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Nerve stimulation in regional anesthesia: theory and practice

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There is now an accumulation of extensive and varied experience with the use of electrical stimulation for verifying the close approximation of needle and nerve, and for increasing the corresponding success rate. The application of this experience has been of proven benefit in the teaching of regional anesthetic techniques, in the performing of difficult nerve blocks, and in the use of novel accesses, resulting in decreased morbidity and a reduced requirement for local anesthetic. Nerve stimulation can also be used in uncooperative patients and in anesthetized individuals or patients under the effects of CNS depressors, although the risk of intraneural injection of local anesthetic is not eliminated in such cases. Putting the accummulated knowledge into practice is not simply a question of using electrical stimulation to elicite an artificial muscle contraction. Sound knowledge of the anatomy of the area to be blocked, the muscle territory subsidiary to the nerve in question, the applied neurophysiology, and the pharmacology of the local anesthetic used are needed. This chapter reviews the most important aspects, from nerve

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anatomy and physiology, to electrical features of the needle, and devices used for the updated clinical application of nerve stimulation in the practice of plexus regional anesthesia.

Keywords: electrical stimulation therapy; evoked potentials; motor; muscle contraction/physiology; needles; nerve block/methods; nerve block; peripheral nerves/physiology.

The performance of peripheral nerve blocks has traditionally involved search for parethesias. The application of nerve stimulation (NS) techniques offers a series of advantages: when performing complicated nerve blocks, as a teaching tool, and for carrying out selective blocks with low doses of local anesthetic.[1–3] NS facilitates the location of peripheral nerves in anesthetized or deeply sedated patients, and in uncooperative subjects[4], and seems to reduce the incidence of paresthesias.[5]

Adequate anatomical and neurophysiological knowledge is essential for the correct clinical use of NS in application to anesthetic block. The variety of NS techniques, the different types of needle, and the different neurostimulators used are responsible for a lack of homogeneity in the results obtained, and controversy often exists over the most appropriate technique for each case.

This chapter reviews the most important aspects of NS and its clinical application to anesthetic block.

ANATOMICAL AND APPLIED NEUROPHYSIOLOGICAL PRINCIPLES

Anatomy and histology of the peripheral nerves

The peripheral nerve system is composed of a series of nerves of different thicknesses and lengths that conduct stimuli from the periphery towards higher nerve centers, and from the latter efferently back to the periphery in the form of motor, secretory, or vegetative responses. Most nerves are of a mixed nature, and comprise sensory, motor and—in some cases—sympathetic fibers.[6]

A peripheral nerve consists of bundles of parallel axons, called fascicles, which are invested by a connective tissue sheath. Axon distribution within the nerve makes up a plexus in which the axons are positioned along the path of the fascicle, establishing a proximity relationship between near axons and their specific location along the nerve. At repeated cuts of a nerve, the topography of the fascicles changes. In general, for a given nerve the number of fascicles increases and the bundle cross-sectional area decreases in regions where the nerve branches detach from and incorporate to the nerve in areas close to joints. On the other hand, the number of fascicles diminishes and their cross-section increases in areas between nerve subdivision points, and in areas between joints.[6] Sunderland and co-workers[7–10] found this fascicle pattern to vary 23 times over a length of only 43 mm. This heterogeneity of the different nerve fascicles causes the nerve fibers to disperse as the nerve advances along its anatomical trajectory. As a result, sensory and motor elements corresponding to one single topographic distribution become located within different fascicles in the same nerve. This phenomenon is important in the clinical application of neurostimulation, and was confirmed by microelectrode stimulation studies[11] involving individualized fascicles of the median nerve at arm

level. In effect, most sensory fibers were seen to be grouped in fascicles differentiated from the motor fibers.

It is important to point out that great variability exists not only in the axonal and fascicular distribution, but also in the proportion of the fascicular component cross-sectional area within a single nerve. On analyzing the proportions of axons and connective tissue within a nerve, a cross-section can show the fascicular area to correspond to 25–75% of the total cross-section, whereas 40–50% corresponds to non-neural elements (connective tissue, endoneural fluid).[6] Using a scanning electron microscope and sciatic nerve samples, Reina et al[12] showed that between fascicles the adipose tissue varied in thickness from 0.5 mm in the central zones to 0.2 mm in the peripheral zones, and was distributed within the epineurium to surround isolated fascicles or groups of fascicles. The adipose tissue within a nerve surrounded the fascicles to form adipose sheaths that separated the fascicles from one another. The thicknesses of these adipose sheaths varied among fascicles. In this context, cells join to conform a compact adipose sheet that can delay the diffusion of an anesthetic block injected near a nerve—thus possibly interfering with the characteristics of anesthetic block.

The different components surrounding the axons are the endoneurium, perineurium, and epineurium. These elements are found along the whole extension of the nerve and become progressively thinner as the nerve divides into its branches. External to the nerve, the epineurium is the connective tissue that surrounds the entire nerve trunk. Its thickness varies according to the nerve involved and to the specific location along its trajectory. The epineurium contains mainly collagen fibrils (oriented longitudinally along the nerve axis), as well as a few elastin fibers, adipose tissue, a few fibroblasts, mast cells, blood vessels (vasae nervorum), lymphatic capillaries, and small nerve endings that supply the vessels that feed the nerve (nervi nervorum).[6] As a general rule, the more numerous the fascicles, the greater the quantity of epineurium.

The next sheath of connective tissue, which is denser and encloses individual nerve fascicles, is known as the perineurium. It is composed of 8–15 concentric layers of cell processes surrounding each bundle; these layers alternate with layers of collagen fibrils.[13] Perineurial cells are flattened, joined together by tight junctions (zonulae occludentes) and hemidesmosomes, and globally constitute a diffusion barrier. The thickness of the perineurium is the result of the number of layers and varies between 10 and 25 μm. Each perineurial cell is 1 μm thick at the core and 0.1 μm thick in the region with no nuclei. The number of layers depends on the size of the nerve fascicle that is ensheathed, and is greater around large fascicles.[14–16]

The endoneurium is a delicate tubular structure surrounding the Schwann cells and each capillary within the fascicles.[12] It is the main element responsible for maintenance of regional homeostasis[17], and is composed of longitudinally oriented collagen fibers. The inner fibers and the fibers closest to the Schwann cells exhibit a more disorganized distribution. A basal lamina separates the endoneurium from the Schwann and endothelial cells. The global endoneurium–Schwann cell structure functions as an insulation unit that avoids interferences from nerve conduction in the neighboring axons.[18]

There are two fundamentally different types of nerve fiber: myelinated and unmyelinated. The latter, also called fibers of Remak, present small axons surrounded by a sheath of flattened cells overlying a basal membrane: the Schwann sheath. Most postganglionic sympathetic fibers, as well as the numerous fibers in the white matter and the spinal ganglionic fibers, are not myelinated. They conduct nerve impulses

Table 1. Classification of nerve fibers.

Feature	Classification				
Type of fiber	Myelinated				Unmyelinated
Groups of fiber	A	A	A	A+B	C
Diameter (μm)	22→1.5				2→0.1
Conduction (m/seconds)	120→60→50→30→4				2→0.5
Subtypes					
Efferent fibers	Aα	Aβ	Aγ	B	C
Afferent fibers	Aα	Aβ	Aγ	Aδ	C

slowly, and are usually classified as C fibers (either afferent or efferent). Nociceptive impulses travel along these fibers to reach the posterior horn of the spinal cord.[19]

Myelinated fibers are distinguished from the above fibers by the presence of a supplementary enveloping component—the myelin sheath—interposed between the Schwann sheath and endoneural sheath. The myelin sheath in turn presents a series of interruptions at regular intervals, known as nodes of Ranvier[20], which allow very rapid 'skipping' conduction of the action potentials between nodes. The diameter of myelinated fibers is highly variable and determines nerve impulse conduction velocity. The latter (in m/s) is approximately equivalent to six times the diameter of the fiber.[19] Although a number of classification systems have been proposed, that developed by Erlanger and Gasser remains the most widely used.[21] This system differentiates nerve fibers into A fibers (fast-conducting myelinated fibers), B fibers (slow-conducting myelinated fibers, corresponding to sympathetic preganglionic efferent fibers), and C fibers (unmyelinated fibers). The myelinated efferents are in turn classified into four groups: Aα (skeletal muscle motoricity fibers), Aβ (extrafusal motoricity), Aγ (intrafusal motoricity), and B (sympathetic preganglionic motor fibers). The myelinated afferent fibers include the first three subdivisions, all represented by the axons that emerge from encapsulated receptors at skin (Aα) and joint level (Aα, Aβ and Aγ), to which are added the Aδ fibers (nociceptive fibers), which are equivalent to the efferent B fibers (Table 1).

Physiology of nerve conduction

The generation and propagation of impulses in nerve fibers and muscle cells depend on ionic current fluxes through channels within the axon plasma membrane. These channels open and close in response to changes in membrane electrical potential, and constitute the target for local anesthetic action.

The potential difference between the two sides of the axon membrane results from the different ion concentrations in the intra- and extracellular environments. When the nerve fiber is stimulated, permeability of the axon membrane to Na^+ ions increases rapidly (depolarization) and the resting potential becomes less negative. When a critical threshold of -50 mV is reached, Na^+ conductance increases considerably and the resting potential becomes positive, reaching $+30$ mV. The Na^+ channel then inactivates spontaneously—a condition that limits the duration of depolarization due to Na^+ influx. K^+ conductance increases more slowly, generating a hyperpolarizing outflux that restores the membrane potential. The membrane is unstable during repolarization—a situation referred to as the refractory period (this is initially absolute

and subsequently relative). Depolarization is completed within 0.1–0.2 seconds, whereas repolarization takes 0.4–0.6 seconds.[22]

The ionic influx generated each time the membrane depolarizes flows through the axoplasma and spreads towards adjacent inactive regions. The latter are in turn depolarized as a result of the action of this 'local current', thus generating an electrical wavefront that conducts the impulse along the nerve fiber. The propagation, or conduction, velocity depends on the diameter of the fiber and is lower for unmyelinated fibers than for myelinated fibers (see Table 1).[23] The magnitude of the electrical current generated within each nerve fiber is 5- to 10-fold greater than the threshold required to stimulate the adjacent axonal segment, thereby ensuring propagation of the impulse along the nerve fiber.[24] This phenomenon is referred to as the nerve conduction safety margin.

Membrane excitability is diminished in certain situations (e.g. metabolic alterations, diseases, drug actions) and nerve impulse propagation slows as a result. When axon current is diminished, the action potentials are of lesser intensity and the conduction velocity decreases. Consequently, nerve impulse transmission worsens and decremental conduction appears.[23] If the reduction is sufficiently important, conduction failure may occur—a situation that can alter nerve response in the context of neurostimulation procedures, as well as local anesthetic action times.

CLINICAL APPLICATION OF NEUROSTIMULATION

Basic principles

As has been described above, nerve fiber depolarization is the origin of action potentials—an electrical phenomenon that gives rise to sensory perception or muscle contraction, depending on the type of nerve fiber involved. In this context, the stimulus triggering depolarization may consist of an external electrical current applied with the purpose of locating a peripheral nerve.[25] A brief description of each is provided below.

The intensity of the electrical stimulus required to trigger an action potential is an important factor and is specific for each particular nerve fiber. The term 'rheobase' (I_r) is used to describe the minimum current intensity capable of inducing an action potential when applied without time limitation to a given nerve fiber. Another factor to be taken into account is the duration of the stimulus, which can be measured as the chronaxie (C), or minimum time for which a direct current equivalent to twice the intensity of the rheobase must be applied to trigger an action potential.[25,26] Thus, the minimum direct current intensity required to trigger an action potential when applied in contact to a nerve fiber is a function of time, and can be expressed by the following equation

$$I_m = I_r(1 + C/t)$$

where I_m is the minimum intensity required, I_r is the rheobase, C is the chronaxie, and t is the time for which the stimulus is applied.[25]

The chronaxie is specific for each type of nerve fiber. In descriptive terms, it is inversely proportional to the degree of fiber myelinization; consequently, the greater the degree of nerve fiber myelinization, the lesser the minimum intensity required to trigger an action potential. In this sense, sensory fibers are less myelinated than motor

fibers—as a result of which their chronaxie is greater. Based on the above considerations, by precisely regulating the intensity of the electrical stimulus, it is possible to trigger action potentials in motor fibers (Aα) without also triggering the sensory fibers (Aδ, C), and therefore without inducing pain or paresthesias.[23,24] The chronaxie values for the different fibers are as follows: type A fibers 0.1–0.2 mseconds; small myelinated fibers 0.3 mseconds; and unmyelinated fibers 0.5 mseconds.[26]

The polarity of the electrical stimulus is another factor to be taken into account. In effect, stimulation is better when the negative electrode (the cathode) is located in the stimulation needle, because the negative current it generates reduces the magnitude of the voltage external to the membrane, causing the resting membrane potential to approach the depolarization values, with facilitation of sodium channel activation and the generation of an action potential.[27,28] By contrast, if the positive electrode (the anode) is positioned at stimulation needle level, nerve fiber resistance will increase as a result of the rise in transmembrane potential difference and the generation of hyperpolarization that tends to reduce fiber excitability (and thus the possibility of triggering an action potential).

The characteristics of the electrical impulse also influence the response obtained. In general, stimulation is performed by delivering rectangular electrical impulses, and avoiding the application of prolonged currents. Following stimulation, the membrane voltage changes exponentially rather than instantaneously. If the duration of the stimulus is too short in relation to the time required by the membrane to load its 'capacitance', the fiber may fail to reach the depolarization threshold when the stimulating current ceases, and no motor or sensory response will be triggered.[26] The ideal parameters for comfortable and effective stimulation comprise a frequency of between 1 and 2 Hz and an impulse duration of 0.1–0.2 mseconds.

The intensity of the electrical stimulus delivered on target (i.e. to the membrane of the nerve fiber) is influenced by passage of the current through the different tissue structures. According to Coulomb's law, the intensity of a current decreases in the course of tissue transmission in inverse proportion to the square of the distance traveled:

$$I_t = K(I/r^2)$$

where I_t is the current intensity at a distance r from the electrical source, K is a constant dependent on the electrical properties of the medium through which the current is transmitted, and I is the current intensity of the electrical source.[25,26] Because the intensity of the current is inversely proportional to the square of the distance, values (r) of over 8 mm would require such a great current intensity that systemic repercussions would result (50 mA for a distance of 2 cm). This explains the need to regulate distance according to the response obtained. The resistance values of the skin located between the active electrode an the electrode on the surface range from 0.5 to 3 kΩ (mean 1.5 kΩ) and the minimum current capable of triggering a response varies from 0.01 to 0.5 mA.[26] It is important to take this skin resistance to the passage of current into account because changes in this parameter could reduce the current intensity delivered on target, thus rendering nerve fiber stimulation ineffective. The resistance of the human body to electrical current passage is variable (1–10 kΩ for wet skin to a maximum of 25 kΩ), and decreases slightly on coming into contact with the dermis (0.5 kΩ). As a result, the stimulation source must possess an internal resistance greater than that of the human body (1 kΩ to ensure that the tissue variations do not modify the current intensity reaching the target nerve trunk).[25,26]

Characteristics of the neurostimulator

The neurostimulators (i.e. peripheral nerve stimulators, PNS) used for peripheral nerve block are characterized by their capacity to generate low-intensity electrical currents for precise location of the different peripheral nerves. Most PNS on the market are able to generate an electrical current with precision when the intensity and resistance ratings are 1 mA and 1–2 kΩ, respectively.[29] The manufacturers usually base their precision ratings on the above-mentioned parameters, although in actual clinical practice lesser current intensities are used. As a result, the characteristics of the stimulus generated can vary, depending on the apparatus used and on the clinical particularities of each individual patient. A description is provided below of the basic PNS characteristics required for peripheral nerve block.

Precision

The capacity of a given PNS to precisely generate the desired current is important for the success of nerve block and for the prevention of complications. As has been mentioned above, the intensity of the electrical current delivered is related to the distance between the needle and the stimulated nerve.[28] Controversy exists over the best intensity for stimulation, although different authors have shown that, with an intensity of 0.1 mA, the needle must be in contact with the nerve to elicit a motor response, whereas when the needle is located at a distance of 2.5 cm the current required for stimulation reaches 2.5 mA. These data indicate that the PNS must offer sufficient precision to generate an electrical current within the intensity range used in clinical practice (0.1–0.5 mA).[30] A lack of such precision can lead to the release of currents of less intensity than the rating actually selected, with the risk of inadvertent neural damage or intraneural injection of the local anesthetic solution as a consequence of excessive needle advancement.[31] These complications can be accentuated when nerve block is performed in patients subjected to deep sedation or general anesthesia, and who are thus unable to perceive paresthesias.[31,32] On the other hand, a PNS that generates currents greater than those actually selected can result in anesthetic solution injection away from the target nerve, thus increasing the risk of block failure.[28]

Duration of the stimulus

As has been described above, chronaxie varies according to the type of nerve fiber involved—a fact that allows us to classify the different fibers according to the characteristics of the electrical stimulus used. The PNS must be able to generate impulses of variable duration to ensure selective stimulation of the different fibers and to elicit motor responses without concomitant sensory or painful effects. In general, a PNS control option is required to be able to regulate the duration of the stimulus in the range of 0.1–1 mseconds.

Morphology of the stimulus

The ideal stimulation current consists of rectangular impulses. Changes in impulse morphology are dependent on changes in resistance; accordingly, modifications in skin characteristics, or the use of dried electrodes, can influence stimulation performance.[29] Such changes can reduce the effective energy delivered by the PNS, although at present the clinical implications of this are not clear.[33]

Frequency of the stimulus

Most PNS offer several stimulation frequencies in the range of 1–5 Hz. In practice, ratings of 1–2 Hz are most commonly used, although in some systems it is not possible to modify this parameter.

Maximum voltage output

Modern PNS make use of technology based on constant current generation, with detection of the difference between the current rating selected by the physician and the current actually generated by the system. When the current detected by the apparatus is lower than that selected, the PNS automatically compensates for the current drop by increasing the voltage output.[29] Such circumstances can arise in clinical practice in situations of increased impedance associated with very dry skin or a dried electrode.[34] In such cases the PNS can generate very important voltages (336 V) to keep the current in line with the selected ratings. This can prove painful for the patient, despite the fact that the current intensity is low, because in such situations excessive voltage is effectively targeted through the needle to a very small area.[33,34] With the high-voltage PNS systems used for neuromuscular monitoring (70 mA or 500 V), there have been reports of skin burns under certain conditions[35], and although this problem has not been observed with the PNS usually used for peripheral nerve block, caution is required and high-intensity or high-voltage currents should be avoided.[29]

Based on the above considerations, an adequately designed PNS should be able to generate brief (0.05–0.1 mseconds) square-morphology electrical impulses of constant intensity (adjustable by means of a potentiometer in the range of 0–5 mA), with a frequency of 1–5 Hz. Additional important characteristics include a battery level indicator, a visual and acoustic signal for each stimulus generated, and good electrode identification (black negative cathode and red positive anode). It would also be desirable to be able to contrast the energy actually delivered for peripheral nerve stimulation with the energy generated by the system and reflected on the display (the only option currently available), because the former is the energy actually responsible for triggering an action potential. In an experimental study by Raymond et al[36], voltage control proportional to the stimulus magnitude was used to indicate the proximity of the needle tip to the nerve. Optimal settings for each control parameter were determined, reflecting both engineering and physiologic tradeoffs. With these settings, the device proved successful in locating nerves, closely tracking needle movements at velocities as high as 2 mm/seconds.

Stimulation modes: technical considerations

Stimulation with low-intensity currents is the most widely adopted approach, although controversy exists over different technical aspects relating to clinical application of the procedure. The positioning of a skin electrode appears to be important for the precise localization of peripheral nerves, although agreement is lacking over the best position. Thus, while some authors recommend positioning the skin electrode as close to the puncture site as possible[37,38], others prefer to position it at a distance.[39] A recent study in healthy volunteers subjected to interscalene and femoral block via stimulation has shown that positioning of the skin electrode (i.e. the positive electrode—anode) does not influence block performance, provided a constant-current PNS is used.[40]

The optimum impulse for correct nerve localization without causing patient discomfort, and the current intensity required to precisely indicate proximity of the needle tip to the target nerve, have not been fully defined to date, although these are clearly critical considerations for correct performance of the technique.[36] Intensities in excess of 0.5 mA can cause block failure because the needle in such situations is not sufficiently close to the nerve, whereas values of under 0.2 mA theoretically increase the risk of intraneural injection.[41] Other authors consider that a current of between 0.5 and 1 mA is sufficient to ensure effective block.[42] Hadzic et al[40] found that an intensity of 0.3 mA with a duration of 0.1 mseconds yielded a satisfactory and comfortable response, with effective nerve block in application to interscalene or femoral block procedures. These authors considered that it is not necessary to stimulate below 0.3 mA because they required only low local anesthetic doses (10 ml), thus indicating proximity of the needle to the target nerve.

It is considered that a short-duration current ($\leq$0.1 mseconds) is able to selectively stimulate the motor components of a nerve[28,33,39,43], whereas a longer-duration current (1 mseconds) will induce sensory stimulation with paresthesias and discomfort for the patient.[42,44] However, a recent study has shown that the duration of the stimulus exerts no important effect on the degree of discomfort[40]; an increase in the duration of the current did not increase patient discomfort when current intensities known to induce a visible motor response without excessive muscle movement were applied. Other authors[45,46] have reported that low-intensity currents do not increase the prevalence of either paresthesias or patient discomfort. According to these investigators, the appearance of discomfort is fundamentally associated with the use of high-current intensities. In this context, currents of 2.1 and 1.7 mA in pulses of 0.1 mseconds induced discomfort when applied to interscalene and femoral block, respectively.[40] Taking the above into account, it appears advisable to deliver low-intensity currents (0.3–0.5 mA) in short pulses (0.1–0.2 mseconds), and at a frequency of 2 Hz.

In some cases, neurostimulation is accompanied by an absence of motor response, with the appearance of paresthesias. Some controversy exists over the use of stimulation and it has been suggested that a degree of contact may exist between the needle and nerve even in the absence of a motor response.[47] It is not known why paresthesias sometimes appear when stimulating at low intensities and in short pulses, although the underlying cause is believed to be mechanical. Nerves are heterogeneous, i.e. non-uniform structures, and at the instant of stimulation the needle tip might lie close to a sensory fascicle, thus resulting in paresthesia induction.[45] Mechanical or electrical stimulation of the nervi nervorum, which play a role in autonomic and nociceptive innervation, could also trigger paresthesias in the absence of a motor response.[48]

The use of different types of needles is an important consideration when performing nerve block with neurostimulation. At present, insulated needles are employed because they allow more precise localization of the target nerve, with less electrical intensity. Non-insulated needles generate an ovoid electrical field, as a result of which the maximum motor response is not achieved at the actual needle tip but rather 1–9 mm behind it, with the risk this implies of traversing the nerve.[49] By contrast, insulated needles generate a circular field with concentration at the tip. As a result, target localization is more precise and the risk of neural puncture less.

Different phases can be defined when performing nerve or plexus block.[26] The plexus 'search phase' begins when inserting the needle through the skin at an intensity according to the expected depth of the plexus. The usual starting intensities are in

the range of 1–2 mA, although some authors recommend starting with 0.5–0.6 mA to avoid patient discomfort due to excessive motor responses.[40,45]

When a motor response is elicited attributable to plexus stimulation, the 'approach phase' is performed until the minimum intensity capable of causing muscle contraction in the territory innervated by the plexus is obtained. The final stimulus current intensity should be in the range of 0.2–0.3 mA to ensure a high success rate.[28]

After adequate localization of the correct motor response as a function of the plexus stimulation site, the selected local anesthetic solution is administered ('injection phase'). Needle immobilization ensures that the administered volume is deposited in proximity to the stimulated nerve trunk and thus close to the plexus within its enveloping aponeurotic sheath. The specific motor-evoked activity disappears after administering 1–2 ml of local anesthetic, and reappears on increasing the stimulation intensity.

Finally, the 'anesthesia phase' is developed. The duration of this phase depends on the location of the stimulated plexus, the anesthetic used, the combined administration of drugs that modify the physicochemical characteristics of the local anesthetic or its intraneural diffusion, and the technique employed.[26] Following the anesthesia phase, the result obtained should be evaluated before commencing surgery.

BRACHIAL PLEXUS BLOCK

Anatomy and motor responses

The upper limb is innervated by a single nerve plexus: the brachial plexus. The latter is composed of the anterior primary divisions of the roots of the last four cervical spinal nerves (C4–C8) and of the first thoracic nerve (T1). On reaching the distal tip of the transverse processes, the roots travel towards the first rib and merge above it to form the three trunks of the plexus. The superior trunk is composed of roots C5–C6, the middle trunk of root C7, and the inferior trunk of roots C8–T1. On passing above the first rib and beneath the collar bone, the trunks in turn divide into two divisions: anterior and posterior. Within these divisions the nerve fibers separate to innervate the anterior flexor muscles and the posterior extensor muscles of the upper limb. On emergence of the plexus below the collar bone, the fibers recombine to form the three fascicles or bundles of the brachial plexus: lateral (composed of the junction of the anterior divisions of the superior and middle trunks), medial (continuation of the anterior division and inferior trunk), and posterior (composed of the posterior divisions of the three trunks). Each of the three fascicles gives rise to a branch that, either alone or in combination with others, comprises the principal nerves of the upper limb. Thus, the lateral and medial fascicles emit branches to form the median nerve, the lateral fascicle terminates as the musculocutaneous nerve, and the medial fascicle ends in the ulnar nerve. The posterior fascicle gives rise to the axillary nerve and terminates as the radial nerve.

Knowledge of anatomy is important when performing neurostimulation. Depending on the approach adopted, the motor responses elicited will differ because distinct structures (trunks, fascicles of nerves) are stimulated. The responses obtained when using an interscalene or supraclavicular approach are of a metameric (homologous segmental) nature, whereas the responses associated with axillary or humeral approaches correspond to those of each of the end-nerves.[26] Another aspect to be

taken into account is that the responses obtained must be distal with respect to the stimulation site, as responses due to direct muscle stimulation or the stimulation of collateral nerves originating outside the plexus may occur.

Table 2 shows the innervation routes of the upper limb and the main motor responses observed when performing brachial plexus block.[26,50]

The aim of neurostimulation is to elicit muscle contraction in one or more of the territories innervated by the nerves to be blocked.[51] In the case of the brachial plexus at axillary level, the typical response is elicited at wrist level or in the fingers. Thus, specific stimulation of the ulnar nerve produces lateral movements of the wrist, as well as flexion of the fourth and fifth fingers, and adduction of the thumb when delivering increased intensities. Median nerve stimulation produces palm flexion and opposition of the thumb, as well as pronation of the hand. Radial nerve stimulation causes extension of the elbow and/or wrist and of the fingers, whereas musculocutaneous nerve stimulation triggers flexion of the forearm on the arm. If an infraclavicular approach is adopted, the plexus is usually localized at a high axillary level; as a result, the responses observed exhibit a distribution similar to that of the end nerves. At this level, a motor response of the musculocutaneous nerve is acceptable for localization because it has not emerged from the brachial plexus. However, motor responses over the shoulder should be regarded as incorrect, because they can be induced by the stimulation of collateral nerves originating in the secondary trunks and which innervate the musculature of the axillary wall region. If a supraclavicular approach is adopted, the plexus is located at division or primary trunk level; as a result, the response elicited may exhibit end-nerve (when stimulus affects the divisions) or metameric characteristics (when stimulus affects the trunks). The responses observed are usually attributable to the uppermost trunks (superior and middle); consequently, the typical motor responses are pronosupination, flexion of the forearm, and carpal flexion–extension. The motor response is to be expected at the wrist joint. If the interscalene technique is performed, the plexus is located at trunk and/or anterior spinal nerve branch level; as a result, the response elicited is clearly metameric. Due to the characteristics of the technique, the commonly observed movements are dependent on the more cephalad roots (C5–C6) or superior trunk, and thus correspond to shoulder (abduction) and elbow (flexion) movements. Typical motor responses of a specific nerve can also be induced.[52–54]

Accumulated evidence of the advantages of neurostimulation

With the introduction of neurostimulation (NS), one of the novel possibilities has been multiple stimulation, i.e. the seeking of various motor responses by stimulating different components of the nerve trunk or plexus.[55] The theoretical advantages of multiple stimulation comprise a shorter latency, fewer failed blocks, and the possibility of using less local anesthetic (and thus reducing the risk of toxicity attributable to the latter). When single stimulation techniques are used, NS is not more effective when compared with the paresthesia technique applied to axillary block of the brachial plexus.[56] Different studies have shown that percentage success with the single injection technique for axillary block is not influenced by the neurovascular compartment identification method used.[56–60] However, the multiple stimulation approach is superior to the paresthesia or transarterial technique. A recent study[61] reported a significantly greater percentage of axillary block (91 versus 76%) when using NS to locate the four nerves, compared with localization of the latter based on the paresthesia induction technique. In addition,

Table 2. Upper limb neural innervation pathways (modified by De Andres[26] from Dumitru[50]).

Muscle	Movement	Root	Trunk	Division	Cord	Peripheral nerve
Spinal nerve origin						
Rhomboid major/minor		C5				Dorsal scapular
Serratus anterior		C5–C6				Long thoracic
Trunk origin						
Supraspinatus-infraspinosus trunk origin		C5–C6	U			Suprascapular
Pectoralis major		C5–C6–C7	U/M	A	Lat	Lateral pectoral
Pectoralis major/minor		C8–T1	L	A	Med	Medial pectoral
Latissimus dorsi		C6–C7–C8	U/M	P	Post	Thoracodorsal
Teres major		C5–C6–C7	U/M	P	Post	Lower subscapular
Peripheral nerve branch origin						
Biceps brachii	Forearm flexion and supination	C5–C6	U	A	Lat	Musculocutaneous
Deltoid	Arm abduction	C5–C6	U	P	Post	Axillary
Triceps	Forearm extension	C7–C8	M/L	P	Post	Radial
Anconeus		C7–C8	M/L	P	Post	Radial
Brachioradialis	Forearm supination	C5–C6	U	P	Post	Radial
Extensor carpi radialis	Carpal extension	C6–C7	U/M	P	Post	Radial
Extensor digitorum	Fingers extension	C7–C8	M/L	P	Post	Radial
Extensor indicis			M/L	P	Post	Radial
Pronator teres	Forearm pronation	C6–C7	M/L	A	Lat	Median
Flexor carpi radialis	Carpal flexion	C6–C7	U/M/L	A	Lat/Med	Median
Pronator quadratus	Forearm pronation	C8–T1	L	A	Med	Median
Opponens pollicis	Thumb opposition	C8–T1	L	A	Med	Median
Flexor carpi ulnaris	Cubital–carpal flexion–lateralization	C7–C8–T1	M/L	A	Lat/Med	Ulnar
Flexor digitorum profundus (III–IV)	Fingers flexion (III–IV)	C7–C8–T1	M/L	A	Lat/Med	Ulnar
Flexor digitorum profundus (I–II)	Fingers flexion (I–II)	C7–C8–T1	M/L	A	Lat/Med	Median

A, anterior; C, cervical; L, lower; Lat, lateral; M, middle; Med, medial; P, posterior; Post, posterior; T, throacic; U, upper.

performance time and time to onset of block were significantly shorter in the NS group. The high percentage success reported is similar to the success rates published by other authors using NS for nerve localization.[59,62] Fanelli et al[63], in a study of 1650 axillary blocks, reported a percentage success rate of over 90% when using multiple stimulation. These results indicate that NS is more objective than the search for paresthesias in locating nerves because it does not require active participation on the part of the patient; indeed, patient fear or anxiety can complicate adequate identification of paresthesias.[64]

Although it seems evident that multiple stimulation offers a series of advantages over other localization methods, it is important to determine how many nerves are to be anesthetized to ensure successful plexus block. In this sense, some authors consider that the musculocutaneous nerve is a separate nerve that should be anesthetized on a preliminary basis before performing any axillary block.[60,65] It seems that triple stimulation (musculocutaneous, median or ulnar, and radial) is superior to double stimulation (musculocutaneous and median, ulnar or radial) when performing axillary block. Coventry et al[65] obtained a 97% success rate with triple stimulation (musculocutaneous, median, and radial) versus only 53% when applying double stimulation (musculocutaneous and median). In another study, Sia et al[66] reported similar results: 90% success with triple stimulation versus 76% with double stimulation. A computed tomography (CT)-based study has shown the existence of great anatomical variability in the septum within the neurovascular space—with the creation of a multicompartment structure that limits diffusion of the local anesthetic solution.[67] Such anatomical peculiarities would help explain the greater percentage success afforded by triple stimulation axillary block.

A new approach has recently been described for brachial plexus block and appears to offer advantages over the axillary approach: midhumeral block.[68] Preliminary studies have obtained greater percentage success rates when compared with the traditional approach (88 versus 54%)[69], performing double stimulation for axillary block and quadruple stimulation for humeral block. A more recent study published by Sia et al[70] was unable to demonstrate differences in success rate using the quadruple stimulation technique with both approaches. These authors consider that the midhumeral technique allows more selective block when administering different anesthetic solutions for each nerve with the purpose of affording selective postoperative analgesia.

Neurostimulation has been used in other approaches to the brachial plexus and has allowed the development of new access routes. Traditionally, interscalene block has been carried out with single stimulation, although in a recent study of 171 interscalene blocks, multiple stimulation was used to obtain three responses (axillary, radial, and musculocutaneous)—yielding a success rate of 94% with a total anesthetic solution volume of 20–25 ml.[63] Gaertner et al[71] reported significantly improved success (87.5 versus 40%) during infraclavicular block with triple stimulation (median, ulnar, radial) compared with single stimulation (median or ulnar or radial)—musculocutaneous nerve stimulation being performed separately. Neuburger et al[72] in turn proposed infraclavicular block by vertical puncture, which yields an 88% success rate, whereas Salazar and Espinosa[73] advocate a technical modification of the classic approach that affords a 95% success rate. Finally, a classic subclavian perivascular approach to the brachial plexus has been reviewed by Franco and Vieira[74], using a nerve stimulator instead of paresthesia for localization, and obtaining 97.2% success in a series of 1001 consecutive blocks. Franco and Vieira emphasized the importance of the use of NS at the site of injection with this technique, where the plexus is reduced to its

smallest components and the sheath is reduced to its smallest volume, thus largely accounting for the success obtained with this block.

There is a concern that the multiple punctures involved in multiple stimulation might cause lesions. However, different studies have reported no cases of neurological damage following axillary block with multiple stimulation.[59,62] A recent observational study[63] described a 1.7% incidence of transient neurological alterations following 3996 blocks performed with the multiple stimulation technique. These data are similar to those published by Selander et al[75], who employed simple stimulation. Needle withdrawal and redirecting does not seem to be associated with an increased incidence of nerve lesions. The role of paresthesias in the development of nerve lesions has not been established. When a needle tip comes too close to a nerve axon, the mechanical effect over the nerve membrane produces paresthesia and hypothetical mechanical damage, thus increasing the risk of permanent neural lesions.[61] Reina et al[76] examined the use of short and long bevel needles over sciatic nerve bundles under scanning electron microscopy. Damage was observed when the needle bevel was introduced 0.3–0.4 mm into the nerve bundle; the needle tip was seen to cut through the perineurium and pierce the nerve bundle. However, the types of epineural lesion caused by short-bevel needles are different from those caused by long-bevel needles. The authors concluded that if the perineurium is damaged, the lesion will also affect the blood–nerve barrier, thereby probably leading to posterior sequelae. No clinical studies have reported a significant increase in nerve lesions associated to the search of paresthesias, even when performing repeated blocks.[77] However, some authors consider that nerve block should be performed avoiding the appearance of paresthesias.[78,79]

LOWER LIMB REGIONAL BLOCK

Anatomy and motor responses

The lower limb is innervated by the lumbar and sacral plexuses. The femorocutaneous, femoral, and obturator nerves are derived from the lumbar plexus. The sacral plexus in turn gives rise to the posterior cutaneous nerve and the sciatic nerve, which leave the pelvis through the sacroiliac foramen. The sciatic nerve is basically an association of the posterior tibial nerve (internal popliteal sciatic, IPS) and common peroneal nerve (external popliteal sciatic, EPS). These two nerves descend as the sciatic nerve along the posterior aspect of the thigh, and then divide at the level of the popliteal space.

To ensure adequate nerve block, it is important to know the different motor responses that might be found as a function of the nerve structure involved (Table 3):

- Sciatic nerve (proximal approaches: Labat, parasacral approach, etc.):
  - plantar flexion of the foot: stimulation of the posterior tibial nerve
  - dorsal flexion of the foot: stimulation of the common peroneal nerve
  - eversion of the foot: stimulation of the superficial peroneal nerve, peripheral branch of the common peroneal nerve
  - inversion of the foot: joint stimulation of the posterior tibial and common peroneal nerves
  - contraction of the biceps femoris: stimulation of the most external part of the sciatic nerve

Table 3. Lower limb neural innervation pathways.

Principal nerves	Muscles	Motoricity	Roots
Lumbar plexus (posterior approach)	Quadriceps	Extension of the leg, traction on patella (femoral n.)	L1–L3
	Adductors of the thigh, vastus internus	Adduction of the hip, contraction vastus internus (obturator n.)	L2–L4
Obturator	Adductors of the thigh, vastus internus	Adduction of the hip, contraction vastus internus	L3–L4
Femoral (inguinal approach)	Quadriceps	Extension of the leg, traction on patella (ideal response)	L2–L4
	Sartorius, adductor longus	Flexion, lateral rotation, adduction of the thigh	L2–L3
Sciatic (proximal approaches)	Plantar muscles of the foot (quadratus plantae, flexor of the toes)	Plantar flexion of the foot (posterior tibial n.)	L4–S3
	Tibialis posterior	Dorsal flexion of the foot (common peroneal n.)	L4–S2
	Extensor of the toes	Eversion of the foot (superficial peroneal n., peripheral branch of the common peroneal n.)	L5–S1
	Peroneus longus and brevis	Inversion of the foot (joint stimulation of the posterior tibial and common peroneal n.)	L4–S3
	Tibialis anterior, extensor of the toes	Flexion of the leg (stimulation of the most external part of the sciatic n.)	L5–S3
	Biceps femoris	Extension of the thigh, flexion of the leg, medial rotation (stimulation of the internal most part of the sciatic n.)	L4–S2
	Semimembranosus and semitendinosus	Extension and lateral rotation of the thigh (stimulation of the lesser sciatic n.)	L5–S2
	Gluteus maximus		
Sciatic (distal approaches)	Plantar muscles of the foot (quadratus plantae, flexor of the toes)	Plantar flexion of the foot (posterior tibial n.)	L4–S3
	Tibialis posterior	Dorsal flexion of the foot (common peroneal n.)	L4–S2
	Extensor of the toes	Eversion of the foot (superficial peroneal n., peripheral branch of the common peroneal n.)	L5–S1
	Peroneus longus and brevis	Inversion of the foot (joint stimulation of the posterior tibial and common peroneal n.)	L4–S3
	Tibialis anterior, extensor of the toes		

  - contraction of the semimembranosus and semitendinosus: stimulation of the internal most part of the sciatic nerve
  - contraction of the gluteus maximus: stimulation of the lesser sciatic nerve.
- Sciatic nerve (distal approaches: lateral popliteal, posterior popliteal approach, etc.):
  - plantar flexion of the foot: stimulation of the posterior tibial nerve
  - dorsal flexion of the foot: stimulation of the common peroneal nerve
  - eversion of the foot: stimulation of the superficial peroneal nerve, peripheral branch of the common peroneal nerve
  - inversion of the foot: joint stimulation of the posterior tibial and common peroneal nerves.
- Femoral or crural nerve (groin):
  - contraction of the quadriceps (movement of the patella): ideal response contraction of the sartorius, contraction of the adductor longus: other responses.
- Obturator nerve:
  - contraction of the vastus medialis of the quadriceps femoris and adduction of the hip: stimulation of the obturator nerve.
- Lumbar plexus (posterior approach):
  - contraction of the quadriceps femoris: stimulation of the femoral nerve
  - contraction of the vastus medialis of the quadriceps femoris, and adduction of the hip: stimulation of the obturator nerve.

The introduction of neurostimulation has resulted in some very important advances in peripheral nerve block of the lower limb, allowing (among others) the following procedures:[80]

- Highly selective block with an important success rate in application to scantly accessible nerve structures (9–14 cm in depth), where the paresthesia technique is very difficult to use.
- Important reduction in the anesthetic volumes required, thereby helping to lessen toxicity.
- Shortened latency.
- Multiple injection of local anesthetic solution, thus improving latency and percentage success.
- Reduced risk of nerve damage.
- Facilitation of the learning curve for anesthesiologists not expert in the use of regional techniques.

Accumulated evidence of the advantages of neurostimulation

In the preceding sections we have seen the possible motor responses that may be observed when stimulating each of the peripheral nerves of the lower limb. When performing femoral nerve block, a number of motor responses may be elicited, although it is well established that motility of the quadriceps femoris is the ideal response for satisfactory block of this nerve.[81] In the same way, when localizing the sciatic nerve, a series of motor responses can be triggered. Which response is to be sought when attempting to block the sciatic nerve? A number of recent studies have dealt with this question. Benzon et al[82] found that when adopting the posterior popliteal approach, inversion of the foot is the motor response that best predicts

complete sensory block, due to proximity of the needle tip to the two branches of the sciatic nerve (posterior tibial and common peroneal nerves). If the observed motor response corresponds to only one of these two branches, the probability of blocking both branches decreases. In relation to the posterior popliteal approach, Benzon et al[82] showed dorsal flexion to predict more complete sensory and motor block than plantar flexion, although when using the lateral popliteal approach, plantar flexion was the motor response that yielded the highest percentage success rate.[83,84] This difference may be due to the different position of the needle tip in the two approaches at the time of injecting the local anesthetic solution. At the gluteal level, and using the posterior approach of Labat, plantar flexion has likewise been shown to predict a greater percentage of successes, with a shorter latency, than dorsal flexion.[85] Further studies are needed to define the true importance of motor response in locating a peripheral nerve, and the possibilities of complete block.

In recent years, many studies have attempted to demonstrate the theoretical advantages of multiple stimulation in application to lower limb block.[63] Casati et al[86] have contrasted the effects of simple stimulation and multiple stimulation (triple stimulation) in terms of the volume of local anesthetic required to block the femoral nerve. The authors found the required solution volume to be less with multiple injection (mean 14 ml; range 12–16 ml) than with simple injection (mean 23 ml; range 20–26 ml), thus contributing to reduce the risk of local anesthetic toxicity. Based on the lateral approach for blocking the sciatic nerve at the level of the popliteal space, Paqueron et al[87] reported a greater percentage success rate after double injection of the local anesthetic solution (in the components of the sciatic nerve) versus single injection. Bailey et al[88] published similar results using the classic posterior gluteal approach. They found an increase in success rate and a shorter latency to sciatic nerve block when using the double-injection technique. Recently, the subgluteal approach has also been used to demonstrate shorter latency with double injection. However, single injection considerably reduced patient discomfort during performance of the technique.[89] It should be remembered that whereas double injection to block the sciatic nerve will probably afford an increased percentage success rate and a shorter latency versus simple injection, the quality of block resulting from double injection will vary, depending on the approach used.[90] Similar considerations also apply to the single-injection technique.[91]

STIMULATING CATHETERS IN PERIPHERAL NERVE BLOCK

Continuous peripheral block has been shown to afford superior analgesia with fewer side effects compared with intravenous analgesia and epidural analgesia.[92,93] One of the main problems posed by the technique is placement of the catheter sufficiently close to the target nerve to ensure effective analgesia with small amounts of local anesthetic. Block failure has been demonstrated in over 10% of cases, despite the administration of large amounts of local anesthetic solution through the catheter.[94] By injecting contrast medium through the catheter, Capdevila et al[95] have shown that whereas the catheters are easily inserted, their directioning when introduced at the femoral level is unpredictable. To avoid this high failure rate, Pham-Dang et al[96] conducted an observational study in 130 patients involving stimulating catheters to confirm correct catheter positioning. This technique was seen to improve the proportion of catheters on target for optimum continuous peripheral block. An active line of research must be

maintained to define the true role of stimulating catheters in continuous peripheral block, and to compare them with the conventional techniques.[97,98]

Practice points

- nerve fiber depolarization is the origin of action potentials. The stimulus triggering depolarization can comprise an external electrical current applied with the purpose of locating a peripheral nerve
- the characteristics of the electrical impulse influence the muscle response obtained
- peripheral nerve stimulators should be able to generate brief (0.05–0.1 mseconds) square-morphology electrical impulses of constant intensity (adjustable by means of a potentiometer in the range of 0–5 mA), with a frequency of 1–5 Hz
- different phases for performing nerve or plexus block: 'search phase' begins when inserting the needle through the skin at an intensity according to the expected depth of the plexus. 'Approach phase' is performed until the minimum intensity capable of causing muscle contraction in the territory innervated by the plexus is obtained. 'Injection phase' for giving local anesthetic in proximity to the stimulated nerve trunk and thus close to the plexus within its enveloping aponeurotic sheath. 'Anesthesia phase' is developed after local anesthetic effect is developed

Research agenda

- multiple stimulation offers a clear advantage over the single-stimulation method only in peripheral nerve blocks. Limited clinical data of its benefit in the roots, trunk, or cords of the nerve plexus suggest caution and further research
- an active line of research must be maintained to define the true role of stimulating catheters in continuous peripheral block, and to contrast them with the accumulated knowledge with conventional techniques
- ultrasound imaging has been found useful in localizing peripheral nerves and in improving the success of nerve blocks. There is an obvious need for studies comparing the ultrasound technique with the nerve stimulator technique in various blocks

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