Background: Dorsal horn neurons of the spinal cord participate in neuronal pain transmission. During spinal and epidural anesthesia, dorsal horn neurons are exposed to local anesthetics and opioids. Droperidol is usually given with opioids to avoid nausea and vomiting. A recently developed method of "entire soma isolation" has made it possible to study directly the action of droperidol on different components of Na⁺ current in dorsal horn neurons.

Methods: Using a combination of the whole-cell patch-clamp recording from spinal cord slices and the entire soma isolation method, we studied the direct action of droperidol on two types of Na⁺ currents in dorsal horn neurons of young rats.

Results: The tetrodotoxin-sensitive Na⁺ current in isolated somata consisted of a fast inactivating (τ₁, 0.5–2 ms; 80–90% of the total amplitude) and a slow inactivating (τ₂, 6–20 ms; 10–20% of the total amplitude) component. Droperidol, at concentrations relevant for spinal and epidural anesthesia, selectively and reversibly suppressed the fast component with a half-maximum inhibiting concentration (IC₅₀) of 8.3 μM. The slow inactivating component was much less sensitive to droperidol; the estimated IC₅₀ value was 809 μM.

Conclusions: Droperidol selectively blocks fast Na⁺ channels, the fast and slow components of the Na⁺ current in dorsal horn neurons are carried through pharmacologically distinct types of Na⁺ channels, and the effects of droperidol differ from those of local anesthetics and tetrodotoxin, which equipotently suppress both components. Droperidol may be suggested as a pharmacologic tool for separation of different types of inactivating tetrodotoxin-sensitive Na⁺ channel. (Key words: Electrophysiology; ion channels; neuroleptics.)

DORSAL horn neurons located in laminae I–III of the spinal cord receive most of their primary sensory input from myelinated Aδ fibers and nonmyelinated C fibers, and therefore participate in processing and transduction of nociceptive information. During epidural and spinal anesthesia, the dorsal horn neurons are exposed to high concentrations of local anesthetics and/or opioids that directly diffuse into the spinal cord. Application of opioids is usually accompanied by side effects such as nausea, emesis, and pruritus. To reduce these side effects and to prolong analgesia, the neuroleptic droperidol is often applied with opioids during epidural and spinal anesthesia. However, the mechanisms of droperidol action on the central nervous system are not completely understood. Although it is generally accepted that droperidol acts on dopaminergic receptors (D2), there are several indications that it also suppresses voltage-gated Na⁺ conductance. For example, a subcutaneous application of droperidol was shown to result in a reversible local anesthesia. Droperidol blocks voltage-gated Na⁺ channels in cardiomyocytes and mammalian nonmyelinated nerve. However, little information is available about the action of droperidol on diverse types of Na⁺ channels expressed in spinal cord neurons.

The recently developed method of "entire soma isolation" (ESI), i.e., isolation of the soma from its neuron during whole-cell recording, has allowed a description of the properties and spatial distributions of two distinct types of inactivating Na⁺ channels in dorsal horn neurons of the spinal cord. In addition, the ESI method provides a possibility to study pharmacologic properties of the channels in identified neurons under conditions where diffusion of the blocker molecules is not impeded by connective tissue surrounding the neuron. In the current investigation we applied the ESI method to dorsal horn neurons from laminae I–III to study the effect of droperidol on fast and slow types of inactivating tetrodotoxin (TTX)-sensitive Na⁺ channel. It has been...
found that the fast Na⁺ channels are two orders of magnitude more sensitive to droperidol than the slow channels and the effect of droperidol differs from that of local anesthetics and TTX, which equipotently suppress both components of the Na⁺ current.

Materials and Methods

Preparation

Experiments were performed by means of the patch-clamp technique on 200-μm-thin slices, cut from the lumbar enlargement (L3-L6) of the spinal cord of 6-12-day-old rats. The animals were rapidly decapitated, and the spinal cords were carefully cut out in ice-cold preparation solution bubbled with 95% O₂-5% CO₂. After removal of the pial membrane with fine forceps, the spinal cord was embedded in a preparation solution containing 2% agar cooled to 39°C. The agar block containing the lumbar enlargement of the spinal cord was cut out and glued to a glass stage fixed in the chamber of the tissue slicer. The spinal cord was sliced in ice-cold preparation solution that was continuously bubbled with 95% O₂-5% CO₂. The slices were thereafter incubated for 1 h at 32°C. The standard procedure of cell cleaning by repetitive blowing and suction of the bath solution through a broken patch pipette was not used because each slice contained numerous dorsal horn neurons with clean surfaces.

The procedures of animal decapitation have been reported to the local veterinarian authority and are in accordance with the German guidelines.

Solutions

Preparation solution contained 115 mM NaCl, 5.6 mM KCl, 2 mM CaCl₂, 1 mM MgCl₂, 11 mM glucose, 1 mM NaH₂PO₄, and 25 mM NaHCO₃ (pH 7.4 when bubbled with 95% O₂-5% CO₂). In the experimental chamber, the slices were perfused with low-Ca²⁺/high-Mg²⁺ solution to reduce spontaneous synaptic activity in neurons. This solution was obtained from the preparation solution by setting the concentration of Ca²⁺ and Mg²⁺ to 0.1 mM and 5 mM, respectively. Tetraethylammonium (TEA⁺) solution used for the investigation of Na⁺ channels (TEA solution) contained 95 mM NaCl, 5.6 mM KCl, 0.1 mM CaCl₂, 5 mM MgCl₂, 11 mM glucose, 1 mM NaH₂PO₄, 25 mM NaHCO₃, and 20 mM TEA-Cl (pH 7.4 when bubbled with 95% O₂-5% CO₂). Stock solution of droperidol (20 mM) was obtained by dissolving this drug in dimethyl sulfoxide. The stock solution was added to TEA solution to achieve the desired drug concentration. The addition of dimethyl sulfoxide did not change the pH value in our experimental solution and had no effect on Na⁺ currents studied here. The local anesthetic lidocaine was directly added to the external TEA solution. The experimental chamber with a volume of 0.4 ml was continuously perfused by external solution at a rate of 2-3 ml/min. Droperidol and lidocaine-HCl were purchased from Sigma Chemical Co. (Deisenhofen, Germany), TTX was purchased from Latoxan (Rosans, France), and TEA was purchased from Merck (Darmstadt, Germany).

Current Recording

Pipettes for whole-cell recording were pulled in two stages from borosilicate glass tube (GC 150; Clark Electromedical Instruments, Pangbourne, United Kingdom) and were fire-polished to give a final resistance of 3-5 MΩ. The patch-clamp amplifier was an EPC-7 (List, Darmstadt, Germany). The effective corner frequency of the low-pass filter was 3 kHz. The frequency of digitization was at least twice that of the filter. The data were stored and analyzed by using commercially available software (pCLAMP; Axon Instruments, Foster City, CA). Transients and leakage currents were digitally subtracted in all recordings using records with hyperpolarizing pulses. Offset potentials were nulled directly before formation of the seal. Errors in the clamped potential evoked by the series resistance of the electrode were not corrected. In experiments performed on the isolated somata, these errors did not exceed 4 mV in most cases. All experiments were conducted at a room temperature of 21-23°C.

Identification of Dorsal Horn Neurons

The dorsal horn neurons were identified in spinal cord slices as multipolar cells with a soma (8-12-μm diameter) located in laminae I-III. Neurons were distinguished from glial cells in voltage-clamp mode on the basis of a procedure described previously. All neurons studied possessed a large Na⁺ current exceeding 1 nA and showed spontaneous synaptic activity. The resting potentials in intact neurons measured just after breaking the membrane and establishing the whole-cell recording configuration (before diffusion of Cs⁺-containing pipette solution into the cell) were between −80 and −50 mV.
Droperidol Selectively Blocks Fast Na⁺ Channels

The Method of Entire Soma Isolation

A detailed description of the ESI method has been published elsewhere. Briefly, in whole-cell recording mode, the entire soma of the neuron was isolated from the slice by slow withdrawal of the recording pipette (see fig. 1). The isolated structure was classified as soma. The isolated structure with one process was identified as soma+axon complex if the remaining Na⁺ current exceeded 90% of the current recorded from the intact neuron in the slice just before its isolation.

Statistical Analysis and Fitting

The normalized amplitudes of peak Na⁺ currents in concentration-effect curves were fitted by means of a nonlinear least squares procedure using a standard isotherm:

\[
\frac{I}{I_0} = \frac{(1 - \text{Res})}{(1 + (c/I_{50}))} + \text{Res} \quad (1)
\]

where \(I\) was the current measured in the presence of a given drug concentration, \(I_0\) was the control current measured in the absence of drug, \(c\) was the drug concentration, \(I_{50}\) was the concentration giving a half-maximum effect, and \(\text{Res}\) was the residual or non-blocked component. The binding of one drug molecule to the receptor was assumed to be sufficient for channel suppression.

Fitting of the inactivation kinetics of the total Na⁺ currents was performed with two exponentials using the following equation:

\[
I(t, c) = I_F(c) \times \exp\left(-\frac{(t - t_0)}{\tau_F}\right) + \left(I_F(c) - I_F(c)\right) \times \exp\left(-\frac{(t - t_0)}{\tau_S}\right) \quad (2)
\]

where \(I(t, c)\) was the current magnitude as a function of time and blocker concentration \(c\), \(t_0\) was the time at which the inward current had reached its maximum, \(I_F(c)\) was the maximum inward current at a given blocker concentration, \(I_F(c)\) was the amplitude of the fast current component at \(t_0\), \(\tau_F\) (0.5-2 ms) was the inactivation time constant of the fast component, and \(\tau_S\) (6-20 ms) was the inactivation time constant of the slow component. For each cell, the values of \(\tau_F\) and \(\tau_S\) had been determined by fitting the recording in control \((c = 0)\) and were kept fixed in all further fittings of currents recorded in the presence of the blocker. By fitting the inactivation kinetics of suppressed currents, the values of \(I_F(c)\) and \(I_F(c)\) for each blocker concentration were determined. The data points plotted on the concentration-effect relations in figure 4B were obtained by normalizing the component amplitudes in the presence of the blocker by the amplitude in control: \(I_F(c)/I_F(0)\) for the fast component and \([I_F(c) - I_F(c)]/(I_F(0) - I_F(0))\) for the slow component, assuming that the amplitude of the slow component \(I_F(c) = I_F(c) - I_F(c)\).

The nonlinear fitting of the steady state inactivation curves (see fig. 5) were performed using a standard Boltzmann equation:

\[
I/I_0 = 1/[1 + \exp\left(-\left(E - E_{50}\right)/k\right)] \quad (3)
\]

where \(I\) was a current measured at a given potential \((E)\), \(I_0\) was the maximum current, \(E_{50}\) was the potential at which half of Na⁺ channels was inactivated, and \(k\) was a steepness factor.

Fig. 1. Scheme of the entire soma isolation (ESI) method. In whole-cell recording mode, the entire soma of the neuron was isolated from the slice by slow withdrawal of the recording pipette. The isolated structure without an attached process was classified as soma. The isolated structure with one process was classified as soma+axon complex if the remaining Na⁺ current exceeded 90% of the current recorded from the intact neuron in the slice just before its isolation.
The present study is based on recordings from 22 intact neurons in the slice, 49 isolated somata, and 10 isolated soma+axon complexes. All numerical values are given as mean ± SEM. The parameters obtained by fitting the data points using a linear least-squares procedure are given as mean ± SE.

**Results**

Na⁺ currents were recorded from the isolated somata of dorsal horn neurons in external TEA solution; the pipettes were filled with high-Cs⁺ solution. Holding potential was set to −80 mV and Na⁺ currents were activated by 50-ms voltage steps to −20 mV after a 50-ms prepulse to −120 mV. The peak Na⁺ currents remaining in the isolated somata after separation from the axon initial segment had a small amplitude of 150–300 pA (10–20% of original Na⁺ current measured in most intact dorsal horn neurons). Therefore, the voltage error caused by the resistance in series was small, and problems of a poor space clamp of the neuronal membrane were avoided. As a consequence of the improved space clamp condition, the kinetics of the Na⁺ current in an isolated soma became considerably faster than in an intact neuron (fig. 2A).

**Pharmacologic Studies with the ESI Method**

The suitability of the ESI method for pharmacologic investigations of ionic channels in spinal neurons was tested in the experiments shown in figure 2. Sensitivities of Na⁺ currents recorded from intact dorsal horn neurons in the spinal cord slice and from their isolated somata to the local anesthetic lidocaine were compared.

To reach the steady state block in experiments with intact neurons, the slices had to be perfused at least 2–5 min with lidocaine-containing solution before the measurements were performed. The hyperpolarizing prepulse to −120 mV was omitted to reduce the amplitude of the Na⁺ current. Lidocaine suppressed the Na⁺ current with an IC₅₀ of 112 ± 8 μM (eight neurons) in intact neurons in the spinal cord slice (fig. 2B).

The IC₅₀ value for lidocaine obtained in experiments with isolated somata was 12.6 ± 1.9 μM (five somata and four soma+axon complexes). It should be noted that a prepulse to −120 mV preceding the depolarization in isolated somata is known to reduce the channel sensitivity to the blocker. Nevertheless, approximately nine times lower concentrations of lidocaine were needed to evoke the same effect as in intact neurons. It is therefore concluded that the connective tissue surrounding the intact neuron in the spinal cord slice remarkably impedes the drug diffusion toward the cell membrane and that the apparent IC₅₀ values measured in pharmacologic experiments performed using the slice preparation represents an underestimation of the real channel sensitivity to the blocker. Therefore, we per-

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formed the following experiments on isolated somata or soma+axon structures.

**Suppression of the Total Na⁺ Current in Isolated Somata**

Inactivating Na⁺ current in isolated somata of dorsal horn neurons consisted of fast inactivating ($\tau_1$, 0.5-2 ms; 80-90% of total current) and slow inactivating ($\tau_2$, 6-20 ms; 10-20% of the total current) components. Both fast and slow components of the transient inward current studied here were carried through Na⁺ rather than Ca²⁺ channels, because they were observed under conditions in which Ca²⁺ currents were suppressed either by lowering Ca²⁺ to 0.1 mM and increasing Mg²⁺ to 5 mM in external solution or by addition of 50 mM F⁻ to the pipette solution. In isolated somata, both components of the Na⁺ current disappeared after substitution of external NaCl with choline-Cl or were completely blocked by 100 nM TTX. Investigation of the steady state Na⁺ channels located in the processes of dorsal horn neurons was beyond the scope of the present study.

Addition of 0.3-300 µM droperidol to the bath solution produced a concentration-dependent reduction of the peak Na⁺ current (fig. 3). It can be seen that 10 and 30 µM droperidol suppressed the fast component of the current, whereas the slow component remained relatively unchanged (fig. 3A). The highest concentration of the drug tested (300 µM) blocked only 83% of the total peak current (fig. 3B). Fitting the data points of the concentration-effect relation with equation 1 gave an IC₅₀ of 11.6 ± 2.0 µM and a Res of 0.17 (12 somata). It is assumed that the droperidol-resistant component of the current was mostly carried through slow inactivating channels.

To test the sensitivity of each component of Na⁺ current to droperidol, we performed a two-exponential fitting of inactivation kinetics of the total Na⁺ current (equation 2) in the presence of different droperidol concentrations (fig. 4A). Suppression of the fast component was complete and could be adequately described using one isotherm (equation 1) with IC₅₀ = 8.3 ± 1.1 µM and Res = 0 (eight somata; fig. 4B). The slow component was much less sensitive to droperidol, being reduced to only 0.83 at 300 µM. Fitting of the data points for the slow component with an isotherm assuming Res = 0 gave an IC₅₀ of 809 ± 247 µM (eight somata; fig. 4B). Thus, the slow component was approximately two orders of magnitude less sensitive to the drug than the fast one.

The two-exponential fitting of inactivation kinetics was further performed to study whether the fast and slow components of Na⁺ current also have different ranges of steady state inactivation. The Na⁺ currents were activated in isolated somata by a voltage pulse to -30 mV after a prepulse (50 or 160 ms long) to different potentials ranging between -150 and -40 mV. For a 50-ms prepulse, the fitting of the data points with equation 3 gave the $E_{H50} = -73.8 ± 0.8$ mV and $k = -8.8$ mV for the fast component and $E_{H50} = -62.9 ± 0.9$ mV and $k = -8.6$ mV for the slow one (fig. 5, five somata). At a 160-ms prepulse, both components inactivated at more negative potentials: $E_{H50} = -84.6 ± 0.5$ mV, $k = -9.0$ mV for the fast component and $E_{H50} = -74.7 ± 0.8$ mV, $k = -8.8$ mV for the slow component (five somata). Thus, the fast Na⁺ currents inactivated at approximately 10 mV more negative potentials than the slow ones.

**Comparison with Effects of TTX and Lidocaine**

To test whether the differential block of fast and slow components of the Na⁺ current is a specific effect of droperidol, the action of 30 nM TTX and 100 µM lidocaine on the currents recorded in isolated somata were
compared (fig. 6). TTX and lidocaine proportionally reduced both fast and slow components, whereas droperidol predominantly suppressed the fast one. This phenomenon can be seen clearly if the peak of the blocked current was normalized to the peak of control current (traces on the right in fig. 6). The traces in 100 μM droperidol were considerably slower than the traces in control, indicating a dominance of the slow component (fig. 6). It can be concluded that neither TTX nor lidocaine are able to produce a differential block of the fast and slow Na⁺ currents.

Use-dependent Block by Droperidol

In the following experiments with isolated somata, we studied the ability of droperidol to produce a use-dependent block of the total Na⁺ current. A train of 10 Na⁺ currents was activated at a frequency of 1 Hz by 50-ms depolarizing pulses from -80 to -20 mV in the absence and presence of 10 μM droperidol (fig. 7A). Droperidol, similar to local anesthetics, produced a use-dependent block of the current. Figure 7B shows the amplitudes of the Na⁺ currents normalized to the amplitude of the first current recorded in control solution (seven isolated somata). In the absence of the drug, the amplitude of the 10th current was reduced by 0.11, presumably because of insufficient recovery of Na⁺ channels from slow inactivation. In the presence of 10
DROPERIDOL SELECTIVELY BLOCKS FAST Na⁺ CHANNELS

Fig. 5. Inactivation characteristics of fast and slow components of Na⁺ current. The inactivation characteristics of the fast (filled symbols) and slow (open symbols) components on Na⁺ currents activated by a voltage step to -30 mV after a 50-ms (upper) or a 160-ms (lower) prepulse to different potentials. The fitting parameters are given in Results.

μM droperidol, the relative amplitude of the Na⁺ current was reduced from 0.59 at the first pulse to 0.35 at the 10th pulse. Thus, slow inactivation and use-dependent block induced by 10 μM droperidol reduced the total Na⁺ current by 41% (10th current vs. first current).

It can be seen in figure 7A that the total Na⁺ current was reduced because of apparent reduction in the amplitude of the fast component, whereas the slow component remained unchanged. To describe the use-dependent block of each component, the two exponential fittings of the inactivation kinetics of the total Na⁺ current were performed. Figure 7C shows the amplitudes of the fast (six somata) and slow (six somata) components in control solution and in the presence of 10 μM droperidol normalized to the amplitude of the corresponding component of the first current activated in a control solution. The data points for the slow component in the presence of the blocker were almost indistinguishable from those in a control solution. The amplitude of the fast component in 10 μM droperidol was reduced from 0.45 to 0.20 (first vs. 10th current). Thus, the use-dependent block of the fast component was 56%.

Discussion

The current study has demonstrated that the ESI method can be adequately used in pharmacologic investigations of ionic channels and that the neuroleptic
droperidol produces a differential block of fast and slow inactivating types of TTX-sensitive Na\(^+\) channel in spinal dorsal horn neurons.

**The ESI Method**

Our experiments show that pharmacologic studies of ionic currents in isolated *somata* had several advantages in comparison with those performed on intact neurons in the spinal cord slice, excised membrane patches, or enzymatically dissociated neurons. First, relatively small amplitudes of the remaining Na\(^+\) current (approximately 150–300 pA in the *somata* compared with 1–20 nA in intact neurons in the slice or in enzymatically dissociated neurons, which usually preserve at least a part of the axon initial segment) allow considerable reduction of the voltage error due to series resistance. On the other hand, remaining currents are sufficiently large to be studied directly, without averaging several consecutive recordings, as typically performed in pharmacologic studies with excised outside-out patches containing only a few channels. Furthermore, ionic currents in isolated *somata* show much less “run-down” effect than in outside-out patches.

Second, simple spherical geometry of the isolated *soma* with a diameter of approximately 10 \(\mu\)m provides adequate space clamp conditions. As a consequence, the
kinetics of Na⁺ channels in isolated somata were considerably faster than in intact neurons. The isolated somata could also be used for measurements of changes in gating kinetics induced by different drugs.

Third, improved conditions for drug perfusion in isolated somata allows precise measurements of the binding constants for the drug investigated; the values obtained for intact neurons in the slice represent a considerable underestimation of the channel sensitivity, since connective tissue impedes diffusion of the blocker.

Fourth, in comparison with nucleated patches,¹⁷ which also provide relatively large ionic currents, the whole isolated somata preserve their good physiologic state, being able to keep the resting potential (when the pipette contains physiologic high K⁺ solution). The ESI methods gives the possibility to study effects of different substances on the somatic excitability under current-clamp conditions.

Fifth, the ESI method enables pharmacologic studies of the channels in the soma of neurons that have been identified before isolation on the basis of their location in the slice or patterns of electrical activity seen during whole-cell recording.

Differential Block of Na⁺ Channels by Droperidol

Droperidol at concentrations between 0.1 and 300 μM suppressed the fast inactivating component of the TTX-sensitive Na⁺ current, whereas the slow inactivating component remained almost unchanged. The IC₅₀ value of 8.3 μM obtained for the fast component was approximately two orders of magnitude lower than that for the slow one (809 μM), indicating that droperidol is a selective blocker of fast Na⁺ channels.

Two-component inactivation kinetics of TTX-sensitive Na⁺ current were observed in a number of neuronal preparations.¹⁰,¹⁸–²¹ In the frog node of Ranvier, the fast component of the Na⁺ current was approximately eight times more sensitive to niflumic acid and approximately three times more sensitive to TTX than the slower one.²₀

In experiments with intact dorsal horn neurons in the spinal cord slice, a differential block of the fast and slow components by 1 μM TTX was only observed during perfusion of the slice with drug-containing solution.¹⁰ The fast component had been completely suppressed within 1 min, whereas blockade of the slow component began several minutes later. In the isolated somata, however, the fast component was only slightly more sensitive to TTX, leading to the conclusion that the differential block of two components seen in experiments with intact neurons in the slice is unlikely to result from different TTX sensitivities of underlying channels but can be better explained by their different spatial distributions over the neuronal membrane. In this case, the connective tissue in the spinal cord slice impedes the diffusion of the blocker, and thus different regions of the neuronal membrane experience different TTX gradients. The idea of the existence of two independent types of inactivating Na⁺ channels in dorsal horn neurons was also supported by single-channel measurements that revealed an approximately 25% larger unitary conductance for the slow channel.¹⁰ Selective suppression of the fast component by droperidol reported here provides further evidence that fast and slow Na⁺ currents in spinal dorsal horn neurons are carried through distinct types of ion channels. Droperidol, with its IC₅₀ value two orders of magnitude lower for the fast channel compared with the slow one, seems to be the only substance described thus far that enables separation of the fast and slow components of TTX-sensitive Na⁺ currents.

In contrast to droperidol, TTX and the local anesthetic lidocaine proportionally reduced both components and were not able to separate the current components in the isolated somata. It can be assumed that droperidol and local anesthetics show different mechanisms of action on Na⁺ channels.

The neuroleptic droperidol and the local anesthetic lidocaine have some structural similarities. They comprise a lipophilic ring system on one end of the molecule that is connected by an aliphatic chain with a tertiary amine on the other end. The intermediate aliphatic chain contains an ester binding in droperidol and an amide binding in lidocaine. Because of the tertiary amine, the droperidol and lidocaine have pKa values of 7.6 and 8.2, respectively, and thus are partly protonated at physiologic pH. Their unprotonated forms are highly lipophilic with a partition coefficient (logP) of 3.5 for droperidol and 2.3 for lidocaine. In contrast, TTX is a permanently charged alkaloid with low lipid solubility. It binds with its charged guanidinium group to the outer mouth of the channel pore.

Numerous studies performed during the last 40 yr have shown that the mechanisms of local anesthetic action during epidural and spinal anesthesia are complex²² and cannot be interpreted as a simple suppression of an ion conductance in the axonal membrane. The dorsal horn neurons of the spinal cord play a key role in neuronal pain transmission. They are exposed to local anesthetics, opioids, and neuroleptics during spinal and epidural anesthesia, and, therefore, suppression of the Na⁺ conductance in dorsal horn neurons by these substances...
contributes to analgesia. Droperidol blocks the fast Na⁺ channels, providing a major portion of Na⁺ current needed for fast membrane depolarization during the action potential. The IC₅₀ value of 8.3 μM is three orders of magnitude lower than the concentration of droperidol injected into the epidural space during analgesia (6 mM syringe concentration, droperidol 2.5 mg/ml), indicating that the clinically applied droperidol may affect the Na⁺ conductance in spinal neurons. In addition, droperidol may be suggested as a pharmacologic tool in studying the properties and physiologic functions of fast and slow inactivating Na⁺ channels.

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