength more easily. Furthermore, it would induce a sensory deficit, such as hypoesthesia or anesthesia in the sole of the foot, which may interfere with a subsequent functional assessment. In order to determine the respective contribution of the different spastic muscle(s) in the deformity (eg. soleus and/or gastrocnemii),

the DNB needs to be more selective at the level of the motor nerve branches innervating each targeted muscle (eg. motor nerve branch to soleus followed if necessary according to the subsequent clinical assessment and improvement by other motor nerve branches). Such a selective DNB would serially suppress spasticity in one muscle after another allowing the correct muscle(s) to be identified and blocked. This then guides the clinician as to whether another DNB is required before proceeding to a definitive treatment. Selective motor nerve branch DNB has been described at the level of the pectoralis major and minor, brachialis, adductor longus, brevis and magnus, gracilis, rectus femoris, vastus intermedius, soleus, gastrocnemius medialis and lateralis and tibialis posterior (Winston et al., 2023). The anaesthetic can also be injected in a muscle to perform an intramuscular diagnostic block. It is recommended for small muscles, whose motor nerve branches are difficult to find and/or are mixed with sensory fibres (e.g. flexor digitorum muscles). This will require a larger dose of anaesthetic and explains why it is not recommended in large muscles, such as soleus muscle. Localization of the tibial nerve trunk and of the motor nerve branch (e.g. soleus motor nerve) has been described on the basis of cutaneous landmarks (Deltombe et al., 2004; Facciorusso et al., 2023; Genet et al., 2017; Yelnik et al., 2019). Ultrasound guidance is increasingly used to visualize the nerve trunk and, in some cases, the smaller motor nerve branches before inserting the needle (Winston et al., 2023).

A Teflon-coated needle for conduction anaesthesia coupled to a portable electrical stimulator or an EMG apparatus is inserted at the level of the targeted nerve. An electrical stimulation with electrophysiological monitoring (M-wave and H-reflex) is used to optimize the targeting. A muscular contraction still visible at a low intensity of stimulation (<10 mA with a 0.001 msec duration of stimulation) means there is a close contact between the top of the needle and the

nerve. This permits the injection of a low dose local anaesthetic (1 - 2 ml), thereby limiting anesthetic diffusion to other motor and/or sensory branches.

DNB dramatically reduces spasticity. After a tibial DNB, a decrease in spasticity has been observed from Ashworth score of 3 to 1 or 0 (Deltombe et al., 2008, 2015; Picelli et al., 2020), in Tardieu spasticity angle (Lamora et al., 2023; Picelli et al., 2020) and in H-Max/M-max ratio from 88% to 51% (Deltombe et al., 2008).

**4) <u>Predictive value of DNB before neurotomy</u>**

Initially, DNB was developed as an assessment tool to confirm the indication of a selective neurotomy and to predict the expected improvement. Neurotomy is a surgical procedure performed under general/spinal anaesthesia consisting in a partial section of a motor nerve branch innervating a spastic muscle. By cutting the afferent Ia fibers included in the motor nerve branch, the neurotomy suppress the myotatic arc reflex and provides a permanent reduction in spasticity and probably co-contraction (Bollens et al., 2013; Lamora et al., 2023; Ploegmakers et al., 2024). As the Ia fibers are now unable to reconnect, the spasticity reduction is permanent or, at least long-lasting. The efficacy of the neurotomy in non-reflex SMO (i.e. spastic dystonia) still needs to be established.

The main indications of neurotomy are the elbow flexion (musculo-cutaneous nerve), the adducted hip (obturator nerve), the stiff knee gait (femoral nerve) and, most of all, the equinovarus foot (tibial nerve). As neurotomy is a surgical procedure with a permanent effect, it

is necessary to be precise on (i) which motor nerve branches require treatment, (ii) the expected functional improvement and (iii) the level of associated contracture, which may necessitate additional tendon surgery (Salga et al., 2023). Several studies have confirmed that DNB predicts the degree of spasticity reduction and the functional improvement obtained after neurotomy, when performed on the same motor nerve branches (Deltombe et al., 2015; Lamora et al., 2023). Therefore, DNB is routinely used in clinical practice to predict the functional improvement expected from a neurotomy.

## 5) Predictive value of DNB before BoNT-A

Determining DNB's predictive value before BoNT-A treatment necessitates studies comparing the outcome obtained after DNB and BoNT-A in spastic patients. In a prospective study of 10 hemiplegic patients suffering from a stiff knee gait, Robertson et al. used gait laboratory analysis to compare the improvement obtained thirty minutes after a rectus femoris DNB and one month after rectus femoris BoNT-A injection (Robertson et al., 2009). They found a similar significant average increase in peak knee flexion of 11° after DNB and 8° after BoNT-A, supporting the predictive value of DNB in such indication. In a prospective study of 14 patients affected by multiple sclerosis also suffering from a stiff knee gait, Baricich et al. found that rectus femoris DNB predicts the improvement in gait speed and endurance obtained after rectus femoris BoNT-A, but underestimates the improvement in balance assessed by a timed-up-and-go-test (Baricich et al., 2024). In a retrospective study of 50 stroke patients suffering from a spastic equinovarus foot, who benefit from a DNB followed by BoNT-A injections in the same selected muscles,

Picelli et al. found a greater reduction in Modified Ashworth (MAS) and Tardieu scores, the Tardieu spasticity angle and a greater improvement in passive range of motion (PROM) immediately after DNB as compared to 1 month after in label BoNT-A dosage injections (Picelli et al., 2020).

The question of whether DNB influences the BoNT-A injection regimen has been studied by Filippetti et al. In a retrospective study, they monitored in 99 adult patients, treated for the first time, the BoNT-A dose per muscle and the BoNT-A cumulative dose in 43 patients assessed by clinical assessment and DNB before injection as compared to 56 patients just assessed clinically. They found that the patients assessed by means of DNB were injected with a higher dose in the flexor digitorum profundus and soleus muscles and received higher BoNT-A cumulative doses in the upper limb with a larger number of injected muscles in clenched fist and adducted thigh patterns (Filippetti et al., 2024).

The determination of patient-centered SMART goals before treatment is a key point in spasticity management (Jacinto et al., 2023). In a case-control study, Filippetti et al. assessed goal achievement in 20 spastic patients assessed by DNB before BoNT-A injections in comparison to 20 spastic patients treated by BoNT-A without prior DNB assessment. They found that the predetermined goals were reached in nearly twice as many patients when the BoNT-A injection strategy was based on DNB and clinical assessment (70% achievement rate) rather than on clinical assessment alone (40% achievement rate) (Filippetti et al., 2024).

## **Conclusion**

Initially developed to assess patients prior to surgery, in order to differentiate spasticity from contracture and to determine the spastic muscles involved in the presenting spastic pattern, DNB is also performed before BoNT-A injections. However, there are only a few low-quality case-controlled studies assessing the role and impact of DNB before BoNT-A injections. In the case of a stiff knee gait, rectus femoris DNB seems to predict knee flexion and gait speed improvement obtained after rectus femoris BoNT-A injections, but underestimates improvements in balance. In case of spastic equinovarus foot, tibial DNB provides a greater reduction in spasticity. DNB assessment prior to BoNT-A injections leads to an increase in the number of injected muscles, in the BoNT-A dose per muscle and in the overall BoNT-A cumulative dose. Finally, DNB may help to increase the goal achievement rate.

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HIGHLIGHTS

Does a diagnostic nerve block predict the outcome of botulinum toxin treatment? A narrative review

Botulinum toxin type A (BoNT-A) is the first line treatment of focal spastic muscle overactivity

Diagnostic nerve block with anaesthetics is a diagnostic tool allowing to identify muscles involved in the spastic pattern and the potential benefit of a treatment

In case of stiff knee gait, rectus femoris diagnostic nerve block seems to predict gait improvement obtained after botulinum toxin injections

In case of spastic equinovarus foot, tibial diagnostic nerve block seems to provide a greater reduction in spastic muscle overactivity than botulinum toxin type A

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The authors have no ethical statement to declare

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**Declaration of interests**

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: