

Nicotinic acetylcholine receptor in skeletal muscle

Summary

This article is a systematic review carried out in order to recognize the importance of the nicotinic acetylcholine receptor in skeletal muscle and the relationship between this and the development of human characteristics such as the development of strength. Strength is one of the fundamental motor skills of athletic performance, in training there are neuromuscular adaptations and metabolic alterations that improve performance during competition, physical strength training, improves the performance of athletes during the competitive period, as well Also the plasticity of the skeletal muscle tissue, thus allowing the manifestation of different adaptations to the functional demands of each athlete linked to processes of a mechanical, metabolic and electrophysiological character specific to any sports modality.

Keywords: acetylcholine, acetylcholinesterase, cholinergic, skeletal muscle fibers

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Introduction

This article is a systematic review carried out in order to recognize the importance of the nicotinic acetylcholine receptor in skeletal muscle and the relationship between this and the development of human characteristics such as the development of strength.

Strength is one of the fundamental motor capacities of sports performance, in training neuromuscular adaptations and metabolic alterations occur that improve performance during competition, physical strength training, improves the performance of athletes during the competitive period, as well as the plasticity of skeletal muscle tissue, thereby allowing the manifestation of different adaptations to the functional demands of each athlete linked to mechanical, metabolic and electrophysiological processes specific to any sport modality.

These motor skills on which sports performance is based are based on the complex and essential action of muscle contraction, in which protein macromolecular complexes act with a single function: to allow movement through the contraction and relaxation of the muscle dependent on the effectiveness of the neuromuscular junctions at the end of the motor plates, in which the release of the neurotransmitter acetylcholine by the nerve cell and its binding to the nicotinic acetylcholine receptor (nAChR) in skeletal muscle play a primary role, hence the importance of this review lies in knowing the functions and characteristics associated with nAChR and the influence on skeletal muscle in order to establish scientific foundations that may be involved in the development of strength, applicable to any sport.

Methods

Search strategy

This review was conducted following the preferred information points for systematic reviews and meta-analyses contained in the statement (PRISMA) (Figure 1). A computerized search was carried out in PubMed, Google Scholar, ScienceDirect and NCBI, (From January 2017 to December 2017) taking as references of analysis articles in English and Spanish, using a combination of keywords: 'Acetylcholine', 'Acetylcholinesterase', 'Colinergycos', 'Physical activity', 'exercise', 'genetics' and 'genes'.

Inclusion and exclusion criteria

To be eligible for inclusion and subsequent review, the selected articles had to meet the following criteria: (a) non-randomized

controlled trials (NRCTs); (b) studies focusing on strength sports; (c) studies with healthy participants, amateurs and elite practice striking competition; and (d) studies written in English and Spanish. Studies where the population under study were adults over 60years of age were excluded, In addition, comments, interviews, letters, posters were excluded.

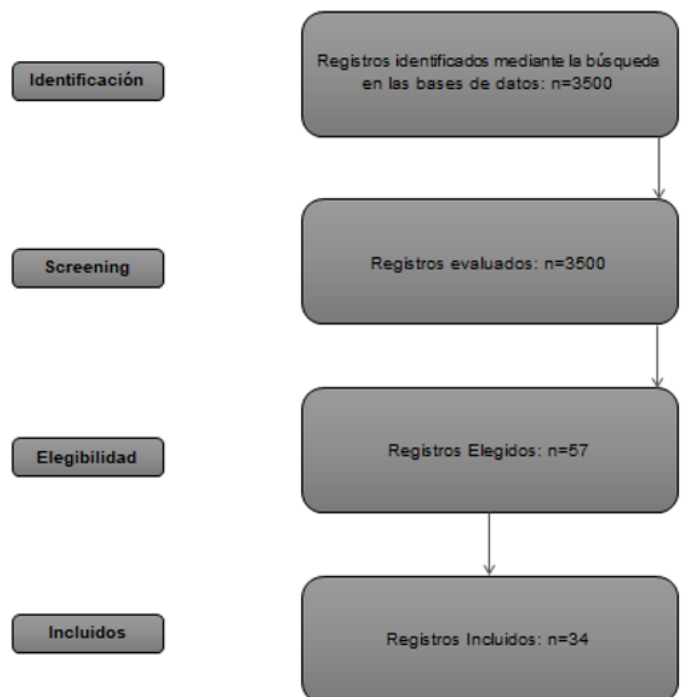


Figure 1 Schematic of the methodology used to select research articles that relate polymorphisms of the nAChR gene in blood, skeletal muscle and brain in Homo Sapiens. Source: Author's Own.

Articles related to genes to exert in humans were selected through RT-PCR studies and microarray genotyping, RNA-Seq. Articles relating polymorphisms of the nAChR gene in blood, skeletal muscle and brain, using cutting-edge methods such as sequencing, RT-PCR and genotyping of microarrays, the detection of polymorphisms in these tissues, show a strong positive correlation for each of the samples. We reviewed studies potentially relevant for eligibility by two reviewers (MS) by examining titles, abstracts and full texts.

Quality assessment

An assessment of the methodological quality of each included article was performed using the modified Downs and black scale, which is appropriate for case-control studies and non-randomised controlled trials. Twenty-seven articles were used to determine the methodological quality control checklist. Twenty-six (26) specific questions of 'yes' or 'no' were asked with a total of twenty-six (26) possible points. In this review, questions were classified into 4 sections: Reporting (10 items), external validity (3 items), study bias (7 articles), and confounding and selection bias (6 items).

History of strength sports in Colombia (Weightlifting)

Pastor F,¹ La Weightlifting, is an Olympic sport of strength framed within the lifting of weights whose objective is the lifting of the maximum possible weight, which is carried out by means of a bar to which at its ends discs are added that are the ones that determine the final weight to be lifted.

Badillo JJ, et.al.,² Weightlifting training requires enhancing a number of characteristics associated with the performance and performance of the athlete such as physical and mental strength, in addition to strengthening the technique and speed at which the movements are made, which for this sport are mainly two: the start and two times.

Marchetti R, et.al.,³ Strength is one of the fundamental motor skills of sports performance, in training neuromuscular adaptations and metabolic alterations occur that improve performance during competition, physical strength training, improves the performance of weightlifting athletes during the competitive period, as well as the plasticity of skeletal muscle tissue, thereby allowing the manifestation of different adaptations to functional demands of each athlete linked to mechanical, metabolic and electrophysiological processes specific to this sport.

Ostrander, et.al.,⁴ These motor skills on which sports performance is based are based on the complex and essential action of muscle contraction, in which protein macromolecular complexes act with a single function: to allow movement through muscle contraction and relaxation dependent on the effectiveness of the neuromuscular junctions at the end of the motor plates, in which the release of the neurotransmitter acetylcholine by the nerve cell and its binding to the nicotinic acetylcholine receptor (nAChR) in skeletal muscle play a primary role, hence the importance of this study lies in knowing the epigenetic and polymorphic variations of the nAChR gene and the tissue or phenotypic variations associated with these genotypic variations, who may be involved in the development of strength in a group of weightlifting athletes from the Valle del del.

Weightlifting is one of the most representative sports in Colombia and in this sport is where more triumphs have been achieved in our nation; This sport consists of two movements the start and two times, in the first the competitor must raise the bar from the platform to the complete extension on the head, in a single movement, being essential that during the final position remains with the arms extended, maintaining balance up to two seconds, when the judges give the signal to replenish the bar on the stage.

In the second, as the name suggests, it is divided into two times, during the first time the participant raises the bar to shoulder height, above the chest, while the legs open well in a flexion, raising the body then, at that moment, with the strength of legs and arms, the athlete must raise the bar, with the full extension of the members,

over the head, until the signal of the judges to lower it. This sport is characterized by technique and strength, the latter being the topic to be evaluated in this article and its relationship with the improvement of sports performance from the study of the nicotinic receptor of acetylcholine in skeletal muscle.

Olympic achievements obtained in Colombia in the modality of weightlifting during the last 16 years

At the 2000 Sydney Olympics it was the first time that women could participate in Olympic weightlifting and the champion was the Colombian Maria Isabel Urrutia, who participated in the 75 kilograms category and won gold. In Athens 2004, once again weightlifting gave medals to Colombia, this time, Mabel Mosquera was the one who won bronze in the 53kg category, at 35years old, this athlete was surprised by her age, but she did it and earned an important place in the history of national sport.

For the year 2008 in Beijing Diego Salazar was the one who shone in the category of the 62 kilograms won the silver and gave the country one of the two medals that were harvested in those Games, followed by this, in London in 2012 Oscar Figueroa won the silver medal in the 62 kilograms, finally in Rio de Janeiro 2016 he took the gold medal with 62 kilograms and that same year Luis Javier Mosquera was in third place taking the bronze.

Relationship between weightlifting and strength

Strength is a basic and fundamental component for sports performance, there are many manifestations or types of this quality, depending on the purpose of the training program you are going to perform, we will describe these classifications to have more knowledge and be able to have a good specific or individualized training plan in strength work, here we will focus on maximum strength and talk about the test to evaluate this manifestation.

Static or isometric strength

Kirsch L,⁵ states: "It is one that occurs as a result of an isometric contraction, in which there is an increase in tension in the contractile elements without detecting a change in length in the muscle structure". Kuznetsov V, 1989. That is to say that the isometric force is one in which a muscle contraction occurs without the muscle making a movement.

Dynamic strength

Lambert,⁶ Es that which occurs as a result of a contraction with change of length in the muscular structure, which can be shortened, resulting in the so-called concentric dynamic force, in which the internal muscular force exceeds the resistance to overcome; or tension in lengthening of the muscle fibers, which would suppose the so-called eccentric dynamic force, where the external force to overcome is superior to the internal tension generated. On the most effective way of working with each of these manifestations of muscle contraction there are no properly contrasted clarifying data.

Explosive force

Cerani J D⁷ also called force-speed and characterized by the ability of the neuromuscular system to generate a high rate of contraction before a given resistance. Generelo E., Tierz O. 1994. In this case, the load to be overcome will determine the preponderance of the force or speed of movement in the execution of the gesture. However, explosive force improvements find a greater correlation in force work than with execution speed improvements.

Strength resistance

Ehlenz H, et al.,⁸ It is the ability to withstand fatigue in performing muscular efforts that can be short, medium and long duration. It supposes, therefore, a combination of the qualities of strength and endurance, where the relationship between the intensity of the load and the duration of the effort will determine the preponderance of one of the qualities over the other.

In this sense, we can talk about the so-called short-term resistance strength, where we try to overcome fatigue at intensities higher than 80% of a maximum repetition (1RM), a circumstance in which local factors dominate and where there is no contribution of oxygen and nutrients through the blood. There seems to be no consensus on the recommended load intensity.

We will talk about strength resistance in the medium term in efforts maintained against loads located between 20% and 40% of 1RM, where the qualities of strength and resistance provide a practically equal value for performance. Finally, note the so-called long-term resistance strength, manifested in efforts maintained below 20% of 1RM, where aerobic energy production pathways acquire clear preponderance in relation to local strength.

Maximum strength

Ozolin N.G.¹⁰ Maximum strength: it is the greatest expression of force that the neuromuscular system can apply to a given resistance. This manifestation of force can be static (maximum static force), when the resistance to overcome is insurmountable or, on the other hand, dynamic (maximum dynamic force) when there is displacement of said resistance. The maximum strength depends on three main factors that are susceptible to be trained, such as muscle cross-section or hypertrophy, intra- and intermuscular coordination, based on an effective activation system of motor units and energy sources for muscle protein synthesis.

Importance of nicotinic acetylcholine receptor in skeletal muscle

Wolfe RR The skeletal muscle plays an important role in all mammals especially in humans since it provides evolutionary characteristics of its species, in addition to the expression of multiple functions, including the ability to perform and maintain movements that guarantee not only the displacement but also maintain the body position of standing that differentiate it from the other members of the animal kingdom and allow exploration and Use of their environment.

Heymsfield SB, et al 1972. Skeletal muscle makes up approximately 40% of the total body weight and is composed of about 50% of proteins that are constantly changing according to the demand and use of them. Skeletal tissue is not only composed of proteins but also of water, mineral salts, carbohydrates and fatty acids that allows each specialized cell of this tissue to fulfill its main function which is muscle contraction, converting chemical energy into mechanical energy, generating in each contraction force and power. Romjin JA, Coyle EF, Sidossi LS, Gastaldelli A, Horowitz JF, Endert E, Wolfe RR 1993. Metabolically muscle contributes to the storage of important metabolic substrates such as amino acids and carbohydrates, for the production of heat for the maintenance of body temperature by consuming oxygen as fuel used during physical activity and exercise.

Ottenheijm, C. A., et al.,¹⁰ For the conversion of chemical energy into mechanical energy that ultimately leads to muscle contraction, multiple proteins are involved. Galpin AJ, Raue U, et al.¹¹ of which the nicotinic acetylcholine receptor (nAChR) stands out; the transmission

of electrical impulses from the nerve to the muscle is closely related to the neurotransmitter Acetylcholine (ACH). Enoka RM¹² which fulfills its fundamental role at the end of the motor plates that connect the nerve bundles with the muscle fibers becoming the first step of muscle contraction.

Rebbeck R, et al.¹³ Neuromuscular transmission ensures that the action potential is generated in the motor neuron and its corresponding communication or synapse with the muscle fiber, said synapse between the skeletal muscle fiber and the termination of the axon of the motor neuron is called neuromuscular junction or motor plate. The structure of the motor plate has characteristics similar to the synapse between neurons, it is formed by a pre-synaptic motor neuron, a synaptic cleft and a muscle fiber. In mammals, each muscle fiber contains only one neuromuscular junction and is therefore controlled by a single neuron.

The endings of the nerve axon have multiple vesicles filled with acetylcholine, which flow into the synaptic cleft, which is rich in mucopolysaccharides where the acetylcholinesterases that bind the muscle fiber are found, said fiber, presents invaginations in the synaptic zone that are called synaptic folds, in which the cholinergic and nicotinic receptors of the ACH are densely located, allowing the transmission of the electrical impulse to the fiber Approximately 107 to 108 receptors with an average function period of 10 days can be found on each motor plate.

Weisleder N, Brotto M, et al.¹⁴ The neurotransmitter ACH released by the nerve fibers at the end of the motor plate, acts inseparably with the nAChR present in the cell membrane of each skeletal muscle cell resulting after its union an increase in ionic permeability in the cell membrane, guaranteeing the transmission of the electrical impulse from the nerve cells and resulting in a depolarization of the skeletal cell membrane that leads to the release of the calcium in the sarcoplasmic reticulum and finally preparing the cell to fulfill its main function of muscle contraction.

Clementi F, Fornasari D, et al.¹⁵ The role of acetylcholine in neuromuscular transmission was demonstrated by electrophysiological methods that showed that the interaction of acetylcholine with a receptor of the postsynaptic membrane caused an increase in the conductance of the membrane to cations, producing a depolarization of the membrane of the muscle cell, which constituted, in short, the initial signal for skeletal muscle contraction. Nachmansohn D,¹⁶ suggested that the postsynaptic acetylcholine receptor could be a protein that when binding the neurotransmitter would undergo a conformational change that would cause the formation of a tunnel or channel for the passage of ions through the membrane. Subsequent results have confirmed this hypothesis.

Genetic aspects. (Factors that can condition the development of high-level athletes)

The genes determine the size of the bottle, while the contextual aspects would represent the content. In this chapter he explains how an athlete can perform and achieve success.

These factors are training, quality and quantity go hand in hand for an athlete to improve, a good structured training where he repeats and corrects his mistakes is essential, it helps him, feel comfortable and confident, have the sports commitment since this factor has to be fun and demanding, that the athlete loves the sport he is doing.

The coach is a fundamental part of sports performance, a good physical trainer plans his sessions with the aim of the practice and skills of each athlete, also influences the psychological field, because it influences the athletes feel comfortable, encouraged, at a certain age

they come to have an affective bond, trust, it is good clear but not lose the demand and respect between themselves.

The family, because the family because it depends a lot on the training and commitment to sport, they give the child to experience several sports by living them and choose where they feel most outstanding, at a certain age the parents support and demand them, and when the child is in adolescence they have a little more commitment depending on the discipline and will of the athletes and the parents already pass a background.

Competition, which influences the improvement of expertise, is an important factor for your performance, Baker J, Côté J, et al.¹⁷ They affirm that one of the most relevant aspects highlighted by athletes when it comes to helping them improve is competition. At the beginning it is important that the fun prevails that the competition, helps to train the athlete, gives positive aspects. Sánchez¹⁸ suggests that competing in top-level or higher-level leagues, as well as simultaneous competitions with players of the same and higher level, becomes a powerful element of skill development. But it can also become a factor against them when there is no balance between the participants, the competition also has to be planned, coherent, especially with the environment and circumstances of the athlete, otherwise he could leave the sports activity for not feeling at an adequate level.

Nicotinic acetylcholine-nAChR receptor

E.X. Albuquerque,¹⁹ The transmission of nerve impulses in skeletal muscle is possible due to the action of the neurotransmitter acetylcholine in the terminal branches of motor neurons, which diffuses through the narrow cleft also formed by the muscle fiber where said neurotransmitter finds the respective receptor in the membrane of the muscle fiber, the consequence of this union results in the increase of the permeability of the membrane allowing the bidirectional flow of ions sodium and potassium. The large amount of information about nicotinic acetylcholine receptors is known thanks to experiments conducted with snake venom such as the one described by Chang and Lee who have reported the action of alpha-bungarotoxin from the snake *Bungarus multicinctus* which irreversibly blocks the action of the receptor.

Miller, P. S., et al.²⁰ Acetylcholine receptors in skeletal muscle have been studied for more than a century, demonstrating that certain substances such as nicotine cause the tonic contraction of some muscles in birds, frogs and toads, this discovery allowed to give the first pins in the search and understanding of the action of a neurotransmitter or pharmacological agonist that when interacting with its receptor produces a molecular intracellular response, Because of this, the actions of muscarine and nicotine are distinguished, leading to the recognition of two families of receptors distinct in their structure and functionally unrelated.

In the seventies, the elucidation and function of nAChR was thanks to biochemical approaches and the abundance of nicotinic synapses in the end plates of skeletal muscle. The alpha-toxins of high affinity as alpha-bungarotoxin allowed to purify the protein nAChR and subsequently study the subunits of which they are conformed.

At the beginning of the 80's these subunits were cloned and began the era of molecular analysis and knowledge of the molecular architecture of nAChR, each of the five subunits that make up the nAChR, cross the lipid membrane forming a channel filled with water, each subunit consists of 4 transmembrane segments form the entire ion channel, the N-Terminal domain is extracellular of each subunit contains a loop, formed by two cysteine residues separated

by 13 amino acids, this loop is involved in the transduction of signals produced by the agonist and that leads to the opening of the channel, the main site of binding with the agonist is the N-terminal domain of the alpha subunits near the adjacent cysteine residues 192 and 193.

E.X. Albuquerque, et al.,¹⁹ Upon binding with the agonist, nAChRs undergo an allosteric transition from closed and resting conformation to an open state that allows an influx of Na⁺, and to a lesser extent Ca²⁺, and a flow of K⁺ under normal physiological conditions. In the closed state, the ion channel is occluded by a "hydrophobic belt" that constitutes a barrier to ion penetration. Agonist binding in the extracellular domain promotes a conformational change that results in rotational motion of the M2 helices lining the pore. The torsion of the belt widens the pore by ~3Å, sufficient for ionic permeation. In the final plate of the muscle, the resulting depolarization causes muscle contraction. Despite the presence of agonist, the nAChR channel closes in a matter of seconds to minutes, to enter a desensitized state. In this condition, nAChR is refractory to activation.

Miller PS, et al.,²⁰ Throughout history, scientific advances in the field of biochemistry and the combination of modern pharmacological techniques and molecular biology have allowed the precise identification of the characteristics of nAChRs, it is known that nAChR proteins belonging to the family of ion channels, which are linked by pentameric ligands, Thanks to advances in molecular biology, through the use of the technique of molecular cloning has been identified that nAChR, is composed of five homologous subunits, with a high degree of similarity in its primary, secondary and tertiary structure, in turn each subunit is made up of five segments composed as follows: an extracellular N-terminal end, three hydrophobic intermembrane domains linked together by small hydrophilic segments, which lead to a broad cytoplasmic domain, said connects with the fourth and last intermembrane segment ending at the extracellular C-terminal end that combine with each other to form monomeric or homomeric receptors, which play with each other with high and low with respect to calcium permeability and affinity with acetylcholine (ACh), thus varying their function with respect to the tissue in which they are found.

Abrams P, et al.²¹ ACh modulates a number of physiological processes in the central and peripheral nervous system, such as in the central nervous system, ACh regulates motor function, sensory perception, cognitive processing, arousal, sleep/wake cycles and nociception, while, in the peripheral nervous system, it regulates heart rate, motility of the gastrointestinal tract and smooth muscle activity.

Harvey AL, Dryden WF, et al.²² nAChR, members of the ligand-linked ion channel superfamily including GABAA and GABAC receptors, are divided into muscular nAChRs at the skeletal neuromuscular junction and neuronal nAChRs, which mediate rapid synaptic neurotransmission throughout the nervous system is a transmembrane protein with four transmembrane domains, of which the P1 protein domain is extracellular and is responsible for binding with ACh in order to increase the opening of ion channels that increase the depolarization of the skeletal cell membrane, on the other hand, between the protein domains P3 and P4 differs the complete molecule since it is the longest part of the protein that is intracytoplasmic and which helps to magnify the nerve impulse.

Polymorphisms associated with the nicotinic acetylcholine-nAChR receptor

With the completion of the human genome project in 1990, it was possible to decipher the complete sequence of the human genome, and it was also possible to evidence the presence of variations or specific changes in said DNA sequence that supported the genotypic

and phenotypic variabilities that characterize each individual, as well as the resistance or individual susceptibility to different diseases, this variability is mainly based on the presence of single nucleotide polymorphisms (SNP's-Single nucleotide polymorphs); and to a lesser extent to insertions, deletions, repeated sequences and/or chromosomal rearrangements, because the human genome is not a passive structure; on the contrary, DNA is exposed to a number of alterations that can result in constant modification that explains the variability between each individual.

These changes in DNA are called mutations, which can be caused by errors in the mechanisms of replication and repair of DNA, as well as by environmental factors, for this reason, mutations can have deleterious effects and cause diseases or give rise to what is known as polymorphisms, which provide allelic variation between individuals and diversity of the same species. A polymorphism is considered as such when the frequency of one of its alleles in the population is greater than 1%. There are several types of polymorphisms (insertions, deletions, changes in the number of repeated sequences), but the most frequent are SNPs.

The different forms of polymorphisms (called "alleles") are more frequent than mutations, that is, at a frequency greater than 1%. The vast majority of SNPs have two alleles which are represented by one base substitution for another. In populations, these types of alleles are classified into main or "wild" allele and rare or mutant allele, classification based on the frequency observed in the populations.

Currently, in the public database of PNS, (dbSNP's for its acronym in English) more than 9 million variants in the DNA sequence have been cataloged. It is described that SNPs occur one every 200 base

pairs in the human genome. Based on this, it would be expected that there were approximately 6 million SNPs in the human genome, many of which have already been described in the dbSNP. SNPs can be present in coding regions and cause a change in an amino acid; this type of SNP's are known as "non-synonymous". Since this type of SNP directly affects the function of the protein, many researchers have focused their attention on genetic association studies in this type of variations.

Likewise, there are functional variations that can produce some disease or susceptibility to it, they can be located in the promoter region of the gene, influencing the transcriptional activity of the gene (modulating the binding of transcription factors), in introns (modulating the stability of the protein) in sites of "splicing" (sites where the elimination of introns and binding of exons occurs) or in intragenic regions.²³⁻⁶²

Another type of SNP's are the so-called "synonyms" (or silent) which do not alter the conformation of the gene; However, it has been described that some of these polymorphisms may have functional consequences due to some type of mechanism still unknown. According to their location in the genome, SNPs are classified into: iSNP, if they are located in intronic regions; cSNP, in coding regions (exons); rSNP, in regulatory regions, and gSNP, located in intergenomic regions. cSNPs can be represented by synonymous (sSNP) or non-synonymous (nsSNP) SNPs. According to the data obtained in the NCBI and filtered by SNP and by articles cited and published in PubMed, 41 different polymorphisms were found for the alpha 4 subunit of the nAChR gene in Homo sapiens, which are listed in Table 1.

Table 1 Relationship of polymorphisms associated with the nAChR gene Alpha 4 subunit

Gene	Combinación de nucleótidos	Posición en el cromosoma	Referencia de la nucleótida	Función/Asociación	Referencia bibliográfica
CHR NA4	AGAGTGGC GAG TGGGTCA TCGTGG C/T GGC GTGGGACCTTACAC ACC AGGA	204338772	m1044383	Variaciones in genes coding for acetylcholine receptor (nAChR) subunits affect cognitive processes and may contribute to the genetic etiology of neurodegenerative disorders.	Mohandeev et al., 2016
CHR NA4	ACAACAC CAG GAAATACCAAGTCTGTC C/T GGC GAG ATCTACCC GAGCATC ACC T	204338733	m1044384	Missense single nucleotide polymorphisms (nAChRs) are important drug targets for the development of drugs for tobacco and drug dependence.	Mohandeev et al., 2016
CHR NA4	CGGTCAAGC CCGCAGCAGCAAGGC A/G CCGCCCC GACCTGTGCC CTGTGGC	204338782	m1044387	Association between the susceptibility to dependence of tobacco and other drugs with the gene (nAChR).	Yang J et al., 2016
CHR NA4	CGAGCCGCAGCCAGAGCCCTGACCC A/G CTCCCTCAGCTGCTGTGTGCC CCG	204338802	m222888	Association between genetic variation response and ANKCT and PND2 genes related to verbal language.	Huber JD et al., 2013
CHR NA4	TGACCCGCCCTTACCCTCTCTCTG C/T GTCC CCGTGGATGTG CCGGCTG AGC	2043388184	m222890	Variation of genes (nAChR) is more influence on	Swan GE et al., 2012
CHR NA4	GAGCGATGGACAGCCGCAAGCC A/G AGGACCCAGCTCC GAGATGTG GCGCA	204338887	m2273804	Effects of tobacco use gene expression differences (nAChR).	Hil NR et al., 2011
CHR NA4	GGTTCAGAGCCGC CCAACACAGCC C/T GGC GCGGG AC TACCCAGAAATCTGT	204338938	m282700	Interaction of genes and proteins with nicotine dependence susceptibility.	Higg J et al., 2010
CHR NA4	CACCGACC TCGCGC GCTTACATGC C/T GGC GCGGG TCCCGG TCCCGC CCGCTT	2043381188	m4080387	Common haplotypes of the (nAChR) α4 subunit gene is associated with vulnerability to nicotine addiction in men.	Feng Y et al., 2004
CHR NA4	TGAGAGCCGCC AACACAGCCATGG A/G CGGG AC TACCCAGAAATCTGTCTC	204338942	m2824284	Association of nicotine and gene variants with nicotine and drug dependence (nAChR).	Wenot J et al., 2010
CHR NA4	CAGAAAGATTCAGAAAGTAGAC A/G CTCCGAGCCAGAGGCTGTGCCA	204338212	m788203	Alkylated risk factor associated with single nucleotide polymorphisms of the gene (nAChR).	Rao SE et al., 2008
CHR NA4	GGGTCCAGACC CTAAGCCAGATGG C/T GTCC GCGGTGGATGCCAGTACTACT	204338213	m788204	Association between genetic variations of the gene (nAChR) and symptoms of nicotine after the first contact in the cigarette.	Pedemonte M et al., 2014
CHR NA4	GCACATGGCTGGTCC AACGACGAC A/G CTGCC CTCTGAA TGGCTGG TCCA	204338280	m2083107	Alkylated risk factor associated with single nucleotide polymorphisms of the gene (nAChR).	Rao SE et al., 2008
CHR NA4	CTCTCCAGCCAGGACAGATGGAG A/G CTCC TCC TCC TACCCCTCATGGCGCC	204338204	m2236186	(nAChR) as a gene associated with the high risk of nicotine dependence.	Zuo L et al., 2014
CHR NA4	CTGC CCAAGG GCGCTCTCTCCAG C/T GTCCAGAGGCGGG CAAAGAC GTCC	204338887	m2273805	Variation in alternative splicing when associated with the risk of tobacco and other drug dependence.	Hancock DE et al., 2018
CHR NA4	TGACCCCTGTGTCTCTTCTTCC C/T GGC GAGCTTCTCATCTACAGCCCT	2043388470	m2273802	C gene relationship between single nucleotide polymorphisms of the gene (nAChR) and addiction from tobacco use.	Squall T et al., 2012
CHR NA4	CTAAGGACAGGTGTG CCGGCATG A/G CGAG CCGCTCTTCCGACCTCCCTT	2043386708	m2273804	(nAChR) and cardiovascular risk and alcoholism severity.	Zhu Y et al., 2014
CHR NA4	CGAGCGGACCTCAGGACAG A/G CTCCGAGCTCC GACCTAC CAG CAG C	2043388826	m2273806	Molecular genetic influencing nicotine abuse and hyperactivity disorder.	Passani EV et al., 2010
CHR NA4	AAGC TGAT GAGC TGGCTCTGGCC A/G CGCCCTTGGAGG TGTCC TGG TCCGAG	204334748	m3787137	Genetic markers implicated in modulating addiction phenotype.	Phygen-Gilley CC et al., 2018
CHR NA4	TGCTCTGATTTTATAGCAATC C/T GGGTCTCTCTGATGGTGTAAACTGAG	204334782	m3787138	genetic gene variants (nAChR) and influence on smoking susceptibility.	Sevens VL et al., 2008
CHR NA4	TAGGACATGACAGCCAGCCCTTCC C/T GGCAGCAGG TGGCC TCGGG TGGG	2043387788	m3787140	susceptibility to nicotine in different Asian populations associated with genetic gene variations (nAChR).	Shi J et al., 2014
CHR NA4	TGCCAGCCGCCGCC CTGCCAC A/G CTCCGAG CCGGTCTTCCAGAAC	2043388042	m3787141	Molecular genetic influencing nicotine abuse and hyperactivity disorder.	Passani EV et al., 2010
CHR NA4	CGTCCTAAGCCAGGAGCTT CCAACC A/G CGGTCAAGAAATG AGTTT TGTGG	2043343128	m2824886	Pharmacokinetics in individuals with dual psychiatric disorders.	Lisak J et al., 2011
CHR NA4	CAGATGGATTCAGCAGCAATG C/G CGTGG TGC ATATATATCTGTACTCC	2043370787	m2808446	Identified genetic loci associated with addiction from tobacco use.	Lee WJ et al., 2012
CHR NA4	AGGACAG TCCAGAG GAGCCACT A/G CGCCAGCTCC AGGACACTGAGCC TG	2043381148	m1010918	Pharmacokinetics of drug addiction.	King DP et al., 2012
CHR NA4	CCCTCC GATTTCTCC ACCCGGAG C/T GGCCTCCAGAAAC TCTGTCTCCAA	2043380798	m1011770	genetic gene variants (nAChR) and influence on smoking susceptibility.	Sevens VL et al., 2008
CHR NA4	TGAGTGGTGTG TGGCCCTCTCC C/T GTCCAGAGTGTGCTCCGAGCCAGAC CG	2043382404	m1011776	Candidate genes in the study of alcoholism in women.	Agrawal A et al., 2011
CHR NA4	CGTCCAGCTCTGATGCCAGCC C/T GGCAGAGTGTGCTCCGAGAGATCTAGCT	2043383870	m1011784	Genetic studies of the gene (nAChR) α4 subunit in tobacco use.	Ho L et al., 2014
CHR NA4	GGATTCAGTGG GGTGGCTGTGTGG A/G CGGACCACTCCGTCAGCTTTTCATC	2043388441	m2082888	Pharmacokinetics of drug addiction.	King DP et al., 2012
CHR NA4	CTTCCAGGGC GACCTCAGTACAG A/G CTCCAGATGGCC ACCCCGACCTTAC	204338822	m2080384	Variation of genes (nAChR) is more influence on (nAChR) and cardiovascular risk and alcoholism severity.	Swan GE et al., 2012
CHR NA4	GGACTCTCTGTGCCCTGCCAGCC C/T GGCCTCCGAGTACC TCCCGAGAGA	2043381884	m1122428	Genetic studies of the gene (nAChR) α4 subunit in tobacco use.	Zhu Y et al., 2014
CHR NA4	CTCCGG GAG TCCCGCTGTCTCT C/T GTCTGGGATCAGAGGAGCTCCGG	2043388804	m2823278	Genetic studies of the gene (nAChR) α4 subunit in tobacco use.	Ho L et al., 2014
CHR NA4	GGAGACAGATGCCAGCCCGCTCC A/G CGAGTGTGCTCCGAGTGTCTCTG	2043388783	m2823280	Genetic studies of the gene (nAChR) α4 subunit in tobacco use.	Ho L et al., 2014
CHR NA4	CAGCGCCCTTCCAGACAGCCAGCC C/T GGCCTCCAGCC TCCCGATGTCACCA	2043388802	m2220882	Genetic studies of the gene (nAChR) α4 subunit in tobacco use.	Ho L et al., 2014

Discussion and analysis

Strength is a fundamental quality for sports performance, it is always involved in many ways that is, several types of strength related to the objective of sport and sportsman, so that the skeletal muscle can perform its function, contraction and relaxation (eccentric), this is due to the signal of the neurotransmitter acetylcholine to the terminal branches of motor neurons, where it produces the activation of the nicotinic receptor in the membrane of the muscle fiber, thus producing the movement of the skeletal muscle.

Through the search carried out in our study we found 41 polymorphisms associated with the Alpha subunit of this gene which will benefit us to the sports field to understand the physiological and biochemical bases of muscle contraction directly associated with strength to identify which athlete will have a good performance or what is its limit for this quality and have the expected achievements.

This study is specified in the maximum strength, where there are the types of concentric contraction, eccentric and there is greater muscle contraction releasing more ATP and calcium producing the hydrolyzation of ATP converting it into ADP that is, the energy necessary for the action of a muscle contraction.

And the type of mutation that is most frequently observed are transitions (change of one purine (Pu) for another purine, or change of a pyrimidine (Pi) for another pyrimide). Since they apparently cause less DNA disorganization and therefore are less recognized as errors and consequently carry a lower probability of being corrected. But generate new alleles, but not all of them cause replacements in the amino acid sequence.

Conclusion

The variation in sports performance is determined by a complex system of interactions of various components, sociocultural, psychological and physiological, which in turn are controlled by both environmental and genetic elements, the study of genetic polymorphisms allows us to understand the mechanisms to which athletes are susceptible and that influence sports performance, With this research it was possible to know some polymorphisms of the nAChR gene reported in international databases, although they have not been reported in skeletal muscle, according to the function played by the protein encoded by said gene it is possible to associate its function and active presence in the contraction processes that allow the realization of sports gestures associated with strength.

As a result of this systematic review, it is important to know and understand that nAChR is involved in the activation of skeletal muscle, allowing the depolarization of the muscle fiber membrane initiating the action on the neuromotor plate, The low report of polymorphisms of this gene in the muscle fiber, could be due to the few investigations in this field; According to the mechanism of action reported for this gene, it is possible to conclude that there is an association between the polymorphisms of the nAChR gene and sports performance in weightlifting athletes in Valle del Cauca, which can be potentiated in order to achieve high achievements that respond to the objectives set by the athlete, the coach and the governmental entres associated with this sports branch.

Recommendations

It is proposed to carry out the development of future field research, since it will contribute to reduce the knowledge gap caused by the low report of polymorphisms of the nAChR gene in the muscle fiber,

the knowledge of the polymorphisms present in the gene expressed in the muscle fiber, opens the door to the development of new training tools based on new technologies, allowing to potentiate the innate characteristics of the athletes of Weightlifting of Valle del Cauca, in order to achieve high achievements that respond to the objectives set, in addition to laying the foundations of control and molecular monitoring of sports training.

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Conflicts of interest

Author declare there are no conflicts of interest towards the article

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