The Physiology of the Nicotinic Acetylcholine Receptor and its Importance in the Administration of Anesthesia

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The nicotinic acetylcholine receptor (nAChR) can be found widely throughout the body. Although the activation of this receptor leads to multiple functions dependent on its location within the body and subunit composition, all nAChRs aid in the communication between the extracellular and intracellular compartments. The nAChR is composed of 3 domains: the extracellular, transmembrane, and intracellular. The receptor functions in response to ligands that act as an agonist or antagonist that binds to the extracellular domain causing activation or inactivation of the receptor. The activation of the nAChR causes a twisting motion of the receptor, which opens a gate allowing for the passage of sodium, potassium, and calcium cations through the cell membrane. The muscle-type nAChR and neuronal-type nAChR have important roles during the administration of anesthesia. The muscle-type nAChR, located in the neuromuscular junction, is the target of neuromuscular blockers and local anesthetics to prevent muscle contraction. General anesthetics affect the neuronal-type nAChR by inhibiting functions of the central nervous system, including memory formation. The importance of the nAChR cannot be underestimated, for it is through the manipulation of this receptor that many anesthetic goals are achieved.

Keywords: Anesthetic effects on nAChR, muscle-type nAChR, nAChR structure, neuronal-type nAChR, nicotinic acetylcholine receptor (nAChR).

Objectives
At the completion of this course, the reader should be able to:
1. Describe the structural makeup of the nicotinic acetylcholine receptor (nAChR).
2. Identify the functions of the nAChR.
3. Discuss the importance of the neuronal-type and muscle-type nAChRs in the administration of anesthesia.
4. Compare and contrast the mechanisms of action of the various types of medications administered by nurse anesthetists.
5. Identify the effects of general anesthesia on the nAChR.

Introduction
The nicotinic acetylcholine receptor (nAChR) is one of the most researched and clearly understood receptors in the human body. This receptor functions in the central nervous system (CNS) and the peripheral nervous system (PNS). The nAChR has many different subunits leading to its compositional diversity throughout the body. Although there are many subtypes of this receptor that perform multiple functions, they are all important in the process of communication between the extracellular and intracellular compartments. Knowledge of this receptor will help nurse anesthetists to understand how and where certain anesthetic agents and adjuncts affect their patients. This course provides a review of the most recent literature published concerning the nAChR and a detailed discussion of its physiology and importance in the administration of anesthesia.

Review of the Literature
There has been extensive research performed on the nAChR. The results and recent advances provide a better understanding of the anatomy and physiology of this receptor. Xu et al reported that the nAChR is the most researched and best understood receptor of the ligand-gated channel family because it was the first receptor to
have been recognized and studied electrophysiologically.

An extensive review of the nAChR based on studies from the electric organs of the torpedo fish nAChRs, mollusk homologous acetylcholine binding proteins, mice nAChRs, and prokaryotic pentameric ligand-gated ion channels was written by Zouridakis et al. In the review, the authors discussed the nAChR structure, domains, ligand binding sites, 3 conformational transitions, and the gating mechanism.

Through a further review of electron microscopy studies on the torpedo and high-resolution x-ray studies of the snail acetylcholine binding protein, Kalamida et al discussed in depth the structure and function of the nAChR. They concluded that the receptor has multiple subtypes consisting of precise combinations of subunits to mediate its assorted physiological functions. In addition, Kalamida et al described the receptor in 3 broad categories: (1) muscle-type receptors that are important in muscle contraction; (2) neuronal-type receptors that are important in cognition, such as learning and memory; and (3) nonneuronal cell receptors that have been found to be important in the cholinergic pathway.

Lecchi et al provided another overview comparable to the 2 previously mentioned studies in which they showed a detailed overview of the structure and function of the nAChR. In addition to the muscle-type, neuronal-type, and nonneuronal-cell-type receptors, Lecchi and associates offered information about several of the sensory functions of the nAChR located in the inner ear and retinal ganglion.

Millar and Harkness wrote a review of studies of the nAChR performed on the torpedo and supplied a detailed discussion of the different subunits of the receptor. They reported 17 subtypes of the subunits, α1 through α10, β1 through β4, ε, γ, and δ. They also found that muscle-type receptors are heteromeric (composed of different subunits) and neuronal-type receptors can be heteromeric or homomeric (composed of the same subunit and subunit subtypes).

In research on snail acetylcholine binding proteins, Gotti et al discovered the ligand binding sites on the nAChR. The nAChR can transform among 3 conformational states based on whether a ligand is bound to the receptor. These conformational states include the following: (1) the resting state with the gate closed, (2) the open state with the gate open, (3) and a desensitized state in which the gate closes after a ligand has remained on the binding site for a period and that can have a fast or slow onset.

Taly reviewed previous studies on the gating mechanism of the nAChR. The gating mechanism has been found to be a twisting motion that occurs between the extracellular domain (ECD) and the transmembrane domain (TMD). The twisting motion between the ECD and the TMD results in the twisting of the M2 α-helices in the TMD, which causes an increase in the diameter of the ion channel and allows the ions to flow through the channel into the cell.

In another study, Shen and Yakel reviewed previous research concerning the nAChR and how activation of the neuronal-type receptor affects calcium signaling in the CNS. Activation of the neuronal nAChR causes direct and indirect calcium influx into the cell, resulting in the calcium signals mediating immediate, short-term, or long-term effects in the CNS.

Wessler and Kirkpatrick reviewed the nonneuronal nAChR, including the synthesis, expression, and cellular functions of the receptor. Like the muscle- and neuronal-type nAChR, the subunit composition of the receptors on nonneuronal cells differed according to function and location. The functions of the nonneuronal nAChR include signal transduction, regulation of phenotypic cell functions, and cholinergic pathway functions. The receptor can be found in mucosal tissue, endothelial cells, immune cells, and mesenchymal cells.

Dilger provided an outline of the muscle-type nAChR at the neuromuscular junction (NMJ) and its function in muscle contraction. Dilger also explained the action of neuromuscular blockers in inhibiting muscle contraction, including the competitive antagonist ligands in nondepolarizing muscle relaxants that compete with acetylcholine at the binding sites and the agonist ligands of depolarizing muscle relaxants, which cause the nAChR to transform into a desensitized state.

Arias and Bhumireddy discussed the experimental evidence about the effects of local and general anesthetics on the nAChR. Local anesthetics work at the NMJ with minimal CNS effects, but general anesthetics have been found to be more sensitive in neuronal receptors. Arias and Bhumireddy observed that general anesthetics have minimal effects at the NMJ.

Wang et al performed a study to determine the suppression of the muscle-type nAChR when local anesthetics and nondepolarizing muscle relaxants were given in combination. Wang et al described how local anesthetics work at the muscle-type nAChR as a noncompetitive antagonist that inhibits ion channel opening to prevent muscle contraction. They concluded that the use of local anesthetics augment the neuromuscular blockade function of nondepolarizing muscle relaxants.

Anatomy and Function of the nAChR

The nAChR is found widely throughout the body. It is located in the CNS as a neuronal-type receptor, in the PNS as a muscle-type receptor, and has additionally been discovered in nonneuronal cells. The nAChR is an integral protein that spans across the cell membrane. According to Millar and Harkness, the nAChR is a part of the ligand-gated ion channel superfamily and the Cys-loop subfamily, which also includes the 5-hydroxytryptamine,
γ-aminobutyric acid, glutamate, and glycine receptors. The nAChR responds to the binding of the neurotransmitter, acetylcholine, but has the ability to become activated through the binding of exogenous ligands, including nicotine, certain medications, and anesthetics. The nAChR is composed of 5 subunits that form a ring, creating an ionic pore in the center of the receptor through which ions flow. These 5 subunits are α, β, γ, δ, and ε; an example is shown in Figure 1. These 5 subunits are further categorized into 17 subtypes, which contribute to the receptor’s complexity (Table 1).

The nAChR is divided into 3 domains. Kalamida et al list the 3 domains as the N-terminal ECD, the TMD, and the intracellular domain (ICD), as shown in Figure 1. The ECD is composed of 10 β strands (known as a β sheet) that are linked with a Cys-loop in addition to containing several other loops. The 2 ligand binding sites for acetylcholine are located in the ECD. The binding sites of a heteromeric nAChR are located at the interface between an α subunit and the adjacent non-α subunit—the γ, ε, or δ subunit. The α subunit is the principal component of the binding site formed by loops A, B, and C, and the non-α adjacent subunit is the complementary component of the binding site formed by loops D, E, and F. In a homomeric nAChR, there are postulated to be 5 binding sites because the nAChR is formed with 5 α subunits. Each α subunit contains the principal and complementary components of the binding sites in the homomeric receptor. Last, the ECD enables the nAChR to be selectively permeable to cations because of the negatively charged amino acid residues that line the inner wall of the ECD. The diameter of the nAChR is 20 to 25 Å with the narrowest portion measuring approximately 7 Å. Arias and Bhumireddy concluded that the diameter of the channel, when the receptor is activated and the gate is open, is wide enough to allow sodium and potassium ions to flow across the cell membrane.

The TMD is the area of the nAChR that spans the cell membrane and forms the ion pore. As shown in Figure 1, the TMD of each subunit consists of 4 α helices (M1, M2, M3, and M4) that span the cell membrane to form the ion channel. There is a covalent bond between β10 of the ECD and M1 of the TMD that joins these 2 domains. M1, M3, and M4 form an outer ring, while the M2 helices of the 5 subunits form an inner ring that lines the channel pore through which ions flow. The ion channel gate is formed by an inward tilt of the M2 helices toward the center of the pore where they come together creating a barrier to ion permeation. The TMD is also lined with negatively charged...
amino acids to selectively facilitate the movement of cations through the receptor.3

The ICD is composed of yet another α helix, MA, which when combined with the 4 MAs from the other subunits, forms the wall of the intracellular vestibule of the nAChR.2 The ICD contains the M3-M4 loop, which is believed to be important for the export of the nAChR from the endoplasmic reticulum and the regulation of trafficking and expression by promoting the clustering of the receptor.2,5 Researchers have also found it instrumental in the assembly and anchoring of the receptors in the cell membrane.11

The ICD aids in modulating the function of the nAChR through the presence of multiple phosphorylation sites.11 As with the ECD and the TMD, the ICD is lined also with negatively charged amino acids to repel anions and facilitate the flow of cations.4

The nAChR can transition among at least 3 conformational states, including resting, activated (open), and desensitized.5,11 When the binding sites on the ECD are free of ligands, the receptor is in the resting state with the gate closed, and it has the ability to be activated.11 Upon ligand binding on the ECD, a conformational change occurs and results in the opening of the gate, allowing cations to flow through the receptor channel.6 One way in which the gate has been found to open is through a twisting mode with opposite rotation of the ECD from the TMD.7 The result is a twisting motion of the internally located M2 helices, causing dilation and an increase in the width of the ion channel, allowing ion passage.7 If the ligands remain on the binding sites, the receptor transitions to a desensitized state, a period in which the receptor is refractory to the ligand and the gate remains closed.11 Once the ligands are removed from the binding sites, the receptor transitions back to the resting state.11

Ligands that bind with the nAChR can have different effects on the action of the receptor. The binding proteins that elicit these different reactions are agonists or antagonists, with the antagonist group being further divided into competitive and noncompetitive antagonists4 (Table 2). As stated by Lecchi et al,4 ligands that have a certain effect on one nAChR may have a different effect on another nAChR with a different makeup of subunits.4

The function of each nAChR depends on numerous factors, including its location in the CNS or the PNS and the subunits and their subtypes that constitute a particular receptor.4 The general function of the nAChR is to transform chemical signals into electrical signals by taking extracellular acetylcholine and using it to generate an electrical signal resulting from the opening of ion channels.7 There are 3 types of nAChRs, including muscle, neuronal, and nonneuronal, that produce electrical signals to carry out specific functions. Each type of nAChR works by opening the ligand-gated channel and allowing an influx of cations into the cell.2

<table>
<thead>
<tr>
<th>Receptor</th>
<th>α subunit</th>
<th>Non–α subunits</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle-type nAChR^5</td>
<td>α1</td>
<td>β1, γ, δ, and ε</td>
<td>α1β1γδ</td>
</tr>
<tr>
<td>Neuronal-type nAChR^5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heteromeric</td>
<td>α2, α3, α4, α5, α6, α7, α8, α9, and α10</td>
<td>β2, β3, and β4</td>
<td>α4β2</td>
</tr>
<tr>
<td>Homomeric</td>
<td>α7, α8, and α9</td>
<td>None</td>
<td>α7</td>
</tr>
<tr>
<td>Nonneuronal-type nAChR</td>
<td>a</td>
<td>a</td>
<td>a</td>
</tr>
</tbody>
</table>

Table 1. Types of nAChRs and Their Subunit Makeup

^5All 17 subtypes listed for the muscle and neuronal types have been found throughout the tissues and cells of the body where the nonneuronal-type nAChR is located.9

Abbreviation: nAChR, nicotinic acetylcholine receptor.

<table>
<thead>
<tr>
<th>Binding protein</th>
<th>Effect</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agonist</td>
<td>Binds to the ligand binding sites activating the receptor</td>
<td>Acetylcholine and succinylcholine^10</td>
</tr>
<tr>
<td></td>
<td>and results in the opening of the gated channel^4</td>
<td></td>
</tr>
<tr>
<td>Competitive antagonist</td>
<td>Binds to the ligand binding sites prohibiting the binding of an agonist and, therefore, the receptor cannot be activated.4</td>
<td>Vecuronium, pancuronium, and mivacurium^10</td>
</tr>
<tr>
<td></td>
<td>This effect is overcome if there is an increase in the concentration of an agonist (acetylcholine) in the area surrounding the nAChR.4</td>
<td></td>
</tr>
<tr>
<td>Noncompetitive antagonist</td>
<td>Does not bind directly to the ligand binding sites and can block the opening of the channel or bind to an allosteric site on the nAChR and cause inhibition of the receptor.4</td>
<td>Lidocaine,^12 procaine,^12 and isoflurane^11</td>
</tr>
</tbody>
</table>

Table 2. Effects of Binding Proteins on the nAChR

Abbreviation: nAChR, nicotinic acetylcholine receptor.
The muscle-type nAChRs are located on the subneural cleft of the NMJ where the motor nerve innervates the muscle,\(^2\) as shown in Figure 2.\(^{10,13}\) The activation of this receptor allows an influx of sodium ions, which depolarizes the muscle cell and brings the resting membrane potential to threshold and causes an action potential to fire, which ultimately leads to muscle contraction.\(^{10}\) The neuromuscular junction is the site of action for local anesthetics, nondepolarizing muscle relaxants, and depolarizing muscle relaxants.\(^{10}\) General anesthetics may also produce some effects at this site.\(^{10}\)

| Abbreviations: PLC, phospholipase C; Ins(1,4,5)P\(_3\) and IP\(_3\), inositol triphosphate; CaBP, calcium sensor proteins; ER, endoplasmic reticulum; RY, ryanodine receptor; ATPase, adenosine triphosphatase. |

The neuronal-type nAChRs are selective to calcium, leading to an increased permeability of calcium into the cell.\(^3\) The activation of this receptor mediates the increase in intracellular calcium by 3 mechanisms: direct permeation of calcium through the nAChR; an influx of calcium into the cell resulting in membrane depolarization, causing the activation of voltage-operated calcium channels (VOCC); and an influx in calcium that triggers further release of calcium from intracellular stores.\(^8\) The increase in intracellular calcium can lead to immediate effects, such as the release of neurotransmitters, or long-term effects, such as the formation of memory or gene expression or metabolism.\(^3,8\)

Figure 2. Nicotinic Acetylcholine Receptor (nAChR) at the Neuromuscular Junction

This figure demonstrates the location of the nAChR in the subneural cleft of the neuromuscular junction. The nAChRs that function in the neuromuscular junction are activated by the ligand binding of acetylcholine from the motor neuron.\(^{10}\) The activation of this receptor allows an influx of sodium ions, which depolarizes the muscle cell and brings the resting membrane potential to threshold and causes an action potential to fire, which ultimately leads to muscle contraction.\(^{10}\) The neuromuscular junction is the site of action for local anesthetics, nondepolarizing muscle relaxants, and depolarizing muscle relaxants.\(^{10}\) General anesthetics may also produce some effects at this site.\(^{10}\) (Adapted with permission from Dubuc.\(^{13}\) See www.thebrain.mcgill.ca.)

Figure 3. Neuronal-type Nicotinic Acetylcholine Receptor (nAChR) and the Influx of Calcium

This figure demonstrates the mechanisms of how calcium enters the cells after stimulation of a neuronal-type nAChR. The neuronal-type nAChRs are selective to calcium, leading to an increased permeability of calcium into the cell.\(^3\) The activation of this receptor mediates the increase in intracellular calcium by 3 mechanisms: direct permeation of calcium through the nAChR; an influx of calcium into the cell resulting in membrane depolarization, causing the activation of voltage-operated calcium channels (VOCC); and an influx in calcium that triggers further release of calcium from intracellular stores.\(^8\)

One difference from the muscle-type nAChR is that the neuronal-type receptor has high calcium selectivity.\(^3\) Calcium signals that can be instigated through the activation of the nAChR include direct calcium influx through the nAChR, activation of voltage-gated calcium channels, and calcium-induced calcium release.\(^8\) These mechanisms are shown in Figure 3.\(^3,8,13\) The direct influx of neurotransmitters from the neuron.\(^3\) Zouridakis et al\(^3\) asserted that the nAChR located in the postsynaptic area activates functions of cell excitability, gene expression, cell differentiation, and survival. On some neurons, the activation of the nAChR can excite the neuron and cause an action potential to fire, while in other neurons, the activation of the receptor may only be facilitative by raising the resting membrane potential closer to threshold without causing the firing of an action potential.\(^4\)

The nAChR has an important role in the CNS functions of neuroprotection and neurodegeneration, learning, memory, reward, motor control, arousal, and analgesia.\(^2,3\) In addition, Lecchi et al\(^4\) emphasized the significance of nAChRs in sensory functions such as in the retina and the innervations of the inner ear. The direct function of nAChR in the retina is not clearly understood, but nAChR is thought to create signal amplification in the outer hair cells of the ear.\(^4\)
of calcium through the nAChR. Another function of the influx of calcium into the cell is the initiation of mechanisms that lead to memory formation.8 Also, the activation of the nAChR results in second-messenger calcium signaling, which influences cell signaling and gene expression and metabolism.3

The nAChRs that are located in nonneuronal cells act in endocrine, endothelial, epithelial, and immune system cells.2 One example is found within nonneuronal cells where the activation of the nAChR helps to mediate autocrine and paracrine regulatory loops.9 Another example is in epithelial cells where the nAChR facilitates cell migration through chemotaxis, control of the cytoskeleton, and cell-to-cell contact; it is also said to have a part in wound healing.9 Last, the activation of the nAChR in immune cells inhibits the release of proinflammatory mediators as part of the cholinergic anti-inflammatory process.9 The expression and function of the nonneuronal nAChRs depend greatly on the receptor subunit composition and on the internal and external environments leading to the variability of the actions of activated nonneuronal cell nAChRs.9

Anesthesia Implications

Anesthesia providers need an understanding of the physiology of the nAChR. This receptor is the site where some of the more commonly used adjunct agents that are administered during anesthesia work to elicit the desired anesthetic outcome or effect. An understanding of the function of the nAChR provides nurse anesthetists with a clearer comprehension of the possible effects that specific agents could have on a patient during surgery.

One result that is desired during many anesthetics is muscle relaxation. This relaxation is attained through administering anesthetic agents and adjuncts that have their effects at the NMJ. The NMJ is a desired site of action because it is where the action potential enters the muscle cell, initiating the process of muscle contraction.10 Dilger10 wrote that for an action potential to be initiated in the muscle, the muscle-type nAChR located at the NMJ is activated from the binding of acetylcholine that is released from the terminal of a motor nerve. This activation of the receptor allows an influx of sodium ions through the sarcolemma into the muscle fiber, causing the muscle to depolarize.10 If the depolarization increases the resting membrane potential enough to reach threshold, an action potential is fired.10 This action potential excites the muscle by traveling along muscle fibers and ultimately results in muscle contraction.10

Different types of muscle relaxants and anesthetics act on the nAChR to accomplish the relaxation or blockage of muscle contraction during surgery. Anesthetics that work at the nAChR in the NMJ include those that act as noncompetitive antagonists, competitive antagonists, and agonists.10,12 These anesthetics are also known as local anesthetics, nondepolarizing muscle relaxants, and depolarizing muscle relaxants.10 Figure 210,13 shows the NMJ and the site of action for these anesthetics.

Local anesthetics primarily inhibit voltage-gated sodium channels, but they also function as noncompetitive antagonists in the nAChR to depress the synaptic transmission from the motor neuron to the muscle.11,12 Researchers disagree about the mechanism of action of local anesthetics. Gotti et al9 state that noncompetitive local anesthetics may bind to an allosteric site on the nAChR without interfering with the direct ligand binding sites for acetylcholine. The binding of the local anesthetic to the nAChR inhibits the channel opening of the ion pore, and, therefore, sodium ions cannot flow into the muscle cell to initiate an action potential, which ultimately prevents a muscle contraction.12 Through experimentation, researchers have also noted that these noncompetitive antagonists may enter the channel and form a blockade that inhibits the flow of sodium ions into the cell.11 Arias and Bhumireddy11 found that local anesthetics have possible actions on neuronal-type nAChRs in the CNS, with effects including sedation, tremors, dysphoria, seizures, and coma.

In addition to local anesthetics, nondepolarizing muscle relaxants also work at the site of the nAChR at the NMJ, but they produce their effects by acting as a competitive antagonist.10 As previously described, a competitive antagonist is a ligand that competes with acetylcholine to bind to the ligand binding sites on the α subunits of the nAChR, and their effects can, therefore, be suppressed by a local increase in the acetylcholine concentration.4,10 This results in the inability of the channel to open and allow an influx of sodium into the muscle to initiate the process of a muscle contraction.10 Because 2 acetylcholine ligands have to bind to the α binding sites on the nAChR, only 1 ligand of the nondepolarizing muscle relaxant needs to bind to the receptor to prevent it from becoming activated and causing the channel to open.10 To properly administer these agents, nurse anesthetists need to recognize that nondepolarizing muscle relaxants have a slow onset, a fade in the train-of-four ratio, and a slow recovery.10

The last type of anesthetic adjunct agent that targets the receptor on the NMJ, known as depolarizing muscle relaxants, produces its effects by acting as an agonist for the muscle-type nAChR.10 An agonist is a ligand that binds to the nAChR and induces a response; in this case, it causes the channel gate to open.4 Depolarizing muscle relaxants require 2 ligands to bind to the binding sites on the α subunits of the nAChR to elicit activation of the receptor.10 Once the gate opens in the channel of the nAChR, sodium ions rush into the muscle and cause an action potential to fire, which results in a muscle contraction.
contraction. The high amount of depolarizing muscle relaxant molecules in the NMJ causes them to equilibrate with the binding sites on the receptor. This high concentration of molecules causes the nAChR to transform into a desensitized state in which the gate is closed, resulting in the inability to fire an action potential and cause the muscle to contract. In contrast with the nondepolarizing muscle relaxants, the depolarizing muscle relaxants have a fast onset, a constant train-of-four, and a fast recovery.

In addition to the muscle-type nAChR, neuronal-type nAChRs have a role in certain CNS effects that occur as a result of general anesthesia, including amnesia, lack of attention, behavioral states, and delirium. General anesthetics produce an inhibitory effect on the nAChR and act as noncompetitive antagonists on certain receptors in the CNS. Their mechanism of action remains to be determined, and they may act in the way that is exhibited by noncompetitive antagonists. The 2 mechanisms by which noncompetitive antagonists may work (which may be the function of general anesthetics) are through the binding of the ligand on an allosteric site of the nAChR that provokes a nonconductional state or through the ligand, which can enter the channel and cause a blockage to inhibit the flow of ions. The impairment of neuronal-type nAChRs during general anesthesia can help prevent the formation of memories. The increased permeability of the neuronal-type nAChRs to calcium ions promotes the activation of mechanisms that lead to memory formation. Through blocking the activation of this receptor, calcium is unable to enter the cell and initiate the process of memory formation. According to Arias and Bhumireddy, neuronal-type nAChRs, more so than muscle-type nAChRs, are sensitive to the action of inhaled anesthetics used for general anesthesia. Although neuronal-type nAChRs may be more sensitive to inhaled anesthetics, these anesthetics have some effect on muscle-type nAChRs, which can lower the dose of muscle relaxants that are required to inhibit muscle contraction.

A summary of the type of nAChRs and the anesthetic agents and adjuncts that affect them is given in Table 3.

It is important for anesthesia providers to understand the functions and physiology of the different nAChRs to elicit desired patient responses during surgery because many administered anesthetic agents and adjuncts target these receptors. If the function of the nAChR is not known, the outcome of giving certain anesthetics cannot truly be understood.

### Conclusion

The nAChR has a complex composition and diverse locations and functions throughout the body. Because of its varied functions from aiding in muscle contractions to assisting in the formation of memory, the nAChR is one of the most important receptors that nurse anesthetists focus on during anesthetic administration. The responses that nurse anesthetists need to elicit are achieved through manipulating the function of the nAChR. Although researchers have made great strides in understanding the physiology and pathophysiology of the nAChR, additional research continues to be performed on this receptor as a target for new drug discovery and drug therapy, including in the field of anesthesia.

### REFERENCES


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