

Request for Reconsideration after Final Action

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SERIAL NUMBER	78970985
LAW OFFICE ASSIGNED	LAW OFFICE 106
MARK SECTION (no change)	
ARGUMENT(S)	
<p>The Examining Attorney has refused registration of the mark NNR THERAPEUTICS (“Applicant’s Mark”) for use with “pharmaceutical preparations for the treatment of central nervous system diseases and disorders, inflammatory diseases and disorders, and addictions” (“Applicant’s Goods”) on the grounds that the mark is merely descriptive. Applicant has disclaimed the word “THERAPEUTICS” and Applicant does not dispute that the letters “NNR” in Applicant’s Mark stand for “neuronal nicotinic receptors.” Nevertheless, Applicant respectfully submits that its mark is not descriptive because the initials “NNR” are not descriptive of Applicant’s Goods.</p> <p>A. Descriptiveness Standard for Acronyms</p> <p>The test for determining whether an acronym or initialism is merely descriptive is whether or not the initials “have become so generally understood as representing descriptive words as to be accepted as <i>substantially synonymous therewith</i>.” <u>Modern Optics, Inc. v. The Univers Lens Co.</u>, 110 USPQ 293, 295 (C.C.P.A. 1956) (emphasis added) (holding that the letters CV were not descriptive of ophthalmic lens blanks and eyeglass lenses because the letters were not accepted as substantially similar with the descriptive words “continuous vision”). The <u>Modern Optics</u> rule has been adopted and applied by the TTAB and other jurisdictions. See, e.g., <u>Welding Services Inc. v. Forman</u>, 85 USPQ2d 1233 (11th Cir. 2007); <u>Anheuser-Busch, Inc. v. The Stroh Brewery Co.</u>, 224 USPQ 657 (8th Cir. 1984); <u>In re Finisar Corp.</u>, 78 USPQ2d 1618 (TTAB 2006); <u>Racine Industries Inc. v. Bane-Clene Corp.</u>, 35 USPQ2d 1832 (TTAB 1994); <u>In re Harco Corporation</u>, 220 USPQ 1075 (TTAB 1984); <u>In re Nissan Jidosha Kabushiki Kaisha, T/A/ Nissan Motor Co., Ltd.</u> (TTAB May 24, 2001), http://www.uspto.gov/web/offices/com/sol/foia/ttab/2eissues/2001/75531325.pdf (non-precedential); <u>Avtex Fibers Inc. v. Gentex Corporation</u>, 223 USPQ 625 (TTAB 1984).</p> <p>In several instances the Trademark Office and the Board have found that acronyms were not descriptive, despite the descriptive or even generic nature of the words for which the initials stood. See <u>In re Council on Certification of Nurse Anesthetists</u>, 85 USPQ2d 1403 (TTAB 2007) (holding that CRNA was not generic even though term “certified registered nurse anesthetist” is generic); <u>In re Nissan</u> (non-precedential) (holding that the letters “SUT” were not descriptive of the applicant’s motor vehicles because the letters were not generally understood as substantially synonymous with the descriptive words “sport utility truck”); <u>Racine Industries</u>, 35 USPQ2d 1832 (holding that the term “PCA” was not descriptive as it is not understood to stand for “Professional Cleaner’s Association”); <u>In re Harco Corporation</u>, 220 USPQ 1075 (holding that CPL was not descriptive of</p>	

"computerized potential log"). Applicant notes that Coley Pharmaceutical's Application Ser. No. 77/747,923, for the mark TLR THERAPEUTICS for use with pharmaceuticals, was allowed for registration on the Principal Register. As the internet abstracts and print-outs from Coley Pharmaceutical's web site illustrate (Exhibit 1), the letters "TLR" stand for "toll-like receptor" and Coley Pharmaceutical's TLR THERAPEUTICS act on these receptors. By allowing this mark to register, the Trademark Office determined that the letters "TLR," although they stand for the descriptive words "toll-like receptors," are not generally understood as substantially synonymous with the words "toll-like receptors." Similarly, while the words "neuronal nicotinic receptors" may be descriptive of a function of Applicant's Goods, the letters "NNR" are not interpreted as substantially synonymous with these words and thus the letters "NNR" are not descriptive of Applicant's Goods.

B. Evidence of Meaning of the Letters "NNR"

The Examining Attorney has introduced acronym definitions from Acronym Finder in support of the contention that "NNR" is a common abbreviation for "neuronal nicotinic receptors." [i] Acronym Finder is a web site operated by a couple from their home. See Exhibit 3. Anyone can submit an acronym to be included in the dictionary and the Acronym Finder's terms of use caution users to "use information from this site at your own risk." See Exhibit 4. While the web site operators confirm the meaning of acronyms submitted by users, their research appears to be based on personal knowledge and other web sites they deem credible. See Exhibit 3. In considering similar evidence regarding the descriptiveness of the letters "SUT" in In re Nissan, the TTAB held that "this on-line Acronym Finder is not the type of material which is reliable enough for us to take judicial notice. Accordingly, we have accorded no weight to this Acronym Finder." Because the Acronym Finder database is composed of acronyms submitted by anyone, and these acronyms appear to be validated primarily by the internet research conducted by two individuals, Applicant submits that these definitions are of little value in determining whether or not "NNR" is descriptive. In In re Nissan, the TTAB considered evidence from several recent dictionaries and acronym dictionaries showing that the letters "SUT" did not appear in any of these references. Similarly, Applicant attaches as Exhibit 5 excerpts from fifteen recent dictionaries and acronym dictionaries showing the pages where the letter "NNR" would appear in those references. Because the letters "NNR" do not appear in any of these dictionaries, Applicant submits that the letters are not generally understood to stand for the words "neuronal nicotinic receptors."

C. Evidence of Use of the Letters "NNR"

In addition to excerpts from dictionaries, the Examining Attorney has introduced ten excerpts from press releases, internet sites, articles and congressional testimony to support the contention that "NNR" is descriptive. Most of these excerpts refer to either Applicant's product and research, or product development and research that Applicant is conducting with other companies. Only one of the excerpts (from neurosearch.com) refers to the use of "NNR" by a party not affiliated with Applicant. In similar cases involving acronyms, the Board has looked at evidence of third party or descriptive use of the acronym in question and has determined that the evidence was insufficient to support a finding that the acronym was descriptive. See Modern Optics, 110 USPQ at 294 ("[w]hile the record shows that there are individuals to whom the letters 'CV' constitute a generic designation of trifocal lenses, we are of the opinion it has not been established that such is the rule rather than the exception."); In re Harco Corp. 220 USPQ at 1077 ("[e]ven granting that in some of these materials 'CPL' is used as an equivalent of the words 'computerized potential log,' the designation 'CPL' is not uniformly so used. Nor is there any other evidence of record that the letters 'CPL' have a generally understood meaning in the field.") Thus, even some evidence of use of the letters "NNR" by third parties in a descriptive sense is not dispositive of the question of whether the letters are generally understood to be substantially synonymous with the underlying terms.

Furthermore, in every one of the introduced excerpts, the author explains that "NNR" means

“neuronal nicotinic receptor” before using the acronym. Thus, the authors of these articles apparently assume that their audience does not know what the letters “NNR” stand for, and conclude that these initials must be explained. If the letters “NNR” were truly descriptive, like the letters “SUV” or “ATV,” then an author would not have to make such an explanation. The fact that the meaning of the letters “NNR” must be explained is strong evidence that the letters are not descriptive under the Modern Optics test.

D. Lack of Competitive Need for the “NNR” Acronym

As noted in the office action, one of the reasons for refusing registration of descriptive marks is the policy of allowing competitors and other businesses to use common descriptive language in describing competing goods and services. In re Abcor Development Corp., 200 USPQ 215 (C.C.P.A. 1978). In this case there are plenty of alternatives that may be used, and that are used, to describe neuronal nicotinic receptors and related products. Applicant attaches as Exhibit 6 abstracts from over twenty articles from PubMed which refer to “neuronal nicotinic receptors,” “neuronal nicotinic acetylcholine receptors” “nicotinic receptors,” “nACHRs,” “neuronal nicotinic ACh receptor,” or “nAchR.”[ii] All of these designations refer to the same biological component, but different terms and abbreviations are used in the scientific community. None of these abstracts use the letters “NNR.” These abstracts illustrate that the letters “NNR” are not generally used to describe neuronal nicotinic receptors and that there are several alternative terms and abbreviations that are used to identify these receptors.

E. Conclusion

In summary, the evidence of record shows that the initials “NNR” are not generally understood to be “substantially synonymous” with “neuronal nicotinic receptors.” Thus, the NNR THERAPEUTICS mark, particularly when considered as a whole, is not a descriptive mark and is entitled to registration on the Principal Register. Finally, as the Board has noted on several occasions, the benefit of the doubt in cases involving a determination of whether a mark is descriptive or suggestive should be given to the applicant. In re Council on Certification of Nurse Anesthetists, 85 USPQ2d at 1415 (“[w]e readily admit that we have doubt as to the character of CRNA, but we believe such doubt should be resolved in applicant’s favor”). Accordingly, Applicant respectfully submits that the application is now in condition for passage to publication, which action is respectfully requested.

[i] The Examining Attorney introduced definitions from two web sites. The first search was conducted through OneLook Dictionary’s web site, but the search results came from Acronym Finder, as evidenced by the URL. The second search was conducted through the Free Dictionary by Farlex, which also uses Acronym Finder. See Exhibit 2.
 [ii] As noted in the description of neuronal nicotinic receptors in the excerpt from targacept.com introduced in the Final Office Action, acetylcholine binds to neuronal nicotinic receptors, and the terms “neuronal nicotinic receptors” and “neuronal nicotinic acetylcholine receptors” are used interchangeably in the literature, including in several of the attached abstracts.

EVIDENCE SECTION

EVIDENCE FILE NAME(S)

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PTO Form 1960 (Rev 9/2007)

OMB No. xxxx-xxxx (Exp. x/xxxx)

Request for Reconsideration after Final Action

To the Commissioner for Trademarks:

Application serial no. **78970985** has been amended as follows:

ARGUMENT(S)

In response to the substantive refusal(s), please note the following:

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B. Evidence of Meaning of the Letters “NNR”

The Examining Attorney has introduced acronym definitions from Acronym Finder in support of the contention that “NNR” is a common abbreviation for “neuronal nicotinic receptors.”[i]

Acronym Finder is a web site operated by a couple from their home. See Exhibit 3. Anyone can submit an acronym to be included in the dictionary and the Acronym Finder’s terms of use caution users to “use information from this site at your own risk.” See Exhibit 4. While the web site operators confirm the meaning of acronyms submitted by users, their research appears to be based on personal knowledge and other web sites they deem credible. See Exhibit 3. In considering similar evidence regarding the descriptiveness of the letters “SUT” in In re Nissan, the TTAB held that “this on-line Acronym Finder is not the type of material which is reliable enough for us to take judicial notice. Accordingly, we have accorded no weight to this Acronym Finder.” Because the Acronym Finder database is composed of acronyms submitted by anyone, and these acronyms appear to be validated

primarily by the internet research conducted by two individuals, Applicant submits that these definitions are of little value in determining whether or not "NNR" is descriptive. In In re Nissan, the TTAB considered evidence from several recent dictionaries and acronym dictionaries showing that the letters "SUT" did not appear in any of these references. Similarly, Applicant attaches as Exhibit 5 excerpts from fifteen recent dictionaries and acronym dictionaries showing the pages where the letter "NNR" would appear in those references. Because the letters "NNR" do not appear in any of these dictionaries, Applicant submits that the letters are not generally understood to stand for the words "neuronal nicotinic receptors."

C. Evidence of Use of the Letters "NNR"

In addition to excerpts from dictionaries, the Examining Attorney has introduced ten excerpts from press releases, internet sites, articles and congressional testimony to support the contention that "NNR" is descriptive. Most of these excerpts refer to either Applicant's product and research, or product development and research that Applicant is conducting with other companies. Only one of the excerpts (from neurosearch.com) refers to the use of "NNR" by a party not affiliated with Applicant. In similar cases involving acronyms, the Board has looked at evidence of third party or descriptive use of the acronym in question and has determined that the evidence was insufficient to support a finding that the acronym was descriptive. See Modern Optics, 110 USPQ at 294 ("[w]hile the record shows that there are individuals to whom the letters 'CV' constitute a generic designation of trifocal lenses, we are of the opinion it has not been established that such is the rule rather than the exception."); In re Harco Corp. 220 USPQ at 1077 ("[e]ven granting that in some of these materials 'CPL' is used as an equivalent of the words 'computerized potential log,' the designation 'CPL' is not uniformly so used. Nor is there any other evidence of record that the letters 'CPL' have a generally understood meaning in the field.") Thus, even some evidence of use of the letters "NNR" by third parties in a descriptive sense is not dispositive of the question of whether the letters are generally understood to be substantially synonymous with the underlying terms.

Furthermore, in every one of the introduced excerpts, the author explains that "NNR" means "neuronal nicotinic receptor" before using the acronym. Thus, the authors of these articles apparently assume that their audience does not know what the letters "NNR" stand for, and conclude that these initials must be explained. If the letters "NNR" were truly descriptive, like the letters "SUV" or "ATV," then an author would not have to make such an explanation. The fact that the meaning of the letters "NNR" must be explained is strong evidence that the letters are not descriptive under the Modern Optics test.

D. Lack of Competitive Need for the "NNR" Acronym

As noted in the office action, one of the reasons for refusing registration of descriptive marks is the policy of allowing competitors and other businesses to use common descriptive language in describing competing goods and services. In re Abcor Development Corp., 200 USPQ 215 (C.C.P.A. 1978). In this case there are plenty of alternatives that may be used, and that are used, to describe neuronal nicotinic receptors and related products. Applicant attaches as Exhibit 6 abstracts from over twenty articles from PubMed which refer to "neuronal nicotinic receptors," "neuronal nicotinic acetylcholine receptors" "nicotinic receptors," "nACHRs," "neuronal nicotinic ACh receptor," or "nAchR." [ii] All of these designations refer to the same biological component, but different terms and abbreviations are used in the scientific community. None of these abstracts use the letters "NNR." These abstracts illustrate that the letters "NNR" are not generally used to describe neuronal nicotinic receptors and that there are several alternative terms and abbreviations that are used to identify these receptors.

E. Conclusion

In summary, the evidence of record shows that the initials "NNR" are not generally understood to be "substantially synonymous" with "neuronal nicotinic receptors." Thus, the NNR THERAPEUTICS mark, particularly when considered as a whole, is not a descriptive mark and is entitled to registration on the Principal Register. Finally, as the Board has noted on several occasions,

the benefit of the doubt in cases involving a determination of whether a mark is descriptive or suggestive should be given to the applicant. In re Council on Certification of Nurse Anesthetists, 85 USPQ2d at 1415 (“[w]e readily admit that we have doubt as to the character of CRNA, but we believe such doubt should be resolved in applicant’s favor”). Accordingly, Applicant respectively submits that the application is now in condition for passage to publication, which action is respectfully requested.

[i] The Examining Attorney introduced definitions from two web sites. The first search was conducted through OneLook Dictionary’s web site, but the search results came from Acronym Finder, as evidenced by the URL. The second search was conducted through the Free Dictionary by Farlex, which also uses Acronym Finder. See Exhibit 2.

[ii] As noted in the description of neuronal nicotinic receptors in the excerpt from targacept.com introduced in the Final Office Action, acetylcholine binds to neuronal nicotinic receptors, and the terms “neuronal nicotinic receptors” and “neuronal nicotinic acetylcholine receptors” are used interchangeably in the literature, including in several of the attached abstracts.

EVIDENCE

Evidence in the nature of Exhibits as mentioned in argument. has been attached.

Original PDF file:

http://tgate/PDF/RFR/2008/03/13/20080313164633569387-78970985-003_001/evi_66193220126-161559636_.NNR_-_Exhibits_1-4.pdf

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SIGNATURE(S)

Request for Reconsideration Signature

Signature: /Randy Springer/ Date: 03/13/2008

Signatory's Name: Randel S. Springer

Signatory's Position: Attorney of Record

The signatory has confirmed that he/she is an attorney who is a member in good standing of the bar of the highest court of a U.S. state, which includes the District of Columbia, Puerto Rico, and other federal territories and possessions; and he/she is currently the applicant's attorney or an associate thereof; and to the best of his/her knowledge, if prior to his/her appointment another U.S. attorney or a Canadian attorney/agent not currently associated with his/her company/firm previously represented the applicant in this matter: (1) the applicant has filed or is concurrently filing a signed revocation of or substitute power of attorney with the USPTO; (2) the USPTO has granted the request of the prior representative to withdraw; (3) the applicant has filed a power of attorney appointing him/her in this matter; or (4) the applicant's appointed U.S. attorney or Canadian attorney/agent has filed a power of attorney appointing him/her as an associate attorney in this matter.

The applicant is filing a Notice of Appeal in conjunction with this Request for Reconsideration.

Serial Number: 78970985

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Abstract;The role of toll-like receptor (TLR) is outlined. "Nonself" in natural immunity system is the molecules such as lipid, protein ; nucleic acid as a constituent of the cell wall of pathogen. TLR is a molecular family which activates the natural immunity system by recognizing them specifically. Simultaneously, cytokine production is accelerated, and the activation of the acquired immunity system is induced. That is to say, TLR plays a role of crosslink between the natural immunity and acquired immunity system. TLR1 and TLR2 and recognize the bacteria-derived lipopeptide, and TLR2 and TLR6 associate and recognize mycoplasma-derived lipopeptide. TLR recognizes flagellum, and TLR4 recognizes bacteria and virus-derived lipopolysaccharide. The single strand RNA incorporated in a viral infection is recognized by TLR7 and TLR8, the double strand RNA by TLR3, and the non-methylated CpG DNA by TLR9. TLR1 TLR6, TLR5 and TLR4 stimulate the production of IL-12, IL-6, and TNF-.ALPHA.. TLR4 also stimulates the production of INF-.BETA. TLR7, TLR8 and TLR9 stimulate the production of IFN-.ALPHA. and IFN-.BETA..

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Research article

Evolution of the chicken Toll-like receptor gene family: a story of gene gain and gene loss

Nicholas D Temperley, Sofia Berlin, Ian R Paton, Darren K Griffin and David W Burt

BMC Genomics 2008, 9:62 doi:10.1186/1471-2164-9-62

Published: 1 February 2008

Abstract (provisional)

Background

Toll-like receptors (TLRs) perform a vital role in disease resistance through their recognition of pathogen associated molecular patterns (PAMPs). Recent advances in genomics allow comparison of TLR genes within and between many species. This study takes advantage of the recently sequenced chicken genome to determine the complete chicken TLR repertoire and place it in context of vertebrate genomic evolution.

Results

The chicken TLR repertoire consists of ten genes. Phylogenetic analyses show that six of these genes have orthologs in mammals and fish, while one is only shared by fish and three appear to be unique to birds. Furthermore the phylogeny shows that TLR1-like genes arose independently in fish, birds and mammals from an ancestral gene also shared by TLR6 and TLR10. All other TLRs were already present prior to the divergence of major vertebrate lineages 550 Mya (million years ago) and have since been lost in certain lineages. Phylogenetic analysis shows the absence of TLRs 8 and 9 in chicken to be the result of gene loss. The notable exception to the tendency of gene loss in TLR evolution is found in chicken TLRs 1 and 2, each of which underwent gene duplication about 147 and 65 Mya, respectively.

Conclusions

Comparative phylogenetic analysis of vertebrate TLR genes provides insight into their patterns and processes of gene evolution, with examples of both gene gain and gene loss. In addition, these comparisons clarify the nomenclature of TLR genes in vertebrates.

The complete article is available as a [provisional PDF](#). The fully

BMC Genomics
Volume 9

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The Journal of Translational Immunology



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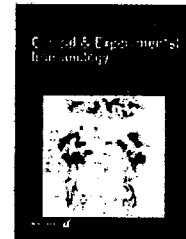
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Clinical & Experimental Immunology

Volume 151 Issue 1 Page 34-41, January 2008

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Clinical & Experimental Immunology 151 (1), 34-41.
doi:10.1111/j.1365-2249.2007.03531.x



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Abstract

ORIGINAL ARTICLE

Increased expression of Toll-like receptor (TLR) 2 and TLR4 in the colonic mucosa of children with inflammatory bowel disease

B. Szebeni,^{*§} G. Veres,^{*§} A. Dezsöfi,^{*K} Rusai,^{*Á} Vannay,[†] M. Mraz,[‡] E. Majorova[‡] and A. Arató^{*}

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[§]Beáta Szebeni and Gábor Veres contributed equally to this work and are both first authors.

Summary

Inflammatory bowel disease (IBD) may result from exaggerated stimulation of the mucosal immune system by luminal bacterial flora. Bacterial products are recognized by pattern recognition receptors such as Toll-like receptors (TLRs), which are key regulators of the innate immune system. Therefore, the expression of TLR2, TLR3 and TLR4 in colonic biopsy samples

taken from children with active IBD were studied and compared to controls. Colonic biopsy samples were collected from macroscopically inflamed and non-inflamed regions of the mucosa of 12 children with freshly diagnosed IBD (fdIBD) and 23 children with relapsed IBD (rIBD). Specimens were also obtained from eight controls. TLR2, TLR3 and TLR4 mRNA expression and protein levels were determined by real-time reverse transcription polymerase chain reaction (RT-PCR) and Western blot. We found higher TLR2 and TLR4 mRNA and protein levels in the inflamed colonic mucosa of children with fdIBD and rIBD compared to controls. In the non-inflamed colonic mucosa of children with fdIBD and rIBD, TLR2 and TLR4 mRNA and protein levels were similar to controls. TLR2 and TLR4 mRNA and protein levels also did not differ between children with fdIBD or rIBD in either inflamed or non-inflamed colonic mucosa. TLR3 mRNA expression and protein levels were similar in all groups studied. Our results of increased levels of TLR2 and TLR4 in the inflamed colonic mucosa of children with IBD confirm the hypothesis that innate immunity has an important role in the pathogenesis of this disease.

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Comparative therapeutic effects of orally administered 1,25-dihydroxyvitamin D₃ and 1alpha-hydroxyvitamin D₃ on type-1 diabetes in non-obese diabetic mice fed a normal-calcaemic diet

J. P. Driver, O. Foreman, C. Mathieu, E. van Etten and D. V. Serreze
Clinical & Experimental Immunology, Volume 151, Issue 1, Page 76-85, Jan 2008, doi: 10.1111/j.1365-2249.2007.03537.x

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Directing the Immune
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TLR Therapeutics™: Directing the Immune System

Coley's proprietary TLR Therapeutics™ drug platform is based on ground-breaking science by Coley co-founder Dr. Arthur M. Krieg. TLR Therapeutics affect important immune system receptors called Toll-like Receptors (TLRs). There are 10 known Toll-like receptors in the human immune system capable of initiating immune responses to viruses and diseases.

Through Coley's understanding of immune system biology, we have developed our drug candidates to either stimulate or block one or more of these receptors. By activating or blocking one or more TLRs with Coley's TLR Therapeutic drug candidates, we are able to induce highly-targeted and appropriate disease-specific immune system responses.

Coley's TLR Therapeutics stimulate or block selective Toll-like receptors. We are focusing our drug development efforts on TLR7, TLR8 and TLR9 for the treatment of various diseases including cancer, asthma and allergy, autoimmune diseases, and to enhance the effectiveness of vaccines. In preclinical testing, we are targeting these receptors for treatment of various infectious diseases and other diseases. We believe the specificity of our drug candidates to these targeted TLRs will offer enhanced safety and efficacy compared to previous immunotherapy approaches.

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The Acronym Finder allows users to decipher acronyms from a database of over 500,000 entries covering computers, technology, telecommunications, and the military. Unlike online glossaries, search engines, encyclopedias, or thesauruses, Acronym Finder exists purely to unravel the bewildering range of acronyms that impact daily life.

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- SSPS - Solid State Protection System
- MPC - Milk Protein Concentrate
- OSL - Open Source Lab
- BDD - Business Desktop Deployment (Microsoft)
- MoFo - Mozilla Foundation
- SPA - Society of Professional Accountants
- WFM - Workflow Management
- ACU - Arithmetic & Control Unit
- BESA - Biomedical Engineering Students Association
- FACS - Frame and Cable System (telecom)
- IBBM - Internet-Based Business Model
- SSBTC - State Street Bank and Trust Company
- WDI - Walt Disney Imagineering
- MMB - Medium Messaging Benchmark
- IFAK - Individual First Aid Kit

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- | | | |
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A Web Site's Traffic Soars As Acronyms Proliferate; Sorting Out 164 CATs

By **BARRY NEWMAN**

ESTES PARK, Colo.—Do your MP3s get tangled in your BVDs? Have you confused an ETF (Exchange-Traded Fund) with an ETF (Effluent-Treatment Facility)? Do you ever order a QPC (Quarter Pounder with Cheese) by mistake at KFC?



Mike Molloy

If so, you might want to check in with Mike Molloy, USAF, Ret. On the World Wide Web, he puts out an exponentially expanding dictionary consulted by bureaucrats, translators, doctors, weapons designers and anyone else who needs help decrypting the wide world's daily output of acronyms. Its HTTP (Hypertext Transfer Protocol) is www.AcronymFinder.com—AF for short.

Unlike acronym sites compiled automatically, AF is "human edited" by Mr. Molloy and his wife, Susan Ebert. Each morning, they settle into the kitchen-office of their home in this Rocky Mountain town and open their computers to a blizzard of new acronyms—200 a day, on average—frequently emailed by the creators themselves.

Often blowing in as well are complaints from lawyers trying to register acronyms with the United States Patent and Trademark Office. Listings on AF have repeatedly convinced USPTO examiners that some jumbles of letters are already in public use, if not public comprehension.

Ms. Ebert, 51 years old, and Mr. Molloy, 52, are dedicated to public comprehension. They have acronyms in their DNA, and Mr. Molloy has a rare gift for recalling what they stand for.

"How about C4ISR?" she said one morning, testing him.

"Command, Control, Communications, Computers, Intelligence, Surveillance, and Reconnaissance," Mr. Molloy replied.

WHAT'S THAT?

A sampling of acronyms and their definitions from AcronymFinder.com:

AWESOME: Angina with Extremely Serious Operative Mortality

BLOAT: Bacon, Lettuce, Onion, Avocado, & Tomato Sandwich

CASANOVA: Carotid Artery Surgery Asymptomatic Narrowing Operation

FATTY: Forward Area Tactical Typewriter

INEPT: Insensitive Nuclei Enhanced By Polarization Transfer

PASTA: Partial Articular Side Tear of the Rotator Cuff

NBF: Nothing But Fun

SMASH: Self-powered Multi-fuel Army Space Heater

WIMPS: Weakly Interacting Massive Particles

"Kinda scary," said Ms. Ebert, as her husband punched C4ISR into AF's search box and got a confirmation.

"This one's a great illustration of why acronyms are needed," Mr. Molloy said. "The ability to precisely express complex concepts in a handful of letters is pretty cool."

AF's editors know that many language guardians (though not all dictionaries) say acronyms must be pronounceable, as in TACO: Texas Anesthesia Conference for Obstetrics.

Mr. Molloy has heard it all. "The fussy word people are fighting a losing battle," he said, scrawling URL—Uniform Resource Locator—on his whiteboard. "Some say, 'What's your *You Are EI?*' Some say, 'What's your *Ear!*?' But most just want to know what the letters stand for. There's a huge need for people to look this stuff up."

In 1985, at Randolph Air Force Base in Texas, Mr. Molloy was integrating computers for the departments of Transportation, Energy and Defense when the need hit him. His first acronym list ran 30 pages. By the time he'd retired and had AF running on the Web in 1997, his list had 43,000 acronyms; at last count, it had 528,000.

The site now pulls in a million visitors a month, attracting advertising from companies whose products and services are often associated with the acronym being looked up. This provides a middle-class income good enough for AF's editors to afford a new SAAB (or Svenska Aeroplan Aktiebolaget.)

AF can barely keep pace with today's overload of "backronyms"—which start as sets of letters and then grope for words to back them up. Congress is a backronym factory. The last one considered the FACT Act (Fair Access to Clinical Trials), the PACT Act (Prevent All Cigarette Trafficking) and the CLASS Act (Community Living Assistance Services and Supports).

Rep. Bob Filner (D., Calif.), who introduced the PAY UP! (Pay for All Your Undocumented Procedures) Act, likes acronyms because "people remember them." He also sponsors the FAIR AIR Act, which stands for "ah, foreign air, ah, reduction something," he says.

That's where acronyms create headaches: The catchwords may be easy to remember, but what they mean is easy to forget. It's helpful to know that ACHE is the American Council for Headache Education, less so that it's also the American Council of Hypnotist Examiners. AF lists 70 SAFEs, 126 FASTs and 164 CATs. Such overlaps can have legal implications since naming conflicts draw brand-protecting lawyers like M&Ms draw kids.

Madison Square Garden went to court in 2005, for instance, claiming trademark rights to MSG as an Internet domain name. The domain's owner, a Minnesota company called F&A, wouldn't give it up. F&A hired Mr. Molloy, who wrote an expert opinion that "monosodium glutamate" and "message" were far more common meanings of MSG, and that MSG also meant 117 other things, including Moe's Southwest Grill. MSG—a k a The Garden—settled out of court last year for an undisclosed sum. Its Web site is now msg.com.

At the patent office, the Trademark Trial and Appeal Board routinely refuses to trademark acronyms that are "merely descriptive." TTAB judges have taken to citing AF listings as evidence of that, annoying some trademark lawyers.

In his "TTABlog" last July, lawyer John Welch tore into the TTAB'S reliance on AF. "This Acronym Finder thing—my complaint was it's user-generated," he says. "Anyone can go on and add acronyms. Why should that be evidence of anything?"

Because, Mr. Molloy shot back on TTABlog, "We do not accept 'made-up' definitions ... our users do NOT create our content." He and Ms. Ebert confirm the meaning of each new acronym with established sources.

First out of the inbox on a recent morning was IASM, defined by an anonymous contributor as "Intelligent Assistant Store Management." Mr. Molloy moved from his breakfast-table laptop to his double-screen desktop and Googled IASM and its alleged meaning with quotation marks around them.

No hits.

Next he removed the quotes and up popped "Intelligent Agent Security Module," a definition AF didn't have either. Its Web address led to something called DODSBIR. "Department of Defense Small Business Innovating Research," said Mr. Molloy. "I happen to know that." Trusting DODSBIR as a reliable acronym source, he added its IASM definition to his list.

Google hit another meaning—"Interdisciplinary Aspects of Survey Methods"—at the equally credible CDC (Centers for Disease Control). And one more: "I Am Sold Myself"—a sales pitch to reluctant customers—that produced 132 hits. Mr. Molloy added both definitions. "Irresistible," he said. "How can you walk away from a new acronym?"

But the day's first IASM was nowhere to be Googled. Mr. Molloy tracked the sender's IP (Internet Protocol) and emailed back, asking for "an authoritative URL reference" to document the definition. Until then, it won't even rate a spot in his

Acronym Attic, a secondary list built by a robot program that harvests acronyms off the Internet. Mr. Molloy and Ms. Ebert edit those in their spare time.

IYWTKTT (if you want to know the truth) they have 2.5 million to go.

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Abbreviation (required) [24 character limit]
Example: NATO

Email address in case we have a question (optional)
This will not appear with the definition.

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Definition (required) [255 character limit] NOTE: We don't accept made-up definitions.
Example: North Atlantic Treaty Organization

Please [Categorize](#) this submission

You can add the above definition now by pressing the **Submit** button, or you can fill out [additional information](#) in the fields below about this abbreviation & definition.

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Acronym to Find (example: ASAP)

Find

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EXHIBIT 5

THE
Oxford
American
Dictionary
of
Current
English

New York Oxford
Oxford University Press
1999

lightfall /nɪtfaʊl/ *n.* the onset of night; the end of day.
light *n.*
light-gown /nɪtɡəʊn/ *n.* 1 a woman's or child's loose garment worn in bed. 2 *hist.* a dressing gown.
light-le /nɪtlee/ *n. colloq.* a nightgown.
light-in-gale /nɪ'tɪŋaɪl/ *n.* any small reddish-brown bird of the genus *Luscinia*, esp. *L. megarhynchos*, of which the male sings melodiously, esp. at night.
light-jar /nɪtʃɑːr/ *n.* any nocturnal bird of the family Caprimulgidae, having a characteristic harsh cry.
light-life /nɪtliːf/ *n.* entertainment available at night in town.
light-ly /nɪtlee/ *adj. & adv.* • *adj.* 1 happening, done, existing in the night. 2 recurring every night. • *adv.* very night.
light-mare /nɪtmɑːr/ *n.* 1 a frightening dream. 2 *colloq.* very unpleasant experience. 3 a haunting fear.
light-mar-ish *adj.* **light-mar-ish-ly** *adv.*
light owl *n. colloq.* a person active at night.
light school *n.* an institution providing evening classes for those working by day.
light-shade /nɪtʃhaɪd/ *n.* any of various poisonous substances, esp. of the genus *Solanum*, including *S. nigrum* and *S. dulcra* (woody nightshade) with black berries, and *S. dulcra* (woody nightshade) with red berries.
light shift *n.* a shift of workers employed during the ht.
light-shirt /nɪtʃɔːt/ *n.* a long shirt worn in bed.
light-spot /nɪtspɒt/ *n.* a nightclub.
light-stick /nɪtstɪk/ *n.* a policeman's club.
light-time /nɪtɪm/ *n.* the time of darkness.
light-ly *adv.* National Institutes of Health.
light-ism /nɪ'tɪzəm, nee-/ *n.* 1 the rejection of all religious and moral principles. 2 a form of skepticism maintaining that nothing has a real existence. • *n.* **light-ist** *n.* **light-istic** *adj.*
light-ly *n.* nothing; no number or amount.
light-ly /nɪmbəl/ *adj.* (nimbler, nimblest) 1 quick and in movement or action. 2 (of the mind) quick to comprehend. • *n.* **light-ly-ness** *n.* **light-ly** *adv.*
light-stratus /nɪmbɒstrə'teɪs, -strətəs/ *n.* (pl. nimbati /-ti/) *Meteorol.* a low dark-gray layer of cloud.
light-stratus /nɪmbəs/ *n.* (pl. nimbi /-bi/ or nimbus) 1 a *Meteorol.* a rain cloud. • *n.* **light-stratus** *adj.*
light-ly /nɪnkəm'pɒp/ *n.* a simpleton; a fool.
light-ly /nɪ/ *n. & adj.* • *n.* 1 one more than eight. 2 a symbol (9, ix, IX). 3 a size, etc., denoted by nine. • *team of nine.* 5 nine o'clock. • *adj.* that it to nine. • *advised to nine* dressed very neatly. **light-nine times out of ten** nearly always. **light-nine** a designation of typical office hours.
light-ninefold /nɪn'fɒld/ *adj. & adv.* 1 nine times as much or y. 2 consisting of nine parts.
light-nine /nɪn'teɪn/ *n. & adj.* • *n.* 1 one more than eight-teen. 2 the symbol for this (19, xix, etc. more than ten. 3 the symbol for this (19, xix, etc. more than ten. 4 a size, etc., denoted by nineteen. • *adj.* that it to nineteen. • *n.* **light-nine-teenth** *adj. & n.*
light-nine /nɪn'teɪn/ *n. & adj.* • *n.* (pl. -ties) 1 the product of ten. 2 a symbol for this (90, xc, XC). 3 (in numbers from 90 to 99. • *adj.* that amount to it.
light-nine-ty /nɪn'ti-eti/ *adj. & n.*
light-nine-ty /nɪn'ti-eti/ *n.* a person skilled in ninjutsu.
light-nine-ty /nɪn'ti-eti/ *n.* one of the Japanese martial arts characterized by stealthy movement and camouflage.
light-nine-ty /nɪn'ti-eti/ *n.* (pl. -nies) a foolish or simpleminded

tallic element occurring naturally in several minerals and used in alloys for superconductors. Also called **coluMBUM**. • *n.* **light-ni-bic** *adj.* **light-ni-bous** *adj.*
light-nip /nɪp/ *v. & n.* • *v.* (nipped, nipping) 1 *n.* pinch, squeeze, or bite sharply. 2 *n.* (often foll. by off) remove by pinching, etc. 3 *n.* (of the frost, etc.) cause pain or harm to. • *n.* 1 a pinch; a sharp squeeze. 2 a bite. 3 biting cold. • *n.* **light-nip and tuck** neck and neck. **light-nip** in the bud suppress or destroy (esp. an idea) at an early stage.
light-nip *adj.*
light-nip /nɪp/ *n.* a small quantity of liquor.
light-nipper /nɪpə/ *n.* 1 a person or thing that nips. 2 the claw of a crab, lobster, etc. 3 (in pl.) any tool for gripping or cutting, e.g., forceps or pincers.
light-nipple /nɪpəl/ *n.* 1 a small projection in which the mammary ducts of either sex of mammals terminate and from which in females milk is secreted for the young. 2 the mouthpiece of a feeding bottle or pacifier. 3 a device like a nipple in function, e.g., the tip of a grease gun. 4 a nipplelike protuberance.
light-nippy /nɪpeɪ/ *adj.* (nippier, nippiest) *colloq.* 1 esp. *Brit.* quick; nimble; active. 2 chilly; cold. • *n.* **light-nippy** *adv.*
light-nirvāna /nɪ'rva:nə, neer-/ *n.* (in Buddhism) perfect bliss and release from karma, attained by the extinction of individuality.
light-nisei /ni'seɪ, neesə/ (also **light-nisei**) *n.* an American whose parents were immigrants from Japan.
light-nit /nɪt/ *n.* the egg or young form of a louse or other parasitic insect, esp. of human head lice or body lice.
light-niter /nɪtər/ *n.* saltpeter; potassium nitrate.
light-nitpick /nɪtpɪk/ *v. intr. colloq.* find fault in a petty manner; criticize. • *n.* **light-nitpick-er** *n.* **light-nitpick-ing** *n.*
light-nitrate /nɪ'treɪt/ *n. & v.* • *n.* 1 any salt or ester of nitric acid. 2 potassium or sodium nitrate when used as a fertilizer. • *v. tr.* *Chem.* treat, combine, or impregnate with nitric acid. • *n.* **light-nit-ration** /-ɪʃən/ *n.*
light-nitric /nɪ'trɪk/ *adj.* of or containing nitrogen, esp. in the quinquivalent state.
light-nitric acid *n.* a colorless corrosive poisonous liquid.
light-nitric /nɪ'trɪk/ *v. tr.* (-fies, -fied) 1 impregnate with nitrogen. 2 convert (nitrogen, usu. in the form of ammonia) into nitrites or nitrates. • *n.* **light-nit-ri-ca-tion** /-fɪkə'sheɪn/ *n.*
light-nitrite /nɪ'traɪt/ *n.* any salt or ester of nitrous acid.
light-nitro- /nɪ'trɒ/ *comb. form* 1 of or containing nitric acid, niter, or nitrogen. 2 made with any of these. 3 of or containing the monovalent -NO₂ group.
light-nitro-ben-zene /nɪ'trɒbɛnzɛn/ *n.* a yellow oily liquid made by the nitration of benzene and used to make aniline, etc.
light-nitro-cellulose /nɪ'trɒsɛlyʊlɒs/ *n.* a highly flammable material made by treating cellulose with concentrated nitric acid.
light-nitrogen /nɪ'trɒdʒɪn/ *n.* *Chem.* a colorless, odorless gaseous element that forms four-fifths of the atmosphere and is an essential constituent of proteins and nucleic acids. • *n.* **light-nitro-genous** /-trɒdʒɪnəs/ *adj.*
light-nitro-glycerin /nɪ'trɒdʒɪsərɪn/ *n.* (also **light-nitro-glycerine**) an explosive yellow liquid made by reacting glycerol with concentrated sulfuric and nitric acids.
light-nitrous /nɪ'trɒs/ *adj.* of, like, or impregnated with nitrous.
light-nitrous oxide *n.* a colorless gas used as an anesthetic (= LAUGHING GAS) and as an aerosol propellant.
light-nitty-gritty /nɪ'tɪgrɪtɪ/ *n. sl.* the realities or practical details of a matter.
light-nitwit /nɪ'twɪt/ *n. colloq.* a stupid person.
light-nix /nɪks/ *n. & v. sl.* • *n.* 1 nothing. 2 a denial. • *v. tr.* 1 cancel. 2 reject.
light-NJ *abbr.* New Jersey (also in official postal use).
light-NM *abbr.* New Mexico (in official postal use).
light-N.Mex. *abbr.* New Mexico.
light-NMR *abbr.* (also nmr) nuclear magnetic resonance.

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nip ~ noblesse

light-No *symp. Chem.* the element nobelium.
light-No /nɒ/ *n.* (also **light-Noh**) traditional Japanese drama with dance and song.
light-No *abbr.* 1 number. 2 North.
light-no /nɒ/ *adj.* 1 not any (there is no excuse). 2 not a; quite other than (is no fool). 3 hardly any (did it in no time). 4 used elliptically as a notice, etc., to forbid, reject, or deplore the thing specified (no parking; no surrender). • *n.* **light-no entry** (of a notice) prohibiting vehicles or persons from entering a road or place. **light-no joy** no satisfaction or success. **light-no man** no person; nobody. **light-no sweat** *colloq.* no bother; no trouble. **light-no trumps** (or trump) *Bridge* a declaration or bid involving playing without a trump suit. **light-no way** *colloq.* 1 it is impossible. 2 I will not agree, etc. ... or no ... regardless of the ... (rain or no rain, I shall go out). **light-there is no ...ing** it is impossible to ... (there is no accounting for taste).
light-no /nɒ/ *adv. & n.* • *adv.* 1 equivalent to a negative sentence: the answer to your question is negative; your request will not be complied with; the statement made or conclusion arrived at is not correct or satisfactory; the negative statement made is correct. 2 (foll. by *compar.*) by no amount (no better than before). • *n.* (pl. **light-noes**) 1 an utterance of the word *no*. 2 a denial or refusal. 3 a negative vote. • *n.* **light-no is no more** has died or ceased to exist. **light-no can do** *colloq.* I am unable to do it. **light-no less** (often foll. by *than*) 1 as much (gave me \$50, no less). 2 as important (no less a person than the president). 3 *disp.* no fewer (no less than ten people). **light-no longer** no now or henceforth as formerly. **light-no more** • *n.* nothing further (have no more to say). • *adj.* not any more (no more wine?). • *adv.* 1 no longer. 2 never again. 3 to no greater extent (is no more an authority than I am). 4 neither (you did not come, and no more did he). **light-no sooner ... than see SOON.** not take no for an answer persist in spite of refusals. or no or not (pleasant or no, it is true). **light-whether or no** 1 in either case. 2 (as an indirect question) which of a case and its negative (tell me whether or no).
light-no-account *adj.* unimportant; worthless.
light-Noah's ark /nɒəz/ *n.* 1 a the ship in which (according to the Bible) Noah, his family, and the animals were saved. 2 an imitation of this as a child's toy. 3 a large or cumbersome or old-fashioned trunk or vehicle. 4 a bivalve mollusk, *Arca noae*, with a boat-shaped shell.
light-Nobel-ist /nɒbəlɪst/ *n.* a winner of a Nobel prize.
light-Nobel-ium /nɒbɛleɪəm/ *n.* *Chem.* a radioactive transuranic metallic element.
light-Nobel prize /nɒbəl/ *n.* any of six international prizes awarded annually for physics, chemistry, physiology or medicine, literature, economics, and the promotion of peace.
light-nobility /nɒbɪlɪteɪ/ *n.* (pl. -ties) 1 nobleness of character, mind, birth, or rank. 2 (prec. by *a, the*) a class of nobles, an aristocracy.
light-noble /nɒbəl/ *adj. & n.* • *adj.* (noble, noblest) 1 belonging by rank, title, or birth to the aristocracy. 2 having lofty ideals; free from pettiness and meanness. 3 of imposing appearance. 4 excellent; admirable (noble horse; noble cellar). • *n.* a nobleman or noblewoman. • *n.* **light-noble-ness** *n.* **light-nobly** *adv.*
light-noble gas *n.* any one of a group of gaseous elements that almost never combine with other elements.
light-noble-man /nɒbəl'mæn/ *n.* (pl. -men) a man of noble rank or birth; a peer.
light-noblesse /nɒblɛs/ *n.* the class of nobles (as of France, etc.). • *n.* **light-noblesse oblige** /ɒblɛ'ʒ/ privilege entails responsibility.

See page xii for the Key to Pronunciation.

—THIRD—

BARNHART
DICTIONARY

OF

*NEW
ENGLISH*

ROBERT K. BARNHART

SOL STEINMETZ

WITH

CLARENCE L. BARNHART

THE H.W. WILSON COMPANY. 1990

Manchester Guardian Weekly 3/9/74, p7 *Said one French diplomat: "Kissinger is attempting to bring the Nine into an Atlantic system whereby they will be able to take only decisions that are approved in Washington."* Time 4/1/74, p26 [1973]

► The European Economic Community, popularly known as the Common Market, or between 1957 and 1973, the Six, comprised Belgium, France, Italy, Luxembourg, The Netherlands, and West Germany. On January 1, 1973, Denmark, Ireland, and Great Britain joined the group, known thereafter as the Nine. Then, in May 1979 Greece was accepted as the tenth member, effective as of January 1, 1981, and the Common Market Nine came to be known as the Ten.

nine-ball, *n.* U.S. Slang. a variety of pocket billiards. See the quotation for details. *For the hustler, nine ball is the best game. The first nine balls—eight solid-colored balls and the nine ball with a yellow stripe—are racked in a diamond with the one ball in front and the nine ball in the middle. The rules are simple: the lowest numbered ball on the table must be hit first, and whoever makes the nine ball wins.* Atlantic 4/70, p67 [1968]

1984, *n.* a date symbolizing a totalitarian society in which all truth and freedom is suppressed and people live in a totally regimented and dehumanized state. *Throughout the campaign, the political uses of television advertising and packaging of candidates were heralded by proponents as the inescapable wave of the future and by doomsayers as the ominous forerunner of 1984.* Time 11/16/70, p14 [1959, from the novel 1984 by George Orwell, 1903-1950, which is set in such a society]

nine-to-five or nine-to-five, *n.* Slang. a person who holds an office job with regular hours, usually nine in the morning to five in the evening. *At Grand Central you can't tell the action crowd from the nine-to-fivers. Singapore Sammy stopped there to put a saw on Carry-Me-Back in the fifth at Roosevelt and wound up on the 5:14 to Greenwich.* Time 4/19/71, p12 *In the course of their rejection, [the hippies] have created a new way of looking at things and a new context in which to live. Dedication to the work ethic has produced the alienation that the hippies see all around them in the "nine-to-fives."* Britannica Book of the Year 1968, p790 [1959]

ninja (nindʒə), *n.* a practitioner of the martial art of making oneself elusive or invisible through disguises and other artifices. *So obsessed was Japan with the secret negotiations surrounding Mr. Nixon's trip to China that for months the Japanese spoke of national-security adviser Henry Kissinger as a ninja—the magician of Japanese legends who performs supernatural acts and practices sorcery.* International Newsweek 9/11/72, p28-29 *Today, ninja practice their art not as espionage, but as a traditional martial art with a nonviolent philosophy.* World Book Encyclopedia (1988), Vol.13, p234 [1972, from Japanese]

nit, *n.* a unit of brightness in the meter-kilogram-second system. See the quotation for details. . . . *let's look at some of the units you get on to when you have sorted out mass and weight . . . I noticed wild things like the Nit "a unit of luminance in the MKS system which is the equivalent to one candela per square metre"; and the Slug "a unit of mass in the foot pound system . . . The slug is also called a gee pound."* Punch 9/11/68, p364 [1953, from Latin *nitēre* to shine]

NIT, abbreviation of NEGATIVE INCOME TAX. *Under the NIT, the tax scales would be continued downward past the zero-tax line . . .* Time 2/8/71, p15 [1967]

Nitinol (nitɪnɔ:l), *n.* a nonmagnetic alloy of titanium and nickel. See the quotations for details. *In 1968 a nickel-titanium alloy, 55-Nitinol, was discovered to have the ability to regain its original shape after being heated and then cooled below a certain temperature, crushed, and subsequently reheated. This "memory" property is expected to make Nitinol a valuable component of fire-extinguisher activators.* 1969 Compton Yearbook, p324 *One of the fascinations of the behavior of plastics is that when certain kinds of plastic are molded in a distinct form, then melted so that the form is lost and then allowed to cool, they resume much the same form. Called "plastic memory," the phenomenon has an analogue in a little-known metallic alloy. The metal is named Nitinol from its constitu-*

ents (nickel and titanium) and the place where it was discovered 10 years ago (the Naval Ordnance Laboratory). Scientific American 3/71, p47 [1968]

nitty-gritty, *n.* 1 the practicalities or details. *But they got bogged down in the nitty-gritties of negotiation . . .* Manchester Guardian Weekly 4/10/71, p1 *How many meetings, finally at the nitty-gritty, are interrupted by your secretary asking if you want to take a call . . . Harper's 3/70, p87 2 get down to the nitty-gritty, to get down to the fundamentals or details. . . . Dr. Swanson . . . can really understand people in a gutsy way. And he's not afraid to get down to the nitty-gritty of unpleasant problems. . . .* NY Times 6/27/67, p20 [1961, of uncertain origin]

Nixon Doctrine. See the first quotation for the meaning. . . . *the Nixon Doctrine [was] enunciated by the President on Guam last July, that the U.S. from then on would avoid military commitments that might lead to ground-combat interventions similar to Viet Nam.* Time 4/13/70, p17 *The Nixon Doctrine, although not officially applicable to Europe, has some worrying implications for Europe. It implies that America is ready to expend money and technology on behalf of her allies but no longer ready to shed her own blood. It also implies that American help is conditional on self-help.* Manchester Guardian Weekly 8/12/72, p15 [1970]

NLP, U.S. abbreviation of neighborhood loan program, a state-sponsored plan that provides low mortgage and down-payment requirements, designed especially for redlined sections of a city. *The neighborhoods eligible for the NLP are chosen in consultation with municipal officials. They have to be basically stable and primarily residential, areas where decay and blight have not reached too advanced a stage and where financing has been difficult.* Ruth Rejnis, Her Home, 1980, p24 [1979]

NOAA (noʊə), *n.* acronym for National Oceanic and Atmospheric Administration (of the United States). *Specifically, NOAA will be concerned with determining atmospheric conditions that make for pollution, the effects of pollution on weather, and contaminants in fish.* Science News 3/27/71, p212 *Formed in 1970, NOAA absorbed the activities of the Environmental Science Services Administration, which was abolished.* 1972 Britannica Yearbook of Science and the Future, p174 [1969]

no-cut contract, U.S. and Canada. a contract in professional sports guaranteeing that the signer will not be eliminated from a team's roster. *Joe Thomas reportedly is demanding a five-year, no-cut contract at more than \$350,000 a year with the Baltimore Colts. Thomas, who has been credited with rebuilding the franchise, is the pro football club's general manager.* NY Times 1/5/77, pA18 [1976]

nod, *n.* on the nod, British. without formality; by tacit agreement or acknowledgment. *The agenda, usually the cause of great friction, was accepted "on the nod".* Sunday Times (London) 1/12/69, p4 *With the Royal Exchange will die more than two centuries of tradition of trading mostly done "on the nod," with scarcely a written contract to be seen.* Manchester Guardian Weekly 7/11/68, p10 [1959]

no-fault or no fault, Especially U.S.—*adj.* 1 of or relating to a form of automobile insurance by which accident victims are compensated for damages or expenses by their own insurance company, whether the accident was their fault or not. *Specifically, the hearings were to focus on a modified no-fault bill introduced by Senator Bernard G. Gordon, a Peekskill Republican. The bill is designed to end much of the current reliance on litigation-oriented settlements for auto accidents.* NY Times 3/5/72, pD4 2 of or denoting a form of divorce which is granted without either party having to prove the other guilty of causing the dissolution of the marriage. *Already accepted by 25 of the United States, the no-fault concept eliminates the adversary role; the courts accept an acknowledgment of irretrievable marriage breakdown by both spouses as sufficient grounds for divorce.* Maclean's 4/19/76, p30 3 of or involving any method of reaching a settlement or awarding damages without having to resort to legal action. *A related "no fault" plan was recently endorsed by the American Medical Associ-*

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nitrogen balance *noun* (1944)
: the difference between nitrogen intake and nitrogen loss in the body or the soil

nitrogen cycle *noun* (1908)
: a continuous series of natural processes by which nitrogen passes successively from air to soil to organisms and back to air or soil involving principally nitrogen fixation, nitrification, decay, and denitrification

nitrogen dioxide *noun* (1885)
: a toxic reddish brown gas NO_2 that is a strong oxidizing agent, is produced by combustion (as of fossil fuels), and is an atmospheric pollutant

nitrogen fixation *noun* (1895)
: the metabolic assimilation of atmospheric nitrogen into ammonia by soil microorganisms and especially rhizobia

nitrogen-fixer *noun* (1912)
: any of various soil microorganisms that are involved in nitrogen fixation

nitrogen-fixing *adjective* (1899)
: capable of nitrogen fixation (*nitrogen-fixing* bacteria)

nitrogen mustard *noun* (1943)
: any of various toxic blistering compounds analogous to mustard gas but containing nitrogen instead of sulfur

nitrogen narcosis *noun* (1937)
: a state of euphoria and exhilaration that occurs when nitrogen in normal air enters the bloodstream at approximately seven times atmospheric pressure (as in deep-water diving) — called also *rapture of the deep*

nitrogen oxide *noun* (circa 1934)
: any of several oxides of nitrogen most of which are produced in combustion and are considered to be atmospheric pollutants: as **a** : NITRIC OXIDE **b** : NITROGEN DIOXIDE **c** : NITROUS OXIDE

nitrogen tetroxide (1885)
: a colorless toxic gas N_2O_4 that is a dimer of nitrogen dioxide and that in liquid form is used as an oxidizer in rocket engines

ni-tro-glyc-er-in or **ni-tro-glyc-er-ine** \ni-trō-'glis-rən, -'gli-sə-\\ *noun* [International Scientific Vocabulary] (1857)
: a heavy oily explosive poisonous liquid $\text{C}_2\text{H}_5\text{N}_2\text{O}_9$ used chiefly in making dynamites and in medicine as a vasodilator

ni-tro-meth-ane \ni-trō-'me-thān, *British* usually -'mē-\\ *noun* (1872)
: a liquid nitroparaffin CH_3NO_2 that is used as an industrial solvent, in chemical synthesis, and as a fuel for rockets and high-performance engines

ni-tro-par-af-fin \-'par-ə-fən\\ *noun* [International Scientific Vocabulary] (1892)
: any of various nitro derivatives of alkanes

nitros- or **nitroso-** *combining form* [New Latin *nitrosus* nitrous]
: containing the group NO (*nitrosamine*)

ni-tro-sa-mine \ni-'trō-sə-'mēn\\ *noun* (1878)
: any of various organic compounds which are characterized by the grouping NNO and some of which are powerful carcinogens

ni-trous \ni-'trās\\ *adjective* [New Latin *nitrosus*, from Latin, full of natron, from *nitrum* natron — more at NITER] (1601)
archaic : of, relating to, or containing niter

nitrous acid *noun* (1676)
: an unstable acid HNO_2 known only in solution or in the form of its salts

nitrous oxide *noun* (1800)
: a colorless gas N_2O that when inhaled produces loss of sensibility to pain preceded by exhilaration and sometimes laughter and is used especially as an anesthetic in dentistry and that is an atmospheric pollutant produced by combustion and a suspected contributor to greenhouse warming — called also *laughing gas*

nit-ty-grit-ty \ni-tē-'gri-tē-, ni-tē-'\\ *noun* [origin unknown] (1963)

: what is essential and basic : specific practical details (get down to the *nitty-gritty* of the problem)

— **nitty-gritty** *adjective*

nit-wit \nit-wit\\ *noun* [probably from German dialect *nit* not + English *wit*] (circa 1922)
: a scatterbrained or stupid person

1nix \niks\\ *noun* [German *nichts* nothing] (1789)
: NOTHING

2nix *transitive verb* (circa 1934)
: VETO, REJECT (the court *nixed* the merger)

3nix *adverb* (circa 1909)
: NO — used to express disagreement or the withholding of permission; often used with *on* (they said *nix* on our plan)

4nix *noun* [German, from Old High German *nihhus*; akin to Old English *nicor* water monster and perhaps to Greek *nizein* to wash] (1833)
: a water sprite of Germanic folklore

1nix-ie \nik-sē\\ *noun* [German *Nixe* female nix, from Old High German *nichessa*, feminine of *nihhus* nix] (1816)
: NIX

2nix-ie also **nixy** \nik-sē\\ *noun*, plural **nix-ies** \nix + -ie\\ (circa 1890)
: a piece of mail that is undeliverable because illegibly or incorrectly addressed

Nix-ie \nik-sē\\ *trademark*
— used for an electronic indicator tube

ni-zam \ni-'zām, 'ni-'zām, ni-'\\ *noun* [Hindi *nizām* order, governor, from Arabic *nizām*] (1768)

: one of a line of sovereigns of Hyderabad, India, reigning from 1713 to 1950

— **ni-zam-ate** \ni-'zā-'māt, ni-'zā-'\\ *noun*

1no \nō\\ *adverb* [Middle English, from Old English *nā*, from *ne* not + *ā* always; akin to Old Norse & Old High German *ne* not, Latin *ne-*, Greek *nē-* — more at AYE] (before 12th century)

1 a chiefly *Scottish* : NOT **b** — used as a function word to express the negative of an alternative choice or possibility (shall we go out to dinner or *no*)

2 : in no respect or degree — used in comparisons

3 : not so — used to express negation, dissent, denial, or refusal (*no*, I'm not going)

4 — used with a following adjective to imply a meaning expressed by the opposite positive statement (in *no* uncertain terms)

5 — used as a function word to emphasize a following negative or to introduce a more emphatic, explicit, or comprehensive statement

6 — used as an interjection to express surprise, doubt, or incredulity

7 — used in combination with a verb to form a compound adjective (*no-bake* pie)

2no *adjective* (12th century)

1 a : not any (*no* parking) (*no* disputing the decision) **b** : hardly any : very little (finished in *no* time)

2 : not a : quite other than a (he's *no* expert)

3 — used in combination with a noun to form a compound adjective (a *no-nonsense* realist)

3no \nō\\ *noun*, plural **noes** or **nos** \nōz\\ (1588)

1 : an act or instance of refusing or denying by the use of the word *no* : DENIAL

2 a : a negative vote or decision **b plural** : persons voting in the negative

No or **Noh** \nō\\ *noun*, plural **No** or **Noh** [Japanese *nō*, literally, talent] (1871)

: classic Japanese dance-drama having a heroic theme, a chorus, and highly stylized action, costuming, and scenery

no-account *adjective* (1845)
: of no account : TRIFLING (her *no-account* relatives)

No-a-chi-an \nō-'ā-kē-ən\\ *adjective* [Hebrew *Nōah* Noah] (1678)

1 : of or relating to the patriarch Noah or his time

2 : ANCIENT; ANTIQUATED

No-ah \nō-ə\\ *noun* [Hebrew *Nōah*]

noble *noun* (1703)
: an Old Testament patriarch who built a city in which he, his family, and living creatures of every kind survived the Flood

1nob \nāb\\ *noun* [probably alteration of *noble*] (circa 1700)

1 : HEAD **1**

2 : a jack of the same suit as the one in a card game that scores one point for the player who has it — usually used in the phrases *his nob* and *no nob*

2nob *noun* [perhaps from *1nob*] (1703)
chiefly *British* : one in a superior position in a game

nob-ble \nā-bəl\\ *transitive verb* **nob-ble** \nā-b(ə-)lɪŋ\\ [perhaps incorrect alteration of *nab*] (1847)

1 *British* : to incapacitate (a racehorse) especially by drugging

2 *slang* *British* **a** : to win over to one's side **b** : STEAL **c** : SWINDLE. CHEAT **d** : to catch

— **nob-bler** \nā-b(ə-)lər\\ *noun* (1788)

nob-by \nā-bē\\ *adjective* **nob-ble** (1788)

: CHIC. SMART

No-bel-ist \nō-'be-lɪst\\ *noun* (1938)
: a winner of a Nobel prize

no-bel-ium \nō-'be-lē-əm\\ *noun* [from Alfred B. Nobel] (1957)

: a radioactive element produced in a nuclear reactor — see ELEMENT table

No-bel prize \nō-'bel-, 'nō-'bel-\\ *noun* (1895)
: any of various annual prizes (as in literature, medicine) established by the Alfred Nobel for the encouragement of scientists who work for the interests of humanity

no-bil-i-ty \nō-'bi-lɪ-tē\\ *noun* [Middle English *nobilite*, from Middle French *nobilité*, Latin *nobilitat-*, *nobilitas*, from *nobilis* noble]

1 : the quality or state of being noble : nobility

2 : the body of persons forming the nobility in a country or state : ARISTOCRACY

1no-ble \nō-bəl\\ *adjective* **no-ble** \nō-'blē-\\ [Middle English *noble*, from Old French, from Latin *nobilis* well-born, noble, from *noscere* to come to know] (13th century)

1 a : possessing outstanding qualities : noble

2 : of high birth or exalted rank : ARISTOCRATIC

3 a : possessing very high or excellent qualities or properties (*noble* wine) **b** : very or excellent

4 : grand or impressive especially in appearance (*noble* edifice)

5 : possessing, characterized by, or resulting from superiority of mind or character : IDEAL

6 : chemically inert or inactive especially toward oxygen (a *noble* metal such as platinum) — compare BASE 6a

synonym see MORAL

— **no-ble-ness** \nō-'blē-nəs\\ *noun*

— **no-bly** \nō-'blē-\\ *adverb*

2noble *noun* (14th century)

1 : a person of noble rank or birth

2 : an old English gold coin equivalent to a penny

noble gas *noun* (1902)

: any of a group of rare gases that include helium, neon, argon, krypton, xenon, and radon and that exhibit great stability and extremely low reaction rates — called also *inert gas*

no-ble-man \nō-'bəl-mən\\ *noun* (14th century)

: a man of noble rank : PEER

noble savage *noun* (1672)

: a mythic conception of people belonging to non-European cultures as having innate moral simplicity and virtue uncorrupted by civilization; also : a person extending this conception

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ovement or action; agile. 2 (of the mind) quick to comprehend; clever, versatile. **nimbleness** *n.* **nimbly** *adv.*
nimble quick to seize *f. nimban* take *f. Gmc.* with **-b-** as **IMBLE**
 gile, lively, active, light, lithe, limber, spry, sprightly, sk, smart, energetic, rapid, quick, swift, adroit, deft, terous, literary volant. 2 agile, clever, versatile, alert, ite, quick-witted, quick, ready-witted, intelligent, n, sharp, smart, brilliant.
stratus /nimbōstrātʏs/, -strātʏs/ *n.* (*pl.* nimbostratid Meteorol. a low dark-gray layer of cloud. [mod.L., *f.* US + STRATUS])
s /nimbəs/ *n.* (*pl.* nimbi /-bi/ or nimbuses) 1 a n cloud or halo investing a deity or person or thing. b halo of a saint, etc. 2 Meteorol. a rain cloud. **nimd** *adj.* [*L.* = cloud, aureole]
f /nimbee/ *abbr. colloq.* not in my backyard.
nimply /nimbeepiminee/ *adj.* feeble, affected; lack vigor. [cf. NAMBY-PAMBY]
 AFFECTED 3, FEEBLE 2.
d /nimrod/ *n.* a great hunter or sportsman. [Heb. *dd* valiant: see Gen. 10:8-9]
npoop /ninkampōop/ *n.* a simpleton; a fool. [17th c. unkn.]
FOOL 1 n. 1.
in /n. & *adj.* ● *n.* 1 one more than eight, or one less ten; the sum of five units and four units. 2 a symbol iis (9, ix, IX). 3 a size, etc., denoted by nine. 4 a set of of nine individuals. 5 the time of nine o'clock (is it yer?). 6 a card with nine pips. 7 (the Nine) the nine s. ● *adj.* that amount to nine. **o dressed** (*Brit. up*) to **nines** dressed very elaborately. **nine days** wonder *n* or thing that is briefly famous. **nine times** out of **early** always. **nine to five** a designation of typical office s. [OE *nigon f. Gmc*]
nd /nɪnfold/ *adj. & adv.* 1 nine times as much or as *n.* 2 consisting of nine parts.
n /nɪnpin/ *n.* 1 (*in pl.*; usu. treated as *sing.*) a game in h nine pins are set up at the end of an alley and bowled an attempt to knock them down. 2 a pin used in this.
en /nɪnteén/ *n. & adj.* ● *n.* 1 one more than eighteen, more than ten. 2 the symbol for this (19, xix, XIX). 3 e, etc., denoted by nineteen. ● *adj.* that amount to **een**. **o talk nineteen to the dozen** see **DOZEN**. **oo ninth** *adj. & n.* [OE *nigontyne*]
ntee /nɪnte/ *n. & adj.* ● *n.* (*pl.* -ies) 1 the product of nine **ten**. 2 a symbol for this (90, xc, XC). 3 (*in pl.*) the **pers** from 90 to 99, esp. the years of a century or of a **n's** life. ● *adj.* that amount to ninety. **o ninety-first**, **nd**, etc., the ordinal numbers between ninetieth and **redth**. **ninety-one**, **-two**, etc., the cardinal numbers **een** ninety and a hundred. **oo ninetieth** *adj. & tyfold* *adj. & adv.* [OE *nigontig*]
ninjʏ /n. a person skilled in ninjutsu. [Jap.]
zu /nɪnjōōtsu/ *n.* one of the Japanese martial arts, char- ized by stealthy movement and camouflage. [Jap.]
'ninee /n. (*pl.* -ies) a foolish or simpleminded person. *f. innocenti*
FOOL 1 n. 1.
neēnon, *neenawn* /n. a lightweight silk dress fabric.
ninth /n. & *adj.* ● *n.* 1 the position in a sequence sponding to the number 9 in the sequence 1-9. 2 thing occupying this position. 3 each of nine equal of a thing. 4 *Mus.* a an interval or chord spanning nine **cutive** notes in the diatonic scale (e.g., C to D an **oc- aigher**). b a note separated from another by this inter- ● *adj.* that is the ninth. **oo ninthly** *adv.*
m /niōbeem/ *n. Chem.* a rare gray-blue metallic tran- s element occurring naturally in several minerals and **in** alloys for superconductors. ¶ *Symb.*: Nb. Also called **MBIUM**. **oo niobic** *adj.* **niobous** *adj.* [*Niobe* daughter of alus: so-called because first found in TANTALITE]
pl /n. sl. *offens.* a Japanese person. [abbr. of NIPPONENSE]

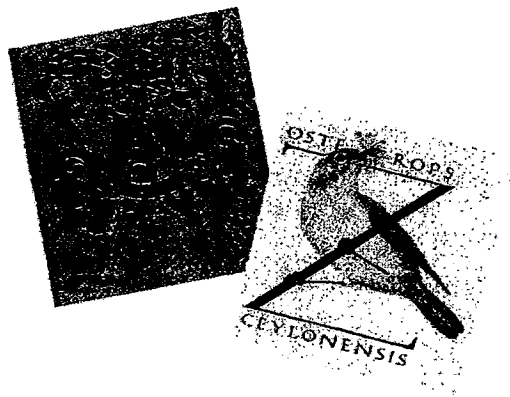
nip /nip/ *v. & n.* ● *v.* (**nipped**, **nipping**) 1 *n.* pinch, squeeze, or bite sharply. 2 *tr.* (often foll. by *off*) remove by pinching, etc. 3 *v.* (of the cold, frost, etc.) cause pain or harm to. 4 *intr.* (foll. by *in*, *out*, etc.) *Brit. colloq.* go nimbly or quickly. 5 *n.* 1 a pinch, snatch. ● *n.* 1 a a pinch, a sharp squeeze. b a bite. 2 a biting cold. b a check to vegetation caused by this. **o nip and tuck** neck and neck. **nip in the bud** suppress or destroy (esp. an idea) at an early stage. **oo nipping** *adj.* [ME, prob. of LG or Du. orig.]
 ● *v.* 1, 2 bite, nibble; pinch, snip, clip, cut, snap, tweak, twitch, trim, lop, crop, shear; grip, squeeze. 3 sting, bite, hurt, pain, pinch; grip. 4 dart, zip, dash, sprint, fly, shoot, speed, skip, hop, leap, flick, whisk, flash, hurry, pop, run, Austral. sl. nick. 5 see STEAL v. 1.
 ● *n.* 1 pinch, squeeze, tweak, snip; bite, nibble, morsel. 2 a chill, coldness, iciness, frost; sharpness, tang, bite. **o nip and tuck** tied, equal, even, colloq. even-steven; see also CLOSE *adj.* 5. **nip in the bud** stop, arrest, check, thwart, obstruct, frustrate, stymie, forestall; quash, squash, crush, stamp on, squelch, suppress, extinguish, put down; scotch.
nip /nip/ *n. & v.* ● *n.* a small quantity of liquor. ● *v. intr.* (**nipped**, **nipping**) drink liquor. [prob. abbr. of *nipperkin* small measure: cf. LG, Du. *nippen* to sip]
 ● *n.* taste, drop, sip, souppçon, portion, swallow, gulp, mouthful, finger, tot, thimbleful, dram, draft, *Brit. peg*, colloq. snort, shot, sl. snifter.
nipa /nɪpə/ *n.* 1 an E. Indian palm tree, *Nipa fruticans*, with a creeping trunk and large feathery leaves. 2 an alcoholic drink made from its sap. [Sp. & Port. *f. Malay nipah*]
nipper /nipər/ *n.* 1 a person or thing that nips. 2 the claw of a crab, lobster, etc. 3 *Brit. colloq.* a young child. 4 (*in pl.*) any tool for gripping or cutting, e.g., forceps or pliers. ● 3 see CHILD 1a. 4 (*nippers*) pincers, tweezers, pliers.
nipple /nipəl/ *n.* 1 a small projection in which the mammary ducts of either sex of mammals terminate and from which in females milk is secreted for the young. 2 the mouthpiece of a feeding bottle or pacifier. 3 a device like a nipple in function, e.g., the tip of a grease gun. 4 a nipplelike protuberance. 5 a short section of pipe with a screw thread at each end for coupling. [16th c., also *neble, nible*, *perh. dimin. f. neb*]
Nipponese /nɪpɒneɪz/, -neəs/ *n. & adj.* ● *n.* (*pl.* same) a Japanese person. ● *adj.* Japanese. [Jap. *Nippon* Japan, lit. "land of the rising sun"]
nippy /niːpi/ *adj.* (**nippier**, **nippiest**) *colloq.* 1 esp. *Brit.* quick, nimble, active. 2 chilly, cold. 3 tending to nip, as a dog. **oo nippily** *adv.* [NIP + -y]
 ● 2 see CHILLY 1.
nirvana /nɪrˈvænə/, neer-/ *n.* (*in Buddhism*) perfect bliss and release from karma, attained by the extinction of individuality. [Skr. *nirvāṇa* *f. nirvā* be extinguished *f. nis* out + *vā-* to blow]
 ● see PARADISE 2.
Nisael /nɪsəˈeɪ/, neesəy/ (also *Niseal*) *n.* an American whose parents were immigrants from Japan. [Jap., lit. "second generation"]
nisi /niːsi/ *adj.* Law that takes effect only on certain conditions (*decreo nisi*). [L., = "unless"]
Nissen hut /nɪsən/ *n.* a tunnel-shaped hut of corrugated iron with a cement floor. [P. N. *Nissen*, British engineer d. 1930, its inventor]
nit /niːt/ *n.* 1 the egg or young form of a louse or other parasitic insect, esp. of human head lice or body lice. 2 *Brit. sl.* a stupid person. [OE *hnitu* *f. WG*]
 ● 2 see FOOL 1 n. 1.
nitrat /niːtrət/ *n.* (*Brit.* nitre) saltpeter, potassium nitrate. [ME *f. OF f. L. mirum* *f. Gk miron*, of Semitic orig.]
nitinol /niːtɪˈnɒl/, -nɔɪl/ *n.* an alloy of nickel and titanium. [Ni + Ti + Naval Ordnance Laboratory, Maryland]
nitpick /niːtpɪk/ *v. intr. colloq.* find fault in a petty manner; criticize. **oo nitpicker** *n.* **nitpicking** *n.*
 ● see QUibble v.
nitrate /niːtreɪt/ *n. & v.* ● *n.* 1 any salt or ester of nitric acid. 2 potassium or sodium nitrate when used as a fertilizer.

● *v. tr.* *Chem.* treat, combine, or impregnate with nitric acid. **oo nitration** /-əˈrɪʃən/ *n.* [F (as NITER, -ATE)]
nitre *Brit.* var. of NITER.
nitric /niːtrɪk/ *adj.* of or containing nitrogen, esp. in the quinquevalent state. **o nitric acid** a colorless corrosive poisonous liquid. ¶ *Chem.* formula: HNO₃. **nitric oxide** a colorless gas. ¶ *Chem.* formula: NO. [F *nitrique* (as NITER)]
nitride /niːtrɪd/ *n. Chem.* a binary compound of nitrogen with a more electropositive element. [NITER + -IDE]
nitriety /niːtriˈeɪ/ *v. tr.* (-ies, -ied) 1 impregnate with nitrogen. 2 convert (nitrogen, usu. in the form of ammonia) into nitrites or nitrates. **oo nitriety** *adj.* **nitriety** /-fɪkəʃən/ *n.* [F *nitrier* (as NITER)]
nitrite /niːtriːt/ *n. Chem.* an organic compound consisting of an alkyl radical bound to a cyanide radical.
nitrite /niːtriːt/ *n.* any salt or ester of nitrous acid.
nitro- /niːtrə/ *comb. form* 1 of or containing nitric acid, niter, or nitrogen. 2 made with or by use of any of these. 3 of or containing the monovalent -NO₂ group (*the nitro groups in TNT*). [Gk (as NITER)]
nitrobenzene /niːtrəˈbenziːn/ *n.* a yellow oily liquid made by the nitration of benzene and used to make aniline, etc.
nitrocellulose /niːtrəˈsɛljʊləs/ *n.* a highly flammable material made by treating cellulose with concentrated nitric acid, used in the manufacture of explosives and celluloid.
nitrogen /niːtrədʒən/ *n. Chem.* a colorless, tasteless, odorless gaseous element that forms four-fifths of the atmosphere and is an essential constituent of proteins and nucleic acids. ¶ *Symb.*: N. **o nitrogen cycle** the interconversion of nitrogen and its compounds, usu. in the form of nitrates, in nature. **nitrogen fixation** a chemical process in which atmospheric nitrogen is assimilated into organic compounds in living organisms and hence into the nitrogen cycle. **oo nitro-**
nitroglycerin /niːtrəˈglɪsərɪn/ *n.* (also **nitroglycerine**) an explosive yellow liquid made by reacting glycerol with a mixture of concentrated sulfuric and nitric acids.
nitrous /niːtrʊs/ *adj.* of, like, or impregnated with nitrogen, esp. in the trivalent state. **o nitrous acid** a weak acid existing only in solution and in the gas phase. ¶ *Chem.* formula: HNO₂. **nitrous oxide** a colorless gas used as an anesthetic (= laughing gas) and as an aerosol propellant. ¶ *Chem.* formula: N₂O. [L. *nitrosus* (as NITER), partly through F *nitreux*]
nitty-gritty /niːteɪgrɪteɪ/ *n. sl.* the realities or practical details of a matter. [20th c.; orig. uncert.]
 ● see POINT n. 13a.
nitwit /niːtwɪt/ *n. colloq.* a stupid person. **oo nitwitty** /-wiːtɪreɪ/ *n.* [perh. *f. NIT + WIT*]
 ● see FOOL 1 n. 1.
nitwitted /niːtwɪtɪd/ *adj.* stupid. **oo nitwittedness** /-wɪtɪdnɪs/ *n.*
nix /niːks/ *n. & v. sl.* ● *n.* 1 nothing. 2 a denial or refusal. ● *v. tr.* 1 cancel. 2 reject. [G, colloq. var. of *nichts* nothing]
 ● *n.* 1 see ZERO n. 1. ● *v.* 2 see VETO v.
nix /niːks/ *n.* (*fem.* *nixie* /niːkseɪ/) a water spirit of German folklore. [G (*fem.* *Nixie*)]
nix /niːks/ *int. esp. Brit. sl.* giving warning to confederates, etc., that a person in authority is approaching. [19th c.; perh. = NIX]
NJ *abbr.* New Jersey (also in official postal use).
NLRB *abbr.* National Labor Relations Board.
NM *abbr.* New Mexico (in official postal use).
nm *abbr.* nanometer.
n.m. *abbr.* nautical mile.
N.Mex. *abbr.* New Mexico.
NMR *abbr.* (also **nmr**) nuclear magnetic resonance.
NNW *abbr.* north-northeast.
NNW *abbr.* north-northwest.

i...i pronunciation ● part of speech	
o	phrases, idioms, and compounds
oo	derivatives
	synonym section
cross-references appear in SMALL CAPITALS or italics	

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of the English Language

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nitroglycerine or **nitroglycerin** ▷ *noun, chem* (formula $C_3H_5(ONO_2)_3$) an explosive liquid compound, used in dynamites, produced by treating glycerine with nitric and sulphuric acids. ① 19c.

nitrous /'naitrəs/ ▷ *adj, chem* relating to or containing nitrogen in a low valency. ① 17c.

nitrous acid ▷ *noun, chem* (formula HNO_2) a weak acid occurring only in solution or in nitrite salts.

nitrous oxide ▷ *noun, chem* (formula N_2O) dinitrogen oxide used as an anaesthetic and popularly known as LAUGHING GAS.

nittler, nittiest and **nitty** see under **NTT**¹

the nitty-gritty /'niti'griti/ ▷ *noun, colloq* the fundamental issue or essential part of any matter, situation or activity, etc. ① 1960s: originally US; perhaps rhyming compound of *grit*.

nitwit /'nitwit/ ▷ *noun* a stupid person. ① 1920s: from German dialect *nit* (variant of *nicht* not) + *wit*¹.

nix ▷ *noun* (*nixes*) *slang* nothing. ▷ *exclamation, N Amer* no. ① 19c; 18c as *nicks*: from colloquial German *nix*, a form of *nichts* nothing.

NJ ▷ *abbreviation, US state* New Jersey. Also written **N.J.**

NL ▷ *abbreviation, IVR* Netherlands.

NM ▷ *abbreviation, US state* New Mexico. Also written **N.Mex.**

nm ▷ *abbreviation* 1 nanometre. 2 nautical mile.

n mile ▷ *abbreviation* (international) nautical mile.

NMR ▷ *abbreviation* nuclear magnetic resonance.

NNE ▷ *abbreviation* north-north-east.

NNW ▷ *abbreviation* north-north-west.

NO ▷ *abbreviation* New Orleans.

No¹, No or no ▷ *abbreviation* number.

No² ▷ *symbol, chem* nobelium.

No³ see **NOH**

no¹ /'nou/ ▷ *exclamation* 1 used as a negative reply, expressing denial, refusal or disagreement. 2 *colloq* used as a question tag expecting agreement □ *It's a deal, no?* 3 used as an astonished rejoinder □ *No! You don't say!* ▷ *adverb* 1 (with comparative) not any □ *no bigger than one's thumb*. 2 used to indicate a negative alternative: not □ *whether he's willing or no*. ▷ *noun* (*noes*) a negative reply or vote □ *The noes have it*. • **no more** 1 destroyed; dead. 2 never again; not any longer. • **not take no for an answer** to continue with an activity in spite of refusals; to insist. ① Anglo-Saxon *na*, from *ne* not + *a* ever.

no² /'nou/ ▷ *adj* 1 not any □ *There's no milk left*. 2 certainly not or far from something specified □ *He's no fool* □ *no easy task*. 3 hardly any □ *do it in no time*. 4 not allowed □ *no smoking*. • **no go** *colloq* impossible; no good. • **no one** no single □ *No one candidate is the obvious choice*. • **no way** *colloq* no; definitely not. ① Anglo-Saxon *na*, variant of *nae* NONE.

no³ or no⁴ /'nou/ ▷ *adverb, Scots* not □ *no bad*.

no⁴ see **No¹**

n.o. ▷ *abbreviation, cricket* not out.

no-account ▷ *adj* worthless; useless.

nob¹ ▷ *noun* in the game of cribbage: the jack of the tumbled-up suit. ① 19c.

nob² ▷ *noun, slang* someone of wealth or high social rank. ① 19c.

nob³ ▷ *noun, slang* the head. ① 17c: probably from **KNOB**.

no-ball ▷ *noun, cricket, baseball, rounders, etc* a ball bowled in a manner that is not allowed by the rules.

nobble /'nɒbəl/ ▷ *verb* (*nobbled, nobbling*) *colloq* 1 horse-racing to drug or otherwise interfere with (a horse)

to stop it winning. 2 to persuade someone by bribes or threats □ *tried to nobble the jury*. 3 to obtain something dishonestly. 4 to catch (a criminal). 5 to swindle someone. ① 19c: possibly from an *hobbler*, later understood as a *nobbler*, meaning 'a person who lames horses'.

nobelium /'nou'bi:liəm/ ▷ *noun, chem* (symbol **No**, atomic number 102) a radioactive element produced artificially from the element **CURIUM**. ① 1950s: named after the Nobel Institute, Stockholm, where it was first produced in 1957.

Nobel laureate ▷ *noun* a winner or past winner of a NOBEL PRIZE.

Nobel prize ▷ *noun* any of the annual prizes, awarded since 1901, for exceptional work in physics, chemistry, medicine or physiology, literature, economics, and the promotion of peace. 1900: instituted by Alfred Nobel (1833-96), Swedish discoverer of dynamite.

nobility /'nou'bi:liti/ ▷ *noun* (*nobilities*) 1 the quality of being noble, in character, conduct or rank. 2 (the nobility) the class of people of noble birth. ① 15c: from Latin *nobilitas*, from *nobilis* noble.

noble /'nəʊbəl/ ▷ *adj* (*nobler, noblest*) 1 honourable. 2 generous. 3 of high birth or rank. 4 grand, splendid or imposing in appearance. ▷ *noun* a person of noble rank. Compare **ARISTOCRAT**, **PEER**¹. • **nobleness** *noun*. • **nobly** *adverb* with a noble manner; honourably. ① 13c: from Latin *nobilis*, originally *gnobilis* knowable, ie well-known.

noble gas ▷ *noun, chem* any of the colourless odourless tasteless gases in group 0 (see **GROUP noun** 5) of the periodic table of the elements, ie helium, neon, argon, krypton, xenon and radon, in order of increasing atomic number. Also called **inert gas**. ① Early 20c.

nobleman and noblewoman ▷ *noun* a member of the nobility.

noble metal ▷ *noun* a metal such as gold, silver or platinum, that is highly unreactive, and so does not easily tarnish on exposure to the air. Opposite of **BASE METAL**.

noble rot ▷ *noun, bot* on white grapes: a rot caused by the fungus *Botrytis cinerea*, which aids the production of sweet white wine.

noble savage ▷ *noun* a romantic and idealized view of primitive human beings.

noblesse oblige /'nɒbləs ɒu'bli:ʒ/ ▷ *noun, usually ironic* it is the duty of those who are privileged to use their privilege to the benefit of the less fortunate. ① 19c: French, meaning 'nobility obliges'.

nobly see under **NOBLE**

nobody /'nɒbdɪ/, -bɒdi/ ▷ *pronoun* no person; no one. ▷ *noun* (*nobodys*) someone of no significance. • **like nobody's business** *colloq* very energetically; intensively □ *She yelled like nobody's business*.

NOC ▷ *abbreviation* National Olympic Committee.

nociceptive /'nɒsi'septɪv/ ▷ *adj, physiol* 1 sensitive to pain. 2 causing pain. ① Early 20c: from Latin *nocere* to hurt, modelled on **RECEPTIVE**.

nock ▷ *noun* a notch, or a part carrying a notch, especially on an arrow or a bow. ▷ *verb* (*nocked, nocking*) 1 to notch. 2 to fit (an arrow) on the string of a bow. ① 14c.

no-claims bonus or **no-claim bonus** ▷ *noun* a reduction in the fee one pays for insurance if one has made no claim for payment over a particular period. Also called **no-claims discount**.

noctambulation /'nɒktæmbju'leɪʃən/ ▷ *noun* sleep-walking. Also called **noctambulism**. • **noctambulist** *noun*. ① 18c: from Latin *nox, noctis* night + *ambulare, ambulatum* to walk.

nocti- /'nɒkti/ or (before a vowel) **noct-** ▷ *combining form, denoting* night. ① From Latin *nox, noctis* night.

English sounds: a hat; ʌ; baa; e bet; ə; ago; ʒ; fur; i fit; i; me; p lot; ɔ; raw; ʌ; cup; u put; u; too; at by

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start work at nine o'clock in the morning and finish at five, which are the hours worked in many offices from Monday to Friday: a *nine-to-five routine*

ninth /naɪnθ/ *determiner, pronoun, adj, adv* [not gradable], *n* • The ninth letter of the alphabet is I. • The school term ends on the ninth (of July). • She currently is/ranks ninth in the world. • A ninth (=one of nine equal parts) of 27 is 3. [C]

999 /ˌnaɪn-naɪn-naɪn/ *n* [U] the number used in Britain when telephoning for the emergency services • a hoax 999 call • There's been an accident - dial 999 and ask for an ambulance.

911 /ˌnaɪn-wʌn-wʌn/ *n* [U] the number used in the US when telephoning for the emergency services • Using my portable phone, I called 911 to summon emergency medical help.

nine-pins *Br* /ˈnaɪn-pɪnz/ *pl n* going down/falling like *ninepins* falling, breaking or being damaged, esp. in large numbers • Trees were going down like *ninepins* in the strong wind.

nineteen /ˌnaɪn-ti:n/ *determiner, pronoun, n* (the number) 19 • eighteen, nineteen, twenty • A group of students were trapped in the cave for nineteen hours. • Simson, aged nineteen, was convicted on two charges of burglary. • I'm looking for a birthday card with a nineteen on it. [C]

nineteenth /ˌnaɪn-ti:ntʃ/ *determiner, pronoun, adj, adv* [not gradable], *n* • She's an expert in nineteenth century industrial history. • "Which century was the cathedral built in?" "The nineteenth." • At the end of the first round, he was (lying) nineteenth. • (byfm) In golf, the nineteenth hole is a bar where people go to socialize after they have finished a game.

nine-ty /ˈnaɪn-ti, \$-tʃi/ *determiner, pronoun, n* (the number) 90 • eighty, ninety, a hundred • Ninety percent of the people surveyed said they were often tired. • We've got about ninety (people) coming to the party. • If something happens ninety-nine times out of a hundred it is almost certain to happen. • See also nine times out of ten at NINE.

nineties /ˈnaɪn-ti:z, \$-tʃi:z/ *pl n* • The nineties is the range of temperature between 90° and 99°. • The nineties is also the period of years between 90 and 99 in any century: Queen Victoria's diamond jubilee was in the nineties (=between 1890 and 1899). • A person's nineties are the period in which they are aged between 90 and 99: She was well into her nineties when she died.

nineteenth /ˈnaɪn-ti:θ, \$-tʃi:θ/ *determiner, pronoun, adj, adv* [not gradable], *n* • Tomorrow is Aunt Elma's nineteenth (birthday). • The team is lying nineteenth in the competition so far. • A nineteenth is one of ninety equal parts of something. [C]

nin-ja /ˈnɪn-dʒə/ *n* [C] (esp. in the past) a Japanese fighter who moves and acts without being seen and usually carries a short sword

ninny /ˈnɪn-i/ *n* [C] *infml* dated a foolish person

ninth /naɪnθ/ *pronoun, n, adj, adv* See at NINE

nip [GO QUICKLY] /nɪp/ *v* [I always + adv/prep] **pp** *Br* and *Aus* *infml* to go somewhere quickly or be somewhere for only a short time • Can you nip out/round to the shop for me? • Nip across to the neighbour's house and see if she's alright. • Shall we nip in to the bar for a bite to eat before the show? • (slightly dated) With the wind behind them they were nipping along (=travelling quickly) on their bikes.

nippy /ˈnɪp-i/ *adj* **Her, -lest** *Br* and *Aus* *infml* • It's a very nippy (=can change speed and direction easily) little car.

nip (obj) [PRESS QUICKLY] /nɪp/ *v* **pp** to press (something) quickly and quite hard between two, often sharp, objects such as teeth or the nails on fingers • It's alright sleeping in the loft - as long as the rats don't nip you! [T] • He dropped the crate which nipped his hand but he wasn't injured. [T] • This type of turtle will often nip at people who try to feed it. [I] • If you nip something in the bud you stop it before it has an opportunity to become established: Many serious illnesses can be nipped in the bud if they are detected early enough.

nip /nɪp/ *n* [C] • I gave my thumb quite a nip when the pliers slipped. • Nip and tuck is *Am* for neck and neck. See at NECK [BODY PART]. • (Am *infml*) Nip and tuck is also another way of saying plastic surgery (=a medical operation to repair or change a person's appearance): You could tell from the magazine photo that he'd had a little nip and tuck to make himself look younger. • (Am *infml*) A nip here and a tuck there means a series of small reductions: The department made a nip here and a tuck there but they were still way over budget.

nip [COLD] /nɪp/ *n* [U] a nip in the air *infml* quite cold • You can tell it's still spring - there's a real nip in the air in the mornings.

nippy /ˈnɪp-i/ *adj* **Her, -lest** *infml* • When the weather is nippy it is quite cold: It's a bit nippy today - you might need a coat.

nip [DRINK] /nɪp/ *n* [C] *Br* *infml* a small amount of strong alcoholic drink • a nip of gin

Nip [PERSON] /nɪp/ *n* [C] *taboo slang* (a very offensive word for) a Japanese person

nipper /ˈnɪp-ə, \$-ə/ *n* [C] *infml* a small child

nipple /ˈnɪp-əl/ *n* [C] the dark part of the skin which sticks out from the breast of a mammal and through which milk is supplied to the young • (Am) A nipple is also a TEAT.

nirvana /ˈnɪr.və.nə, \$nə-/ *n* [U] (in Buddhism) a high spiritual state of freedom from all suffering which is achieved by removing all personal desires, or (fig.) a state of perfection • (fig.) In her speech the candidate promised a nirvana of better jobs, less crime, and more education.

Nissen hut /ˈnɪs-ən/ *n* [C] a building shaped like a tube cut along the middle made from CORRUGATED iron sheets

nit [PERSON] /nɪt/ *n* [C] *Br* and *Aus* *infml* disapproving a NITWIT

nit [EGG] /nɪt/ *n* [C] the egg of an insect, esp. a LOUSE, which is sometimes found sticking to people's or animal's hair

nit-picking /ˈnɪt.pɪk-ɪŋ/ *adj, n* *infml* disapproving (showing) too much interest in unimportant details, esp. as a way of criticizing • a nitpicking attitude • If you spend less time nitpicking you'd get more work done. [U]

nit-pick /ˈnɪt.pɪk/ *v* [I] • Must you nitpick (=find fault with details) all the time?

nit-pick-er /ˈnɪt.pɪk-ə, \$-ə/ *n* [C]

nitrate /ˈnaɪ-treɪt/ *n* a chemical which includes NITROGEN and oxygen, often used as a FERTILIZER (=a substance which helps plants to grow) • potassium/sodium nitrate • If too much nitrate is used on an area it can contaminate local water supplies. [U] Nitrogen is converted into nitrates in the soil which plants can then use. [C]

nitric acid /ˈnaɪ-trɪk/ *n* [U] a very acidic transparent colourless liquid which is used in making many chemicals, esp. FERTILIZERS and explosives

nitrogen /ˈnaɪ-trɒ-dʒən/ *n* [U] a gaseous element having neither colour nor taste which forms about 78% of the Earth's ATMOSPHERE and is a part of all things which live

nitro-glycerine /ˈnɪ.trəʊˈglɪs-ɪn, \$-trouˈglɪs-ə-, Am also **nitro-glycer-in** *n* [U] a very powerful liquid explosive

nitty-gritty /ˈnɪ.tɪˈgrɪt-i, \$nɪ.tɪˈgrɪt-i/ *n* [U] the nitty-gritty *infml* the basic facts of a situation • Let's get down to the nitty-gritty - when can you finish the building and how much will it cost?

nitwit /ˈnɪt-wɪt/, **nit** *n* [C] *infml* disapproving a foolish or stupid person • You're such a nitwit - you're bound to fall off your bike if you ride it on ice. • Get down from that tree right now, nitwit! [as form of address]

nix obj /nɪks/ *v* [T] *Am* *infml* to stop, forbid or refuse to accept (something) • The film studio nixed her plans to make a sequel.

nix /nɪks/ *n* [U], *adv* [not gradable] *Am* *infml* • All that effort for nix (=nothing). • I suppose mom will say nix to us going (=say we cannot go) to the movies.

no [NOT ANY] /nəʊ, \$nou/ *determiner* not any; not one; not a • There's no butter left. • No trees grow near the top of the mountain. • That's my kind of holiday - no telephone, no TV and no worries. • Not surprisingly no life forms were detected on the planet. • There's no chance (=no possibility) of us getting there by eight. • She no longer goes (=does not continue to go) to music lessons. • There is no doubt in my mind that he is the person I saw with the gun. • In signs and official notices, 'no' is used to show that something is not allowed: No smoking/fishing • This waiting is the worst part - the audition itself will flash by in no time (=very quickly). • (infml) We're so pleased you came, you cheered us up no end (=a lot). • (infml) They tried for hours to persuade her to come down from the roof, but it was no go (=impossible or hopeless). • (infml) "Will you be able to repair the light?" "Yeah, no problem/sweat (=without any serious difficulties)." • (infml) If someone says there's no knowing/telling/saying they mean it is not possible to know what will happen: She's very unpredictable so there's no knowing how she'll react to the news. • (Am *infml*) No-account means (a person who is) of little use. • In cricket and some other games a no-ball is when the ball is BOWLED (=thrown) in a way which is not allowed by the rules. • (Br

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camouflage. [Japanese, from *nin* 'stealth' + *jutsu* 'art, science']

ninny *n.* (pl. **-ies**) *colloq.* a foolish or simple-minded person.

ninth *n.* **1** the position in a sequence corresponding to the number 9 in the sequence 1-9. **2** something occupying this position. **3** each of nine equal parts of a thing. *adj.* that is the ninth. *n* **ninthly** *adv.*

niobium *n.* *Chem.* a rare grey-blue metallic element occurring naturally. [named after Niobe, daughter of Tantalus, because first found in tantalite, rare black mineral]

nip *v.* (**nipped**, **nipping**) **1** *tr.* pinch, squeeze, or bite sharply. **2** *tr.* (often foll. by *off*) remove by pinching etc. **3** *tr.* (of the frost etc.) cause pain or harm to. **4** *intr.* (foll. by *in*, *out*, etc.) *Brit. colloq.* go nimbly or quickly. *n.* **1** *a* a pinch, a sharp squeeze. **b** a bite. **2** biting cold. *n* **nip in the bud** suppress or destroy (esp. an idea) at an early stage. [Middle English] *n* **nipping** *adj.*

nip *n.* a small quantity of spirits.

nip and tuck *n.* *colloq.* a cosmetic surgical operation. *adv.* *N. Amer.* neck and neck.

nipper *n.* **1** a person or thing that nips. **2** the claw of a crab, lobster, etc. **3** *Brit. colloq.* a young child. **4** (in pl.) any tool for gripping or cutting.

nipple *n.* **1** *a* a small projection in which the mammary ducts of female mammals terminate and from which milk is secreted for the young. **b** an analogous structure in the male. **2** the teat of a feeding bottle. **3** a device like a nipple which disperses liquids. **4** a device on the casing of a bearing through which grease is introduced using a grease gun. **5** a nipple-like protuberance. [16th-century coinage]

nipplewort *n.* a yellow-flowered weed, *Lapsana communis*.

nippy *adj.* (**nippier**, **nippiest**) *colloq.* **1** quick, nimble, active. **2** chilly, cold. *n* **nippily** *adv.*

nirvana *n.* (in Buddhism) perfect bliss and release from karma, attained by the extinction of individuality. [from Sanskrit *nirvāṇa*]

nisei /nee-say/ *n.* (also **Nisei**) *US* an American whose parents were immigrants from Japan. [Japanese, literally 'second generation']

Nissen hut *n.* a tunnel-shaped hut of corrugated iron with a cement floor. [named after P. N. Nissen, British engineer, 1871-1930, its inventor]

nit *n.* **1** the egg or young form of a louse or other parasitic insect. **2** *Brit. colloq.* a stupid person. [Old English]

niter *US* var. of **NITRE**.

nit-picking *n.* *S* *adj. colloq.* criticizing in a petty manner. *n* **nit-pick** *v.intr.* **nit-picker** *n.*

nitrate *n.* **1** any salt or ester of nitric acid. **2** potassium or sodium nitrate when used as a fertilizer. *v.tr.* *Chem.* treat, combine, or impregnate with nitric acid. *n* **nitration** *n.*

nitre *n.* (*US* **nitrate**) saltpetre, potassium nitrate. [from Greek *nitron*]

nitric *adj.* of or containing nitrogen.

nitric acid *n.* a colourless or pale yellow corrosive poisonous liquid acid.

nitric oxide *n.* a colourless toxic gas, involved in physiological processes in minute quantities, and forming nitrogen dioxide in air.

nitride *n.* *Chem.* a compound of nitrogen with another element or radical.

nitri *v.tr.* (**-ies**, **-ied**) **1** impregnate with nitrogen. **2** convert into nitrites or nitrates. [from French *nitrifier*] *n* **nitrication** *n.*

nitrile *n.* *Chem.* an organic compound consisting of an alkyl radical bound to a cyanide radical.

nitrite *n.* any salt or ester of nitrous acid.

nitro- *comb. form* **1** of or containing nitric acid, nitre, or nitrogen. **2** made with or by use of any of these. **3** of or containing the monovalent -NO₂ group. [Greek]

nitrobenzene *n.* a yellow oily liquid made by the nitration of benzene and used to make aniline etc.

nitrocellulose *n.* a highly flammable material made by treating cellulose with concentrated nitric acid.

nitrogen *n.* *Chem.* a colourless odourless unreactive gaseous element that forms four-fifths of the earth's atmosphere. [from French *nitrogène*] *n* **nitrogenous** *adj.*

nitrogen cycle *n.* *Ecol.* the series of processes by which nitrogen is absorbed from and returned to the atmosphere by biological systems.

nitrogen dioxide *n.* a reddish-brown poisonous gas.

nitroglycerine *n.* (also **nitroglycerin**) an explosive yellow liquid made by reacting glycerol with a mixture of concentrated sulphuric and nitric acids.

nitrous *adj.* of, like, or impregnated with nitrogen.

nitrous acid *n.* a weak acid existing only in solution and in the gaseous state.

nitrous oxide *n.* a colourless gas used as an anaesthetic and as an aerosol propellant.

nitty-gritty *n.* *slang* the realities or practical details of a matter. [20th-century coinage]

nitwit *n.* *colloq.* a stupid person. *n* **nitwitty** *n.*

nix *slang* *n.* **1** nothing. **2** a denial or refusal. *v.br.* **1** cancel. **2** reject. [German, colloquial variant of *nichts* 'nothing']

NMR *abbr.* (also **nmr**) nuclear magnetic resonance.

NNE *abbr.* north-north-east.

NNW *abbr.* north-north-west.

No *1* *ymb.* *Chem.* the element nobelium.

No *2* *var.* of **NOH**.

No. *abbr.* **1** number. **2** *US* North. [sense **1**: from Latin *numero* 'by number']

no *1* *det.* **1** not any (there is no excuse). **2** not a, quite other than (is no fool). **3** hardly any (did it in no time). **4** used elliptically in a notice etc., to forbid, reject, or deplore the thing specified (no parking). *n* **by no means** see **MEANS**. *n* **dice** see **DICE**. *n* **no doubt** see **DOUBT**. *n* **no end** see **END**. *n* **no fear** see **FEAR**. *n* **no little** see **LITTLE**. *n* **no man** no person, nobody. *n* **no place** *US* nowhere. *n* **no small** see **SMALL**. *n* **no sweat** *colloq.* no bother, no trouble. *n* **no thoroughfare** an indication that passage along a street, path, etc., is blocked or prohibited. *n* **no through road** = *no thoroughfare*. *n* **no time** see **TIME**. *n* **no way** *colloq.* **1** it is impossible. **2** I will not agree etc. *n* **wonder** see **WONDER**. ... or **no** ... regardless of the ... (rain or no rain, I shall go out). *n* **there is no ...ing it is**

Abbreviations Dictionary

Tenth Edition

Dean Stahl
Karen Kerchelich

Originated by Ralph De Sola

★ Abbreviations ★ Acronyms ★ Airlines and Airports ★ Appellations
★ Astronomical Terminology ★ Bafflegab Divulged (euphemisms
explained) ★ Birthstones ★ Chemical Elements ★ Citizen's-Band Call
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- nni noise and number index (sound pollution)
- NNI Norwegian Nobel Institute
- NNI *Nederlands Normalisatie Instituut* (Dutch—Netherlands Standards Institute)
- nnk (NNK) notify next of kin
- NNL Nigerian National Line
- NNLC National Negro Labor Council
- nnm next new moon
- NNMC National Naval Medical Center
- nnn no national name; no native named
- NNN Nihon News Network; Novy-Nicolle-McNeal (bacteriological culture)
- NNNR Noss National Nature Reserve (Shetlands)
- NNO National Night Out
- NNO *noord noordoost* (Dutch—north northeast)
- NNOC Nigerian National Oil Company
- n. nov. nomen novum* (Latin—new name)
- nnp (NNP) net national product
- NNP Nairobi National Park (Kenya); Ngezi National Park (Zimbabwe), Nimule National Park (Sudan)
- NNPA National Negro Press Association; National Newspaper Promotion Association; National Newspaper Publishers Association; Nuclear Non-Proliferation Act (1978)
- n-n p-i-f* never-never pay-in-full (installment plan)
- NNPP Naval Nuclear Propulsion Program (USN)
- NNPT Nuclear Non-Proliferation Treaty
- NNR New and Nonofficial Remedies
- NNRC Neutral Nations Repatriation Commission
- NNRI National Nutrition Research Institute
- NNRO *Norske Nasjonalkomite for Rasjonell Organisasjon* (Norwegian National Committee for Scientific Management)
- nns (NNS) Navy navigation satellite
- nn's nubile nymphs
- n N's nice Nellyisms, euphemisms
- n-N's neo-Nazis
- N Ns Newport News
- NNS National Newspaper Syndicate
- NNSC Neutral Nations Supervisory Commission
- NNS & DDC Newport News Shipbuilding and Dry Dock Company
- NNSL Nigerian National Shipping Line
- nnsn no national stock number
- NNSS Navy Navigational Satellite System
- NNTO Netherlands National Tourist Office; Norwegian National Travel Office
- NNTT National New Technology Telescope
- NNW north northwest
- NNW *noord noordwest* (Dutch—north northwest)
- NNWR Necedah National Wildlife Refuge (Wisconsin); Noxubee National Wildlife Refuge (Mississippi)
- nnws non-nuclear weapon states
- NNWSI Nevada Nuclear Waste Storage Investigation
- no natural order; normally open; north; number
- no (NO) neuromyelitis optica
- n-o not or
- n/o no orders
- no norsk* (Dano-Norwegian—Norwegian); *nummer* (Dutch—number)
- nº número* (Spanish—number)
- no. numero* (Latin—number)
- No nobelium; Norskie (Norwegian-American); Norway; Norwegian; number
- NO Naval Observatory; Naval Officer, New Order; New Orleans; nitrous oxide; North Central Airlines; Norway (Internet code); Nuffield Observatory (Jordrell Bank, England); Nursing Officer
- NO *noordoost* (Dutch—northeast); *Nordosten* (German—northeast); *noroste* (Spanish—northwest)
- No 1 first; first quality; first rate; first person; most important; most important person; number one
- No 2 next in line; next-in rank; number two; second; second person; second quality; second rate
- NO₂ nitrogen dioxide
- No 10 Number 10 Downing Street (London residence of the British prime minister)
- noa net operating assets; new obligational authority (NOA); not operationally assigned; not otherwise authorized
- n-o-a not-or-and
- NOA National Onion Association; National Opera Association; National Optical Association; National Orchestral Association
- NOAA National Oceanic and Atmospheric Administration
- NOAB National Outdoor Advertising Bureau
- NO-AB New Orleans-Algiers Bridge
- NOADS Newspapers Opposed to Advertising Death by Smoking
- NOAH New Opportunities for Animal Health scientists
- NOAL National Order of Arts and Letters
- noala noise-operated automatic level adjustment
- NOAOs National Optical Astronomy Observatories
- NOASSR North Ossetian Autonomous Soviet Socialist Republic
- nob no open burning; nobility; noble; not on board
- nob nabob* (Urdu—viceroy)
- nob. nobis* (Latin—to us)
- NOB National Oil Board; Naval Operating Base; Naval Order of Battle
- NOB *Nationaal Orkest van Belgie* (Flemish—National Orchestra of Belgium)
- Nobelst Nobelstiftelsen* (The Nobel Foundation)
- no biz no business
- NOBLEE National Organization of Black Law Enforcement Executives
- Noble Patria Noble Patria' tu hermosa bandera* (Spanish—Noble country, your lovely flag)—Costa Rican anthem
- NOB spread price differential between Treasury notes and Treasury bonds
- NOBE Nordstrom Incorporated
- noc not otherwise classified; notation of content(s)

T H E

Barnhart
Abbreviations
Dictionary

Edited by
Robert K. Barnhart



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Ref
PE1693
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NMU National Maritime Union.

NN or **N.N.** neutralization number *chemistry*.

N/N or **n/n** not to be noted *commerce*.

nn. 1 also **NN.** names. [Latin *nomina*] 2 nerves *medicine*. 3 notes.

n.n. no name.

NNA National Newspaper Association.

N.N.D. New and Nonofficial Drugs (publication).

NNE or **N.N.E.** or **n.n.e.** north-northeast.

NNI or **n.n.i.** noise and number index (in acoustic evaluation of ambient noise).

n. nov. new name *taxonomy*. [Latin *nomen novum*]

NNP Net National Product (Gross National Product after deduction for depreciation and value of capital and business services used in production).

NNPA National Newspaper Publishers Association.

N.N.R. New and Nonofficial Remedies (publication).

NNSS Navy Navigation Satellite System.

NNW or **N.N.W.** or **n.n.w.** north-northwest.

NO 1 also **N.O.** natural order (family in plant classification) *botany*. 2 naval officer. 3 Navigation Officer. 4 also **N.O.** New Orleans. 5 also **N/O** no orders *commerce*. 6 also **n.o.** normally open: **NO** circuit or switch. 7 also **N/O** not operating.

No 1 an abbreviation for: 1 also **No.** north, northern. 2 number. [Latin *numero*]

II a symbol for: nobelium (chemical element).

no 1 net. [German *netto*] 2 also **no.** north, northern. 3 nose (esp. in horse racing). 4 also **n.o.** not out *cricket*. 5 also **no.** number. [Latin *numero*]

NOA 1 betanaphthoxyacetic acid (plant growth hormone). 2 also **N.O.A.** National Opera Association. 3 new obligation authority (U.S. Government commitment to future expenditures). 4 also **n.o.a.** not otherwise authorized.

NOAA (nō'a) National Oceanic and Atmospheric Administration (of U.S. Department of Commerce).

NOAO National Optical Astronomy Observatories.

Nob. noble.

nob. for or on our part. [Latin *nobis*]

NOC 1 National Olympic Committee. 2 also **n.o.c.** not otherwise classified.

Noct. nocturne *music*.

noct. during the night *pharmaceutics*. [Latin *nocte*]

NOD night observation device.

NODC National Oceanographic Data Center.

NODL National Office for Decent Literature (of the Catholic Church in the U.S.).

NOE or **n.o.e.** not otherwise enumerated.

NOFI National Oil Fuel Institute.

NoHo (nō'hō') North of Houston Street (area in New York City that is a center of avant-garde art, music, film, and fashion).

NOHP or **n.o.h.p.** not otherwise herein provided.

NOIBN or **n.o.i.b.n.** not otherwise indexed by name (esp. of goods subject to tariff) *commerce*.

nok or **NOK** next of kin.

NOL Naval Ordnance Laboratory.

noI. con. I do not wish to contend *law*. [Latin *nolo contendere*]

noI. pros. will not continue or not willing to prosecute *law*. [Latin *nolle prosequi*]

nom. 1 nomenclature. 2 nominal. 3 nominated. 4 nominative *grammar*.

NOMA National Office Management Association.

NOMAD Navy Oceanographic Meteorological Automatic Device (fixed broadcasting station for monitoring oceanic conditions of temperature, barometric pressure, and wind speed and direction).

nom. cap. nominal capital *commerce*.

nomen. nomenclature.

nomin. nominative *grammar*.

nom. nov. new name *taxonomy*. [Latin *nomen novum*]

nom. nud. name alone (unsupported by technical description) *taxonomy*. [Latin *nomen nudum*]

NOMSS National Operational Meteorological Satellite System.

Non. nones (the religious office or hour once celebrated about nine hours after sunrise or the ninth day before the ides in the calendar of ancient Rome).

noncom (non'kom') or **military NONCOM** noncommissioned officer.

non cul. not guilty *law*. [Latin *non culpabilis*]

non obs. or **non obst.** notwithstanding. [Latin *non obstante*]

non pros. he or she does not prosecute *law*. [Latin *non prosequitur*]

non rep. do not repeat *pharmaceutics*. [Latin *non repetatur*]

non res (non'rez') or **Non Res.** nonresident: *non res. num.* = *nonresident number*.

non seq (non'sek') it does not follow (of the logic or subject of a statement or argument). [Latin *non sequitur*]

nonstand or **nonstd** nonstandard.

non-U (non'yū) not upper class (original British informal usage for something tending to be common or informal).

NOO Naval Oceanographic Office.

no op or **No op 1** nonoperational. 2 no operation *computers*.

NOP 1 British National Opinion Polls. 2 a no operation *computers*. b nonoperation, nonoperational. 3 also **n.o.p.** not otherwise provided for. 4 not our publication.

NOPA National Office Products Association.

no par. no paragraph (in preparing copy).

NOPEC (nō'pek) non-OPEC (of oil-producing countries, not members of OPEC).

NOPHN National Organization for Public Health Nursing.

NOR 1 not operationally ready, also in combination: **NORS** = *not operationally ready (until) supplied*. 2 **NOT-OR** (logic operator) *mathematics, computers*.

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AND SYMBOLS

compiled and edited
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ELSEVIER

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1 NNF National Nanofabrication Facility

Micro-engineering - The NNF started about twenty years ago at Cornell University - U.S.A.

NNISS National Nosocomial Infections Surveillance System - U.S.A.

NNMC National Naval Medical Center - U.S.A.

N-N-O Nord-Nord-Ovest

NNRLIS *Library Associations* - National Natural Resources Library and Information System

NNS Non-Native Speakers

Linguistics

NO Nitric Oxide

Inorganic Chemistry

NO₂ Nitrogen Dioxide

Inorganic Chemistry - Nitrogen Dioxide is a brown gas that has a melting point of -9.3°C. It is used mainly in the production of nitric acid

No The chemical symbol for Nobelium

Symbols

N-O Nord-Ouest

NO Novara, Italy

NOAA National Oceanic and Atmospheric Administration - U.S.A.

NOCLA *Library Associations* - Negroes Occidental Library Association

NODC National Oceanographic Data Center

NOD mice Nonobese Diabetic mice

nod The above acronym was coined using the English word: "nod"

NOE Nuclear Overhauser Effect

Noè The above acronym was coined accidentally using the Italian word "Noè" which means: Noah

NOLM Nonlinear Optical Loop Mirror

Materials Science

NOMLAC Newsletter On Military Law And Counseling - U.S.A.

NORAD system North American Air Defence system

NATO acronym - The air defence of Canada and the United States is coordinated in the North American Air Defence system

(*App. 8 - n° 49*)

NORC National Opinion Research Center - U.S.A.

Of the University of Chicago, U.S.A. - NORC was established in 1941. During the war it carried out hundreds of surveys for government agencies. Since the war it has become a major university-affiliated social research organization.

NORD National Organization for Rare Disorders - U.S.A.

nord The above acronym was coined accidentally using the Italian word "nord" which means: north (*Geodesy*)





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NICOTINE PATCH

you could raise interest from foreign investors who wanted into that niche.

—*European Investor* May 1990, p. 10

Mr Kitayama believes that Japan's banks will fall into two groups: those 'offering the full range of financial services to the entire market' and 'niche players'.

—*Economist* 2 May 1992 (Survey of World Banking Supplement) p. 49



Niche marketing and strategic alliances can give you greater clout in the markets of the Middle East and Pan Pacific.

—advertisement in *Esprit de Corps* (Ottawa, Ontario) Aug. 1994, p. 38

The company now specialises in one of the UK's most substantial niche markets, dealing primarily with individual clients and landed estates.

—*Guardian* 26 Apr. 1995, section 1, p. 15

nicotine patch  see PATCH

nigga /'nɪgə/ noun  

A black man.

A representation of American Black English pronunciation of the word *nigger*.

This and other forms of *nigger* have long been in use within the AFRICAN-AMERICAN community and have been recorded in print since the twenties. However, recent usage of *nigga*, and its plural form *niggaz*, represents a conscious, politically motivated reclamation by blacks of the term *nigger*. This term, which had been regarded as typifying offensive and derogatory attitudes within the white community, was adopted by the black community as a form of self-assertion, with the aim of reducing the term's derogation. (A similar development may be seen in the adoption of the word *queer* by the gay community; see QUEER NATION.) The recent uptake of the term *nigga* has been given impetus by its use in rap lyrics and within the HIP-HOP culture, and by its adoption as a name by some black groups, notably the Los Angeles trio *Niggaz with Attitude* (or *N.W.A.*). Its use is largely restricted to the black community, and both *nigga* and *nigger* remain offensive when used by white people.

Further use of this vernacular respelling of the *-er* element may be seen in terms such as *GANGSTA*, in the name of the group *Gravediggaz*, and in the formulation *brotha*. Further respellings, such as *dat* for *that* and *tha* for *the*, are similarly used in affirmation of contemporary black culture.

After South Central Los Angeles was plastered with posters promoting N.W.A.'s new '100 Miles and Runnin' album with the tag line 'Tha Niggaz R Back', some of the most immediate response came not from fans but from alleged white supremacists who were unable to define the posters' origins.

—*Los Angeles Times* 15 Oct. 1990, section D, p. 2

These guys were in shock—they had no idea that black people sometimes call each other nigga as a term of endearment. They saw the brothers at the party shouting 'What's up nigga?' to one another and one of my white friends got so excited he started yellin'. 'Hey! How you niggas doing?' The music stopped and everyone looked at them.


—*The Face* Sept. 1993, p. 69

Niggas would come to school with them in their back pockets, and I would read 'em and think, 'Oh my God, it's the phattest shit in the world', because it's exactly what hardcore rap is: it's the lingo, it's life, it's the whole life we live.

—Brian Cross *It's Not About a Salary* (1993), p. 182

We went through a regular struggle, a lot of niggaz got chopped off in the process, and seein' that, we was able to make us stronger.

—*Represent* Apr. 1995, p. 31

no-fly /nəʊ 'flaɪ/ adjective 

Designating an area in which military, and occasionally civil, aircraft are forbidden to fly; especially in the phrase **no-fly zone**. Also, designating the order to enforce, or the enforcement of, such an area.

The determiner *no* is used elliptically with the verb *fly* to form an adjective, following the model of *no-go*.

Use of this formulation has been recorded since the late eighties. The term *no-fly zone* has been made familiar to the general public through its frequent use in reports of recent conflicts,

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mething that nips: as **a** *archaic*: a sharp biting or stinging cold (a ~ in the air) **c**: a biting or sting (cheese with a ~) **2**: the act of nipping the region of a squeezing or crushing device (as a rolls or jaws are closest together **4**: a small por-

kin, a liquor container) (ca. 1796): a small quantity: a very small bottle of liquor
 to take liquor in nips: **TIPPLE** (1887): to take liquor in nips: **TIPPLE**
ip, fr. It, fr. Malay *nipah* nipa palm) (1779): thach: nipa palm
 (d)-tək\adj or adv (1832): being so close that the fits rapidly from one opponent to another
 a southeast Asian palm (*Nipa fruticans*) growing and estuaries and having a short underground pinnate leaves
51 **1**: any of various devices (as pincers) for in pl. **2** **a** chiefly Brit: a boy employed as a help-awker **b**: CHILD; **esp**: a small boy
HARE, CHILLING (a ~ wind) — **nip-ping-ly** -lē

lier noble, nible, prob. dim. of *neb, nib*) (ca. 1530) of a mammary gland upon which in the female open and from which milk is drawn **2** **a**: an artificial a bottle-fed infant nurses **b**: a device with which the discharge of a liquid can be regulated **3** resembling or suggesting the nipple of a breast **4** rough which oil or grease is injected into machining consisting of a short piece of threaded tubing
iz, -'nēs\adj [*Nippon*, Japan] (1859): JAPANESE

pi-er; -est (1575) **1**: marked by a tendency to risk, quick, or nimble in movement: **SNAPPY** **3** **d**: CHILLY, CHILLING (a ~ day) — **nip-pily** -pi-nēs\ **nip-pé-nās** **n**
38 **1**: a spring from a supine position to a stand-

nar-\n, often cap [SKT *nirvāna*, lit., act of extinguish it blows — more at **WIND**] (1801) **1**: the if-scends suffering, karma, and *samsara* and b through the extinction of desire and individual: a place or state of oblivion to care, pain, or ex-CESS, **HEAVEN** **b**: a goal hoped for but apparent — **nir-van-ic** -vā-nik, -'vā-adj
v [*Heb Nisan*] (14c): the seventh month of the onth of the ecclesiastical year in the Jewish cal-
nd [first *often cap* [*JP*, lit., second generation, fr. ion] (1929)]: a son or daughter of Japanese in-nd educated in America and esp. in the U.S.
SS, fr. *ne- not* + *st* [*IG*] (ca. 1836): taking effect at previously modified or avoided by cause shown, a condition fulfilled (ca. decree ~)
Peter N. Nissen 1930 Brit. mining engineer) shelter with a semicircular arching roof of con-nd a concrete floor
 itute of Standards and Technology
SUS -'sās, -'sūs\ **n**, fr. *mit* to lean, rely, striv-; **nk** — more at **CONVINE**] (1699): a mental or an end: a persuasive urge or endeavor
DE hntiu: akin to OHG *hntiz* nit, Gk *konid*, *ko-* of a louse or other parasitic insect; also: the **2**: a minor shortcoming
it: **NITWIT**
ional Tournament

atron, fr. MF, fr. L *nitrum*, fr. Gk *nitron*, fr. POTASSIUM NITRATE **2** *archaic*: CHILE SALT

-t-rē\n, pl **nitr-er-ies** [nīte + *ery* (as in *eateny*): *ary*] (ca. 1934) **n**: NIGHTCLUB
idus — more at **NEAT**] (1619): BRIGHT, LUS-

v **n** [nickel + titanium and -*nol* (fr. *Naval Ordnance*) (1968)]: a nonmagnetic alloy lat after being deformed returns to its original ed
ck-formation fr. *nit-picking* **vi** (1966) **to** **en**: to criticize by nit-picking — **nitpick** **n** -ky\ -pi-kē\adj
n [*nit*] (1956): minute and usu. unjustified

nter **1**: nitrogen (*nitride*) **2** usu *nitro-* gen compound NO₂ (nitrobenzene)
[F, fr. *nitrique*] (1788): a salt or ester of nite-ate or potassium nitrate used as a fertilizer
odium nitrate used as a fertilizer
1 (1887): the process of adding a nitro group
 — **nit-rate** -ni-'trāt\ **vi** — **nit-ra-tor** -vā-

nitri-fi-ca-tion \ni-'trō-'fi-kā-shən\ **n** (1827): the oxidation (as by bac-teria) of ammonium salts to nitrites and the further oxidation of ni-rites to nitrates
itri-fy-ing \ni-'trō-'fi-(ə)-iŋ\ **n** (1903): any of the nitrifying bacteria
itri-fy-ing \ni-'trō-'fi-lj\ **adj** [*F* *nitrifier* to convert into nitrite, fr. *nitr-*] (1827): active in or relating to nitrification (~ organisms)
nitrifying bacteria **n** (1925): bacteria of a family (Nitrobacteraceae) comprising gram-negative bacteria commonly found in the soil and ob-taining energy through the process of nitrification
nitro \ni-'trō-, -tri-(ə)-\ **n** [*ISV* *nitr-* + *-il*, *-ile* (fr. L *-iliv* -ite)] (1848): an organic cyanide containing the group CN which on hydrolysis yields an acid with elimination of ammonia
nitrite \ni-'tri't\ **n** (1788): a salt or ester of nitrous acid
nitro-ni-(ə)trō \ni-'trō-'ni-(ə)-\ **adj** [*nitr-*] (1881): containing or being the monovalent group NO₂ united through nitrogen
nitro-ni \ni-'trō-'ni-\ **n** (1903): any of various nitrated products; **specif**: **NI-TROGLYCERIN**
nitro-ben-zene \ni-'trō-'ben-zēn-, -ben-'n\ **n** [*ISV*] (1868): a poisonous yellow oily liquid C₆H₅NO₂ with an almond odor that is used esp. in chemical synthesis (as of aniline)
nitro-cell-u-lo-se \ni-'trō-'sēl-yə-'loz-, -'lōz\ **n** [*ISV*] (1882): any of several nitric-acid esters of cellulose used esp. for making explosives, plastics, and varnishes
nitro-fu-ran \ni-'trō-'fyū-rən-, -fyū-'rən\ **n** (1930): any of several nitro-derivatives of furan used as bacteria-inhibiting agents
nitro-gen \ni-'trō-'jən\ **n**, often *nitri* [*F* *nitrogen*, fr. *nitre* niter + *-gēn*] (1794): a colorless tasteless odorless element that as a diatomic gas is relatively inert and constitutes 78 percent of the atmosphere and that is a constituent of organic compounds found in all living tissues — see ELEMENT table — **nitr-er-ous** -ni-'trē-rə-'nēs\ **adj**
nitro-ge-nase \ni-'trō-'jə-'nās-, -ni-'trō-'jə-, -'nāz\ **n** (1934): an enzyme of various nitrogen-fixing bacteria that catalyzes the reduction of molecu-lar nitrogen to ammonia
nitrogen balance **n** (1944): the difference between nitrogen intake and nitrogen loss in the body or the soil
nitrogen cycle **n** (1908): a continuous series of natural processes by which nitrogen passes successively from air to soil to organisms and back to air or soil involving principally nitrogen fixation, nitrification, decay, and denitrification
nitrogen dioxide **n** (1869): a toxic reddish brown gas NO₂ that is a strong oxidizing agent, is produced by combustion (as of fossil fuels), and is an atmospheric pollutant (as in smog)
nitrogen fixation **n** (1895): the metabolic assimilation of atmospheric nitrogen into ammonia by soil microorganisms and esp. rhizobia
nitrogen-fixer **n** (1912): any of various soil microorganisms that are involved in nitrogen fixation
nitrogen-fixing \ni-'trō-'fiks-iŋ\ **adj** (1899): capable of nitrogen fixation (~ bacteria)
nitrogen mustard **n** (1943): any of various toxic blistering com-pounds analogous to mustard gas but containing nitrogen instead of sulfur
nitrogen narcosis **n** (1937): a state of euphoria and confusion similar to that of alcohol intoxication which occurs when nitrogen in normal air enters the bloodstream at increased pressure (as in deep-water diving) — called also *rupture of the deep*
nitrogen oxide **n** (1869): any of several oxides of nitrogen most of which are produced in combustion and are considered to be atmo-spheric pollutants: **a**: NITRIC OXIDE **b**: NITROGEN DIOXIDE **c**: NITROUS OXIDE
nitrogen tetroxide **n** (1869): a colorless toxic gas N₂O₄ that is a dimer of nitrogen dioxide and that in liquid form is used as an oxidizer in rocket engines
nitro-glyc-er-ol or **ni-tro-glyc-er-ine** \ni-'trō-'glis-er-ən-, -'gli-sē-'n\ **n** [*ISV*] (1857): an oily explosive poisonous liquid C₂H₅N₃O₇ used chief-ly in making dynamite and in medicine as a vasodilator
nitro-meth-ane \ni-'trō-'mē-'thən-, Brit usu -'mē-'n\ **n** (1872): a liquid nitro-para-ffin CH₃NO₂ that is used as an industrial solvent, in chemical syn-thesis, and as a fuel for rockets and high-performance engines
nitro-par-af-fin \ni-'trō-'pā-rə-'fən\ **n** [*ISV*] (1892): any of various nitro-derivatives of alkanes
nitros- or **nitroso-** *comb form* [*NL* *nitrosus* nitrous]: containing the group NO (*nitrosamine*)
ni-tro-sa-mine \ni-'trō-'sə-'mēn\ **n** (1878): any of various organic com-pounds which are characterized by the grouping NNO and some of which are powerful carcinogens
nitrous \ni-'trō-'s\ **adj** [*NL* *nitrosus*, fr. L, full of natron, fr. *nitrum* na-tron — more at **NITER**] (1601) *archaic*: of, relating to, or containing ni-trous acid **n** (1788): an unstable acid HNO₂ known only in solution or in the form of its salts or esters
nitrous oxide **n** (1798): a colorless gas N₂O that when inhaled produc-es loss of sensibility to pain preceded by exhilaration and sometimes laughter, that is used esp. as an anesthetic in dentistry and as a fuel, and that is an atmospheric pollutant and greenhouse gas produced by com-bustion — called also *laughing gas*
nitry-grit-ty \ni-'trī-'grī-tē-, -grī-tē-\ **n** [*origin unknown*] (1956): what is essential and basic: specific practical details (get down to the ~ of the problem) — **nitty-gritty** **adj**
nit-wit \ni-'wit\ **n** [*prob. fr. G dial. nit not + E wit*] (ca. 1922): a scat-terbrained or stupid person
NIU abbrev network interface unit
nix \nix\ **n** [*G* *nichts* nothing] (1789): **NOTHING**
nix **vi** (ca. 1903): **NETO**, **REJECT** (the court ~ed the merger)
nix **adj** (1902): **NO** — used to express disagreement or the withholding of permission; **often used with on** (they said ~ on our plan)
nix **n** [*G*, fr. OHG *nihhus*; akin to OE *nicor* water monster and perh. to Gk *niein* to wash] (1833): a water sprite of Germanic folklore
nixie \nix-'ē\ **n** [*G* *Nix* female *nix*, fr. OHG *nichessa*, fem. of *nihhus* oix] (1816): **NIX**
ni-zam \ni-'zām-, -ni-'zām-, -ni-'zām-\ **n** [*Hindi* & *Urdu nizam*, order, govern-our, ultim. fr. *Ar* *nihzam*] (1768): one of a line of sovereigns of Hyder-abad, India, reigning from 1713 to 1950 — **ni-zam-ate** -ni-'zā-'māt-, -zā-'n\ **n**
NJ abbrev New Jersey
NK cell \ven-'kā-\ **n** (1979): NATURAL KILLER CELL

NKVD *abbr* [*Russ* *Narodnyj komissariat vnutrennikh del*] People's Com-missariat of Internal Affairs
NL *abbr* **1** National League **2** Newfoundland and Labrador
NLCS *abbr* National League Championship Series
NLF *abbr* National Liberation Front
NLRB *abbr* National Labor Relations Board
nm *abbr* **1** nanometer **2** nautical mile
NM *abbr* New Mexico
NMDA \nem-'(d)jə-'dā-\ **n** [*N-methyl-D-aspartate*] (1986): a synthetic amino acid C₇H₉NO₄ that binds selectively to a subset of glutamate re-ceptors on neurons where the binding of glutamate results in the open-ing of calcium channels
N Mex *abbr* New Mexico
NMHA *abbr* National Mental Health Association
NMI *abbr* no middle initial
NMR *abbr* nuclear magnetic resonance
NNW *abbr* north-northwest
no \nō\ **adv** [*ME*, fr. OE *nā*, fr. *ne* not + *ā* always; akin to ON & OHG *ne* not, L *ne*, Gk *nē* — more at **AYE**] (bef. 12c) **1** **a** chiefly *Scot*: **NOT** **b** — used as a function word to express the negative of an alternative choice or possibility (shall we go out to dinner or ~) **2**: in no re-spect or degree — used in comparisons (you're ~ better than the rest of us) **3**: not so — used to express negation, dissent, denial, or refusal (~, I'm not going) **4** — used with a following adjective to imply a meaning expressed by the opposite positive statement (in ~ uncertain terms) **5** — used as a function word to emphasize a following nega-tive or to introduce a more emphatic, explicit, or comprehensive state-ment (it's big, ~, it's gigantic) **6** — used as an interjection to express surprise, doubt, or incredulity **7** — used in combination with a verb to form a compound adjective (*no-bake* pie) **8**: in negation (shook his head ~)
2 **no** **adj** (12c) **1** **a**: not any (~ parking) (~ disputing the decision) **b**: hardly any: very little (finished in ~ time) **2**: not a: quite other than a (he's ~ expert) **3** — used in combination with a noun to form a compound adjective (*a no-nonsense* realist)
3 **no** \nō\ **n**, pl **noes** or **nos** \nōz\ (1588) **1**: an act or instance of refus-ing or denying by the use of the word **NO**: **DENIAL** (received a firm ~ in reply) **2** **a**: a negative vote or decision **b** pl: persons voting in the negative
4 **no** *abbr* **1** north; northern **2** [*L* *numero*, abl. of *numerus*] number
5 **no** *var* of **NOH**
NO *symbol* nobelium
NOAA *abbr* National Oceanic and Atmospheric Administration
no-account *adj* (1845) **1**: of no importance: **TRIFLING** **2**: not amounting to anything: **SHUFFLESS** (her ~ relatives) — **no-account** **n**
No-a-chi-an \nō-'ā-kē-'ān\ **adj** [*Heb* *Noah*] (1678) **1**: of or relat-ing to the patriarch Noah or his time **2**: ANCIENT, ANTIQUATED
No-ah \nō-'ā-\ **n** [*Heb* *Noah*] (bef. 12c): an Old Testament patriarch who built the ark in which he, his family, and living creatures of every kind survived the Flood
no-b \nō-b\ **n** [*prob. alter. of knob*] (ca. 1700) **1**: **HEAD** **2**: a jack of the same suit as the starter in cribbage that scores one point for the holder — usu. used in the phrases *his nob* or *his nob*
2 **no-b** **n** [*perh. fr. 'nob*] (1703) chiefly *Brit*: one in a superior position in life
no-ble \nō-'blē-\ **n** **no-bled**; **no-bling** \-b(ə)-lɪŋ\ [*perh. irreg. freq. of nab*] (1847) **1** *Brit*: to incapacitate (a racehorse) esp. by drugging **2** *slang, Brit* **a**: to win over to one's side **b**: **STEAL** **c**: **SWINDLE**, **CHEAT** **d**: to get hold of: **CATCH** — **no-bler** \-b(ə)-lɪr-\ **n**
no-bly \nō-'blē-\ **adj** **no-bli-er**; **-est** (1788): **CHIC**, **SMART**
no-bel-ist \nō-'bē-'lɪ-st\ **n** (1938): a winner of a Nobel Prize
no-bel-i-um \nō-'bē-'lē-'əm-\ **n** [*NL*, fr. Alfred B. *Nobel*] (1957): a radio-active metallic element produced artificially — see ELEMENT table
no-bel Prize \nō-'bē-, -nō-'bē-'n\ (1900): any of various annual prizes (as in peace, literature, medicine) established by the will of Alfred No-bel for the encouragement of persons who work for the interests of hu-manity — called also *Nobel*
no-bil-i-ty \nō-'bi-li-'tē-\ [*ME* *nobilitē*, fr. *AF* *nobilitē*, fr. L *nobilitat-*, *nobilitas*, fr. *nobilis*] (14c) **1**: the quality or state of being noble in character, quality, or rank **2**: the body of persons forming the noble class in a country or state: **ARISTOCRACY**
no-ble \nō-'blē-\ **adj** **no-bler** \-b(ə)-lɪr-\; **no-blest** \-b(ə)-lɪst\ [*ME*, fr. *AF*, fr. L *nobilis* well-known, noble, fr. *nascere* to come to know — more at **KNOW**] (13c) **1** **a**: possessing outstanding qualities: **ILLUS-TRIOUS** **b**: **FAMOUS**, **NOTABLE** (~ deeds) **2**: of high birth or exalted or impressive esp. in appearance (~ edifice) **3**: possessing, character-ized by, or arising from superiority of mind or character or of ideals or morals: **LOFTY** (a ~ ambition) **6**: chemically inert or inactive esp. toward oxygen (a ~ metal such as platinum) — compare **BASE** **6a SYN** see **MORAL** — **no-ble-ness** \-blē-nēs-\ **n** — **no-bly** \-blē-'lē-\ **adv**
2 **noble** **n** (14c) **1**: a person of noble rank or birth **2**: an old English gold coin equivalent to 6s 8d
noble gas **n** (1902): any of a group of rare gases that include helium, neon, argon, krypton, xenon, and usu. radon and that exhibit great sta-bility and extremely low reaction rates — called also *inert gas*
no-ble-man \nō-'blē-'mən\ **n** (14c): a man of noble rank: **FRER**
noble rot **n** (1905): a botrytis fungus (*Botrytis cinerea*) that infects vari-ous usu. overripe wine grapes causing shriveling which results in in-creased sugar and flavor content and is responsible for the character-istic flavor of sauternes and related wines
noble savage **n** (1670): a mythic conception of people belonging to non-European cultures as having innate natural simplicity and virtue

\ə\ **abut** \ə\ **kitten**, **F** table \ər\ **further** \ə\ **ash** \ā\ **acc** \ā\ **mop**, **mar** \a\ **out** \ch\ **chin** \ē\ **bet** \ē\ **easy** \ē\ **go** \i\ **hit** \i\ **ice** \i\ **job** \o\ **sing** \ō\ **go** \ō\ **law** \ō\ **boy** \ō\ **thin** \θ\ **the** \θ\ **loot** \l\ **foot** \u\ **yet** \z\ **viston**, **beige** \k\ **ce**, **ce**, **ce** \i\ see **Guide to Pronunciation**

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- NNNGB** New York Genealogical and Biographical Society, New York, NY [Library symbol Library of Congress] (LCLS)
NNNH National Health Agencies Library, New York, NY [Library symbol Library of Congress] (LCLS)
NNNH Naval History Society, New York, NY [Library symbol Library of Congress] (LCLS)
NNNM New York Medical College, Flower and Fifth Avenue Hospitals, New York, NY [Library symbol Library of Congress] (LCLS)
NNMCA New Museum of Contemporary Art, New York, NY [Library symbol Library of Congress] (LCLS)
NNNPsan New York Psychoanalytic Institute, New York, NY [Library symbol Library of Congress] (LCLS)
NNNPSC National No-Nukes Prison Support Collective (EA)
NNNPsi New York State Department of Mental Hygiene, Psychiatric Institute, New York, NY [Library symbol Library of Congress] (LCLS)
NNNS New School for Social Research, New York, NY [Library symbol Library of Congress] (LCLS)
NNNSB National Society for the Prevention of Blindness, New York, NY [Library symbol Library of Congress] (LCLS)
NNNT New York Theological Seminary, New York, NY [Library symbol Library of Congress] (LCLS)
NNNTSH Naukove Tovarystvo Imeni Shevchenka (Shevchenko Scientific Society, Inc.), New York, NY [Library symbol Library of Congress] (LCLS)
NNWA N. W. Ayer & Son, New York, NY [Library symbol Library of Congress] (LCLS)
NNO Naga Nationalist Organization [India]
NNO No New Orders [Medical Records] (DAVI)
NNO Nord-Nord-Ouest [North-Northwest] [French]
NNO Northern Orion Explorations [Vancouver Stock Exchange symbol]
NNOA National Naval Officers Association (EA)
NNOC National Network Operations Center [Ottawa, ON] [Telecommunications] (TSSD)
NNomAE Albany Avenue Elementary School, North Massapequa, NY [Library symbol Library of Congress] (LCLS)
NNomEE Eastplain Elementary School, North Massapequa, NY [Library symbol Library of Congress] (LCLS)
NNomPH Plainsedge High School, North Massapequa, NY [Library symbol Library of Congress] (LCLS)
NNomPJ Sylvia Packard Junior High School, North Massapequa, NY [Library symbol Library of Congress] (LCLS)
NNOPE Naturists and Nudists Opposing Pornographic Exploitation (EA)
NNopo Northport Public Library, Northport, NY [Library symbol Library of Congress] (LCLS)
NNopo-E Northport Public Library, East Northport Branch, East Northport, NY [Library symbol Library of Congress] (LCLS)
NNopoHS Northport High School, Northport, NY [Library symbol Library of Congress] (LCLS)
NNopoJH Northport Junior High School, Northport, NY [Library symbol Library of Congress] (LCLS)
NNopoVA United States Veterans Administration Hospital, Northport, NY [Library symbol Library of Congress] (LCLS)
NNOR Nonnuclear Ordnance Requirement (MCD)
NNorP Norwich Pharmacal Co., Norwich, NY [Library symbol Library of Congress] (LCLS)
nNOS Neuronal Nitric Oxide Synthase [An enzyme]
NNosCE Sea Cliff Elementary School, North Shore, NY [Library symbol Library of Congress] (LCLS)
NNosJH North Shore Junior High School, North Shore, NY [Library symbol Library of Congress] (LCLS)
NNosSH North Shore Senior High School, North Shore, NY [Library symbol Library of Congress] (LCLS)
NNot New York Orthopaedic Hospital, New York, NY [Library symbol Library of Congress] (LCLS)
NNot North Tonawanda Public Library, North Tonawanda, NY [Library symbol Library of Congress] (LCLS)
NNotD DeGraff Memorial Hospital, North Tonawanda, NY [Library symbol Library of Congress] (LCLS)
NNotHC Hooker Chemicals & Plastics Corp., Durez Division Library, North Tonawanda, NY [Library symbol Library of Congress] (LCLS)
NNotL Lawless Container Corp., North Tonawanda, NY [Library symbol Library of Congress] (LCLS)
NNotP North Tonawanda Public Library, North Tonawanda, NY [Library symbol Library of Congress] (LCLS)
n nov Nomen Novum [New Name] [Latin] [Pharmacy] (DAVI)
N NOV Nomen Novum [New Name] [Latin] (BABM)
NNP Needle-Nosed Probe
NNP Negative Node Point
NNP Neonatal Nurse Practitioner (DAVI)
NNP Nerve Net Pulse [Neurobiology]
NNP Net National Product [Economics]
NNP Nuveen New York Performance Plus Municipal [NYSE symbol] (SPSG)
NNP Nuveen NY Perform Plus Muni [NYSE symbol] (TTSB)
NNPA National Negro Press Association [Defunct] (EA)
NNPA National Newspaper Promotion Association [Later, INPA] (EA)
NNPA National Newspaper Publishers Association (EA)
NNPA Nuclear Nonproliferation Act [1975]
NNPA Port Authority of New York and New Jersey, New York, NY [Library symbol Library of Congress] (LCLS)
NNParS Parsons School of Design, New York, NY [Library symbol Library of Congress] (LCLS)
NNPaul Paul, Weiss, Rifkind, Wharton & Garrison, Law Library, New York, NY [Library symbol Library of Congress] (LCLS)
- NNPaW** Payne Whitney Clinic, New York, NY [Library symbol Library of Congress] (LCLS)
NNPC Nigerian National Petroleum Corp. (ECON)
NNPC Pace College, New York, NY [Library symbol Library of Congress] (LCLS)
NNPC-L Pace University, Law Library, White Plains, NY [Library symbol Library of Congress] (LCLS)
NNPE-NC National Council of the Protestant Episcopal Church, New York, NY [Library symbol Library of Congress] (LCLS)
NNPennie Pennie, Edmonds, Morton, Taylor & Adams, New York, NY [Library symbol Library of Congress] (LCLS)
NNPI Carl H. Pforzheimer Library, New York, NY [Library symbol Library of Congress] (LCLS)
NNPH-0 Institute of Ophthalmology, Presbyterian Hospital, New York, NY [Library symbol Library of Congress] (LCLS)
NNPHR New York City Public Health Research Laboratory, New York, NY [Library symbol Library of Congress] (LCLS)
NNPHW National New Professional Health Workers [Later, NPSAPHA] (EA)
NNPI Naval Nuclear Propulsion Information (MCD)
NNPIA Polish Institute of Art and Sciences in America, Inc., Research Library, New York, NY [Library symbol Library of Congress] (LCLS)
NNPlan Planning Assistance, Inc., New York, NY [Library symbol Library of Congress] (LCLS)
NNPM Pierpont Morgan Library, New York, NY [Library symbol Library of Congress] (LCLS)
NNPopC Population Council, New York, NY [Library symbol Library of Congress] (LCLS)
NNPPFA Planned Parenthood Federation of America, Inc., Katharine Dexter McCormick Library, New York, NY [Library symbol Library of Congress] (LCLS)
NNPPNYC Planned Parenthood of New York City, Inc., Abraham Stone Memorial Library, Margaret Sanger Center, New York, NY [Library symbol Library of Congress] (LCLS)
NNPRM United Presbyterian Mission Library of the United Presbyterian Church in the USA, New York, NY [Library symbol Library of Congress] (LCLS)
NNPS Navy Nuclear Power School (DNAB)
NNPS Norco Nuclear Power Station (NRCH)
NNPSPP National Non-Point Source Pollution Program (GNE)
NNPTU Naval Nuclear Power Training Unit (DNAB)
NNPU Naval Nuclear Power Unit [Obsolete]
NNR City College of City University of New York, New York, NY [Library symbol Library of Congress] (LCLS)
NNR National Nature Reserve [British]
NNR National Number Routed [Telecommunications] (TEL)
NNR Nearest-Neighbor Rule [Mathematics]
NNR Nevada North Resources [Vancouver Stock Exchange symbol]
NNR New and Nonofficial Remedies [A publication]
NNR Nordiska Nykterhetsradet [Nordic Temperance Council - NTC] (EAO)
NNR Northern NORAD [North American Air Defense] Region (SAA)
NNRA National Negro Republican Assembly [Defunct]
NNRB National Neurological Research Bank [Veterans Administration Medical Center] [Research center] (RCD)
NNRB Recording for the Blind, Inc., New York, NY [Library symbol Library of Congress] (LCLS)
NNRDC National Nuclear Rocket Development Center [Also known as NRDS]
NNRDF National Nuclear Rocket Development Facility (AAG)
NNRocA National Recreation Association [Later, NRPA], New York, NY [Library symbol Library of Congress] (LCLS)
NNreP Regional Plan Association, Inc., Library, New York, NY [Library symbol Library of Congress] (LCLS)
NNRF National Neurological Research Foundation (EA)
NNRG Nevada Energy Co., Inc. [NASDAQ symbol] (SAG)
NNRGA Nevada Energy [NASDAQ symbol] (TTSB)
NNRH Roosevelt Hospital, Medical Library, New York, NY [Library symbol Library of Congress] (LCLS)
NNRIS Nebraska Natural Resources Information System [Nebraska State Natural Resources Commission] [Lincoln] [Information service or system] (IID)
NNRd Theodore Roosevelt Association, New York, NY [Library symbol Library of Congress] (LCLS)
NNRocF Rockefeller Foundation, New York, NY [Library symbol Library of Congress] (LCLS)
NNRocFA Rockefeller Family & Associates, Inc., Office Library, New York, NY [Library symbol Library of Congress] (LCLS)
NNRoi Rochdale Institute, New York, NY [Library symbol Library of Congress] (LCLS)
NNRom Romanian Library, New York, NY [Library symbol Library of Congress] (LCLS)
NNRRB R. R. Bowker Co., New York, NY [Library symbol Library of Congress] (LCLS)
NNRT Non-Nucleoside Reverse Transcriptase [Biochemistry]
NNRT Racquet and Tennis Club, New York, NY [Library symbol Library of Congress] (LCLS)
NNRTI Non-Nucleoside Reverse Transcriptase Inhibitor [Biochemistry]
NNRU Rockefeller University, New York, NY [Library symbol Library of Congress] (LCLS)
NNRU-P Rockefeller University, Population Council, Bio-Medical Library, New York, NY [Library symbol Library of Congress] (LCLS)
NNRY Nunnery (ABBR)
NNRYS National Network of Runaway and Youth Services (EA)
NNS National Narrowcast Service [Public Broadcasting Service] [Arlington, VA] [Telecommunications service] (TSSD)
NNS National Natality Survey

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ORIGIN 1940s: from Japanese, lit. 'second generation'.
nisi /'naɪsai/ ● adj. [postpos.] law (of a decree, order, or rules valid or taking effect only after certain conditions are met.
- ORIGIN C19: from L., lit. 'unless'.
Nissen hut /'nɪs(ə)n/ ● n. chiefly Brit. a tunnel-shaped hut of corrugated iron with a cement floor.
- ORIGIN C20: after the Brit. engineer Peter N. Nissen.
nit' ● n. informal 1 the egg or young form of a louse or other parasitic insect, especially the egg of a human head louse. 2 Brit. a stupid person.
- DERIVATIVES **nitty** adj.
- ORIGIN OE *hnttu*, of W. Gmc origin.
nit' ● exclam. Austral. informal used as a warning that someone is approaching.
- PHRASES **keep nit** keep watch.
- ORIGIN C19: prob. from **NIX**.
niter ● n. US spelling of **NITRE**.
nitrite /'naɪtrɪt/ ● n. (pl. **-ites**) informal a nightclub.
nitinol /'nɪtnɒl/ ● n. an alloy of nickel and titanium.
- ORIGIN 1960s: from the chemical symbols Ni and Ti + the initial letters of *Naval Ordnance Laboratory* (in Maryland, US).
nit-picking ● n. informal fussy or pedantic fault-finding.
- DERIVATIVES **nit-pick** v. **nit-picker** n.
nitrate Chemistry ● n. /'naɪtreɪt/ a salt or ester of nitric acid. ● v. /'naɪtreɪt/ treat with nitric acid, especially so as to introduce the group =NO.
- DERIVATIVES **nitration** n.
- ORIGIN C18: from Fr. (see **NITRE**, **-ATE**).
nitrazepam /'naɪtreɪzəpəm, -'træz-/ ● n. Medicine a short-acting drug used to treat insomnia.
- ORIGIN 1960s: from *nitro* + *azep* + *amide*.
nitre /'naɪtrə/ (US **niter**) ● n. potassium nitrate; saltpetre.
- ORIGIN ME: from OFr., from L. *nitrium*, from GK *nitron*.
nitric acid ● n. Chemistry a colourless or pale yellow acid with strong corrosive and oxidizing properties. [HNO₃]
nitric oxide ● n. Chemistry a colourless toxic gas made by reduction of nitric acid, reacting immediately with oxygen to form nitrogen dioxide. [NO]
nitride /'naɪtraɪd/ ● n. Chemistry a compound of nitrogen with another element or group.
nitri-fy /'naɪtrɪfaɪ/ ● v. (-ies, -ied) Chemistry convert (ammonia or another nitrogen compound) into nitrites or nitrates.
- DERIVATIVES **nitri-fication** n.
- ORIGIN C19: from Fr. *nitri-fier*.
nitrite /'naɪtrɪt/ ● n. Chemistry an organic compound containing a cyanide group -CN bound to an alkyl group.
- ORIGIN C19: from **NITRE** + *-ite* (alt. of **-YL**).
nitrite /'naɪtrɪt/ ● n. Chemistry a salt or ester of nitrous acid.
nitro ● n. short for **NITROGLYCERINE**.
nitro- /'naɪtrəʊ/ ● comb. form 1 of or containing nitric acid, nitrates, or nitrogen: *nitrogenous*. 2 Chemistry containing the group =NO; *nitrobenzene*.
nitrobenzene ● n. Chemistry a yellow oily liquid made by nitrating benzene, used in chemical synthesis.
nitrocellulose ● n. Chemistry a highly flammable material made by treating cellulose with concentrated nitric acid, used to make explosives and celluloid.
nitrochalk ● n. a mixture of chalk and ammonium nitrate, used as fertilizer.
nitrogen /'naɪtrədʒ(ə)n/ ● n. the chemical element of atomic number 7, a colourless, odourless unreactive gas that forms about 78 per cent of the earth's atmosphere. (Symbol: N)
- DERIVATIVES **nitrogenous** adj.
- ORIGIN C18: from Fr. *nitrogène* (see **NITRO-**, **-GENE**).
nitrogen cycle ● n. Ecology the series of processes by which nitrogen and its compounds are interconverted in the environment and in living organisms.
nitrogen dioxide ● n. Chemistry a reddish-brown poisonous gas formed when many metals dissolve in nitric acid. [NO₂]
nitrogen fixation ● n. Biology the chemical processes by

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which atmospheric nitrogen is assimilated into organic compounds, especially by certain micro-organisms as part of the nitrogen cycle.
nitrogen narcosis ● n. Medicine a drowsy state induced by breathing air under pressure, e.g. in deep-sea diving.
nitroglycerine (also **nitroglycerin**) ● n. an explosive yellow liquid made by nitrating glycerol, used in dynamite.
nitrosamine /'naɪtrəʊsəmi:n/ ● n. Chemistry a compound containing the group =NNO attached to two organic groups.
- ORIGIN C18: from *nitroso-* (relating to nitric oxide in combination) + **AMINE**.
nitrous /'naɪtrəs/ ● adj. of or containing nitrogen.
- ORIGIN C17: from L. *nitrosus* 'nitrous'.
nitrous acid ● n. Chemistry an unstable, weak acid made by the action of acids on nitrites. [HNO₂]
nitrous oxide ● n. Chemistry a colourless gas with a sweetish odour which produces exhilaration or anaesthesia when inhaled and is used as an anaesthetic. [N₂O]
nitty-gritty ● n. Informal the most important aspects or practical details of a matter.
- ORIGIN 1960s: of unknown origin.
nitwit ● n. informal a silly or foolish person.
- DERIVATIVES **nitwitted** adj. **nitwittedness** n. **nitwittory** n.
- ORIGIN C20: appar. from **NIT** + **WIT**.
NIV ● abbrev. New International Version (of the Bible)
nival /'naɪv(ə)l/ ● adj. of or relating to regions of perpetual snow.
- ORIGIN C17: from L. *nivalis*, from *nix*, *niv-* 'snow'.
nivation /'naɪveɪʃ(ə)n/ ● n. Geography erosion beneath or beside a snow bank, mainly as a result of alternate freezing and thawing.
- ORIGIN C20: from L. *nix*, *niv-* 'snow' + **-ATION**.
niveous /'nɪviəs/ ● adj. poetic/literary snowy; like snow.
- ORIGIN C17: from L. *niveus* (from *nix*, *niv-* 'snow') + **-OUS**.
nix informal ● prep. nothing. ● exclam. 1 expressing denial or refusal. 2 Brit. dated used as a warning that a person in authority is approaching. [perch. from the obs. phr. *keep nix 'to watch, guard'*] ● v. put an end to; cancel: *he nixed the deal*.
- ORIGIN C18: from Ger., colloq. var. of *nichts* 'nothing'.
nixie ● n. a female water spirit.
- ORIGIN C19: from Ger.; rel. to the archaic Engl. word *nicker*, denoting a water demon.
Nizam /'nɪzəm/ ● n. historical 1 the title of the hereditary ruler of Hyderabad. [abbrev. of Urdu *nizām-al-mulk* 'administrator of the realm'] 2 (the **nizam**) the Turkish regular army [abbrev. of Turk. *nizām askeri* 'regular soldier']
Nizari /'nɪzəri/ ● n. a member of an Ismaili Muslim sect led by the Aga Khan.
- ORIGIN named after the C12 Egyptian Ismaili imam *Nizar*.
NJ ● abbrev. New Jersey (in official postal use).
NL ● abbrev. the Netherlands (international vehicle registration).
NLP ● abbrev. 1 natural language processing. 2 neuro-linguistic programming.
NM ● abbrev. New Mexico (in official postal use).
nm ● abbrev. 1 nanometre. 2 (also **n.m.**) nautical mile.
NMR ● abbrev. Physics nuclear magnetic resonance.
NNE ● abbrev. north-north-east.
NNP ● abbrev. net national product.
NNW ● abbrev. north-north-west.
No' ● symb. the chemical element nobelium.
No' ● n. variant spelling of **Now**.
No. ● abbrev. 1 US North. 2 (also **no.**) number. [from L. *numerus*, ablative of *numerus*.]
no ● det. 1 not any. 2 quite the opposite of: *it was no easy task*. 3 hardly any. ● exclam. used to give a negative response. ● adv. 1 [with comparative] not at all: *they were no more able to do it than I was*. 2 Scottish not. ● n. (pl. **noes**) a negative answer or decision, especially in voting.
- PHRASES **no can do** informal I am unable to do it. **no**

longer not now as formerly **no place** N. Amer. nowhere. **no through road** an indication that passage along a street is blocked or prohibited. **not take no for an answer** persist in spite of refusals. **no two ways about it** no possible doubt about something. **no way** informal under no circumstances; not at all. **no worries** informal, chiefly Austral. all right; fine. or no or not.
- ORIGIN OE *nō*, *nā* (adv.), from *ne* 'not' + *ō*, *ā* 'ever'.
n.o. ● abbrev. Cricket not out.
no-account ● adj. informal, chiefly N. Amer. unimportant or worthless.
Noachian /nəʊ'eɪkɪən/ ● adj. of or relating to the biblical patriarch Noah or his time.
noah ● n. Austral. informal a shark.
- ORIGIN 1940s: from rhyming sl. *Noah's ark*.
nob' ● n. Brit. informal a person of wealth or high social position.
- DERIVATIVES **nobby** adj.
- ORIGIN C17 (orig. Scots as *knab*): of unknown origin.
nob' ● n. informal a person's head.
- ORIGIN C17: appar. a var. of **knob**.
no-ball Cricket ● n. an unlawfully delivered ball, counting as an extra run to the batting side if not scored from. ● v. (of an umpire) declare (a bowler) to have bowled a no-ball.
noble ● v. Brit. informal 1 try to influence or thwart by underhand or unfair methods. > tamper with (a race-horse) to prevent it from winning a race. 2 accost (someone). 3 obtain dishonestly; steal. > seize.
- ORIGIN C19: prob. a var. of dial. *knobbie*, *knubble* 'knock, strike with the knuckles'.
nobbler ● n. informal 1 Brit. a person who nobbles someone or something. 2 Austral./NZ a drink of liquor.
Nobel /nəʊ'beɪlɪst/ ● n. chiefly N. Amer. a winner of a Nobel Prize.
nobelium /nəʊ'bi:liəm, -'beɪ-/ ● n. the chemical element of atomic number 102, an artificial radioactive metal of the actinide series. (Symbol: **No**)
- ORIGIN 1950s: from the name of Alfred Nobel + **-IUM**.
Nobel Prize ● n. any of six international prizes awarded annually for outstanding work in physics, chemistry, physiology or medicine, literature, economics, and the promotion of peace.
- ORIGIN named after the C19 Swed. chemist and engineer Alfred Nobel, who endowed the prizes.
nobiliary /nəʊ'bi:lɪəri/ ● adj. of or relating to the nobility.
- ORIGIN C18: from Fr. *nobiliaire*, based on L. *nobilis* (see **NOBLE**).
nobility ● n. (pl. **-ities**) 1 the quality of being noble. 2 the aristocracy.
noble ● adj. (-er, -est) 1 belonging by rank, title, or birth to the aristocracy. 2 having fine personal qualities or high moral principles. 3 imposing; magnificent. ● n. 1 (especially in former times) a person of noble rank or birth. 2 historical a former English gold coin.
- PHRASES **the noble art** (or **science**) (of self-defence) chiefly archaic boxing.
- DERIVATIVES **noblesse** n. **nobly** adv.
- ORIGIN ME: from OFr., from L. (*g*)*nobilis* 'noted, high-born'.
noble gas ● n. Chemistry any of the gaseous elements helium, neon, argon, krypton, xenon, and radon, which form compounds with difficulty or not at all.
nobleman (or **noblewoman**) ● n. (pl. **-men** or **-women**) a man (or woman) who belongs to the aristocracy; a peer (or peeress).
noble metal ● n. Chemistry a metal (e.g. gold, silver, or platinum) that resists attack by acids and other reagents and does not corrode.
noble rot ● n. a grey mould (*Botrytis cinerea*) cultivated on grapes in order to perfect certain wines.
- ORIGIN 1830s: translation of Fr. *pourriture noble*.
noble savage ● n. a representative of primitive mankind as idealized in Romantic literature.
noblesse /nəʊ'bles/ ● n. the nobility of a foreign country.

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1: Neurosci Lett. 2004 Nov 30;372(1-2):1-5.

ELSEVIER Links FULL-TEXT ARTICLE

Identification of molecular variants at the promoter region of the human alpha 7 neuronal nicotinic acetylcholine receptor subunit gene but lack of association with schizophrenia.

Li CH, Liao HM, Chen CH.

Department of Psychiatry, Tzu-Chi General Hospital, and Tzu-Chi University, 701 Section 3, Chung-Yang Road, Hualien City 970, Taiwan, ROC.

The human alpha7 neuronal nicotinic receptor subunit gene has been considered as a candidate gene for P50 sensory gating deficit in schizophrenic patients. Because P50 sensory gating deficit is a common neurophysiological dysfunction in patients with schizophrenia and schizophrenia spectrum disorders, it is conceivable to hypothesize that the human alpha7 neuronal nicotinic receptor subunit gene might be a susceptible gene for schizophrenia. Researchers have reported that mutations in the protein-coding sequences of the human alpha7 neuronal nicotinic receptor subunit gene are very rare. Therefore, we searched for mutations at the promoter region of the human alpha7 neuronal nicotinic receptor subunit gene and performed a genetic association study in 249 unrelated Han Chinese schizophrenic patients and 273 non-psychotic subjects from Taiwan. Two molecular variants were identified and designated g.-213G>A and g.-324A>G, respectively. The g.-213G>A variant was found to obliterate a putative NF-1 transcription factor binding site using computer analysis. One out of 249 patients was detected to be a heterozygote for this variant, but none of 273 control subjects was. The g.-324A>G variant was also very rare in both patients and control subjects, only one heterozygote of this variant was identified in 249 patients and 273 control subjects, respectively. Hence, in this study, we did not find mutations in the human alpha7 neuronal nicotinic receptor subunit gene that are associated with schizophrenia in our population.

PMID: 15531077 [PubMed - indexed for MEDLINE]

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- Sensory gating and alpha-7 nicotinic receptor gene allelic variants in m J Med Genet B Neuropsychiatr Genet. 2007]
- The promoter -194 C polymorphism of the nicotinic alpha 7 receptor gene has a protective effect against the P50 sensory gating deficit. [Mol Psychiatry. 2004]
- Linkage disequilibrium for schizophrenia at the chromosome 15q13-14 locus of the alpha7-nicotinic acetylcholine receptor subunit gene (CHR 15) J Med Genet. 2001]

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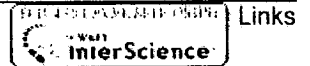
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Age-related loss of neuronal nicotinic receptor expression in the aging mouse hippocampus corresponds with cyclooxygenase-2 and PPAR gamma expression and is altered by long-term NS398 administration.

Gahring LC, Persiyanov K, Days EL, Rogers SW.

Salt Lake City VA-Geriatrics Research, Education and Clinical Center, Salt Lake City, Utah, USA.

Age-related changes in the mammalian dorsal hippocampus are associated with diminished expression of neuronal nicotinic acetylcholine receptors (nAChR), which is particularly severe in pathologies such as those associated with dementias, including Alzheimer's disease. Because the mouse is a useful model for age-related decline in nAChR expression in the basal forebrain and limbic system, we used immunohistochemistry to examine the influence of long-term (12-month) oral administration of nicotine and/or the cyclooxygenase-2 (COX-2) preferring non-steroidal anti-inflammatory drug (NSAID) NS398 on nAChR alpha4, alpha5, alpha7, and beta4 expression in the C57BL/6 mouse. Inhibitory neurons of the dorsal hippocampus that express nAChRs also constitutively express COX-2 and the peroxisome proliferator-antagonist receptor subtype gamma-2 (PPAR gamma2) which is also a target of NS398. Administration of NS398 correlated with retention of nAChR alpha4 and to a lesser extent nAChR beta4, but not nAChR alpha5 or alpha7, but nicotine exhibited no similar effect. Nicotine and NS398 co-administration abolished the NS398-related effect on nAChR alpha4 retention. These results provide evidence that the interaction during aging between oral administration of nicotine and NSAIDs are not straightforward and could even be antagonistic when combined. Copyright 2004 Wiley Periodicals, Inc.

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Mouse strain-specific nicotinic acetylcholine receptor expression by inhibitory interneurons and astrocytes in the dorsal hippocampus. [J Comp Neurol. 2004]
Age-related changes in neuronal nicotinic acetylcholine receptor subunit alpha4 expression are modified by long-term nicotine administration. [J Neurosci. 1998]
Nicotine increases the expression of high affinity nerve growth factor receptors in both in vitro and in vivo. [Life Sci. 2002]
Differential expression of nicotinic acetylcholine receptor subunits in fetal and neonatal mouse thymus. [J Neuroimmunol. 2002]

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[FULL-TEXT ARTICLE](#)

Potentiation of human alpha4beta2 neuronal nicotinic receptors by a *Flustra foliacea* metabolite.

Sala F, Mulet J, Reddy KP, Bernal JA, Wikman P, Valor LM, Peters L, König GM, Criado M, Sala S.

Instituto de Neurociencias, Universidad Miguel Hernández-CSIC, Sant Joan d'Alacant, Apdo, Correos 18, 03550 Alicante, Spain.

The effects of various *Flustra foliacea* metabolites on different types of human neuronal nicotinic acetylcholine receptors (nAChRs) expressed in *Xenopus* oocytes were investigated. Whereas most of the compounds tested had a small blocking effect, one of them, deformylflustrabromine, selectively increased the current obtained in alpha4beta2 receptors when co-applied with acetylcholine (ACh). The current increase was reversible and concentration-dependent. This potentiating effect was still present at saturating concentrations of acetylcholine, and no changes in single-channel conductance or reversal potential were observed, thus suggesting a modification in the gating of alpha4beta2 receptors. Dwell time analysis of single channel records indicates that the mechanism of action of deformylflustrabromine could be both an increase of the opening rate constant and a decrease of the closing rate constant on alpha4beta2 receptors. Thus, deformylflustrabromine may constitute an excellent starting point for the future development of related agents able to potentiate human neuronal nicotinic receptor function.

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Association of a nicotinic receptor mutation with reduced height and blunted physostigmine-stimulated growth hormone release.

Fedi M, Bach LA, Berkovic SF, Willoughby JO, Scheffer IE, Reutens DC.

FRACP, Southern Clinical School, Monash Medical Centre, 246 Clayton Road, Clayton, Victoria 3168, Australia.
David.Reutens@med.monash.edu.au.

Background: Pulsatile GH secretion from the anterior pituitary is a key mediator of human growth regulation and is affected by a number of genetic and environmental factors. Activation of neuronal nicotinic acetylcholine (nACh) receptors promotes GH release, but the role of these receptors in growth regulation is unknown. Aim: Our aim was to assess the effect of a mutation in the alpha4 subunit of the nACh receptor on cholinergic-mediated GH release. Methods: Forty-one healthy volunteers (24 male, age 36.2 +/- 12.2 yr, mean +/- sd) and 13 subjects with the alpha4-Ser248Phe mutation (four male, age 43.2 +/- 16.8 yr) were studied. Serum levels of GH, LH, FSH, prolactin, TSH, free T(4), and cortisol were measured at baseline and at regular intervals after infusion of physostigmine. Height and weight were recorded in all participants as well as from additional family members with (n = 11, four male) and without (n = 16, seven male) the mutation. Results: Subjects with the mutation were shorter (1.62 +/- 0.08 vs. 1.72 +/- 0.09 m, P < 0.05) and had a greater body mass index (31 +/- 6 vs. 24 +/- 3 kg/m(2), P < 0.05) than healthy volunteers and unaffected members of the pedigree. In controls, physostigmine markedly increased the serum levels of GH (mean increase, +732%). In contrast, the response to physostigmine was markedly blunted in subjects with the mutation (+104%, P > 0.2 vs. control). Conclusions: These findings suggest a role of the nACh receptor in human growth regulation.

PMID: 18042647 [PubMed - in process]

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- Role of alpha-amino-3-hydroxy-5-methylisoxazole-4-propionic acid receptors in the control of prolactin, growth hormone and gonadotropin secretion in prepubertal rats. [J Endocrinol. 1999]
- Effects of megestrol acetate on pituitary function and end-organ hormone secretion: a post hoc analysis of serum samples from a 12-week study. [Arch Gen Psychiatry. 2005]
- A paradoxical gender dissociation within the growth hormone/insulin-like growth factor I axis during puberty. [J Clin Endocrinol Metab. 2000]
- Tripartite neuroendocrine activation of the human growth hormone (GH) axis in women by continuous 24-hour GH-releasing peptide infusion: pulsatile, entropic, and nocturnal. [J Clin Endocrinol Metab. 1999]

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Nicotinic receptor subunits alpha 3, alpha 4, and beta 2 and high affinity nicotine binding sites are expressed by P19 embryonal cells.

Cauley K, Marks M, Gahring LC, Rogers SW.

Molecular Biology and Virology Laboratory, Salk Institute for Biological Studies, San Diego, California 92186, USA.

Controlled exposure to retinoic acid (RA) induces the murine embryonal carcinoma cell line P19S1801A1 (P19) to differentiate into a variety of cell types. One of the cell types exhibits neuronal-like morphology and expresses neuronal markers including neurofilament proteins, glutamate receptors, and the cholinergic enzymes choline acetyl-transferase and acetylcholinesterase. In this study we use Northern blot analysis, double-label immunocytochemistry, and single cell RNA analysis using polymerase chain reaction to show that RA-treated P19 cells with neuronal-like morphology also express neuronal nicotinic acetylcholine receptor (nAChR) subunits alpha 3, alpha 4, and beta 2. Greater than 80% of RA-treated P19 cells with a neuronal-like phenotype express nAChR alpha 4 subunit transcripts and both alpha 4 and beta 2 protein. The RA-induced expression of alpha 3 transcripts accounts for a comparably small number of nAChR-containing cells (< 20%) of which half coexpress alpha 4 transcripts. Expression of high-levels of alpha 4 RNA is dependent upon both cell-cell contact and RA exposure. The appearance of nAChR subunits also coincides with RA-induced expression of high affinity [3H]-nicotine binding receptors. The P19 cell line offers an inducible neuronal cell system to study mammalian neuronal nicotinic receptor expression and the development of high affinity nicotinic binding sites similar to those expressed in the mammalian central nervous system.

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Characterization of nicotinic acetylcholine receptors expressed in primary cultures of cerebellar granule cells. *Mol Brain Res*. 1995

Stable expression, pharmacologic properties and regulation of the human neuronal nicotinic acetylcholine alpha 4 beta 2 receptor. *J Pharmacol Exp Ther*. 1996

Developmental expression of functional GABAA receptors containing the gamma 2 subunit in neurons derived from embryonal carcinoma cells. *Mol Brain Res*. 1996

Induction of expression of the alpha v beta 1 and alpha v beta 3 integrin heterodimers during retinoic acid-induced neuronal differentiation of murine embryonal carcinoma cells. *J Biol Chem*. 1991

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Rapid nongenomic effect of corticosterone on neuronal nicotinic acetylcholine receptor in PC12 cells.

Shi LJ, He HY, Liu LA, Wang CA.

Department of Physiology, Beijing Medical College of PLA, Beijing, 100071, China. l.j.shi@263.net

The effects of corticosterone, a natural glucocorticoid of rat, on the acetylcholine (ACh)-induced current (I(ACh)) were studied in pheochromocytoma (PC12) cells by using whole-cell clamp technique. The I(ACh) proved to be generated through neuronal nicotinic receptor. ACh (30 microM) induced an inward current at a holding potential of -80 mV. When cells were preincubated with corticosterone (0.1-100 microM) for 4 min, an inhibitory effect of corticosterone on the peak of I(ACh) was found. This effect was reversible, concentration-dependent, and voltage-independent. Intracellular application of corticosterone through the patch electrode did not affect the I(ACh). Extracellular application of 10 microM corticosterone neither shifted the dose-response curve of the peak I(ACh) to the right (dissociation constant (K(d)) = 16.5 microM) nor affected its coefficient (1.8) but inhibited the curve amplitudes by approximately 49% in the cells pretreated with corticosterone for 4 min. Bovine serum albumin-conjugated corticosterone (0.1-10 microM) had the inhibition similar to corticosterone. The inhibitor of transcription, actinomycin D (10 microM), and the protein synthesis inhibitor, cycloheximide (50 microM), had no effect on the inhibition induced by corticosterone on I(ACh). These results suggest that corticosterone has rapid inhibitory effect on I(ACh) in PC12 cells, which is mediated by a nongenomic mechanism. It indicates that corticosterone binds to the specific site on the outer cell membrane, probably on the neuronal nicotinic receptor-coupled channel, and inhibits the I(ACh) in a noncompetitive manner, thus controlling the immediate catecholamine release from the sympathetic cells. Copyright 2001 Academic Press.

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- Modulation of neuronal nicotinic acetylcholine receptor function by corticosterone [Arch Biochem Biophys. 2002]
- Decrease in acetylcholine-induced current by neomycin [Arch Biochem Biophys. 2002]
- Inhibitory effect of the kinase inhibitor chelerythrine on acetylcholine-induced current in PC12 cells [Arch Biochem Biophys. 1999]
- [Rapid inhibitory effect of glucocorticoids on ACh-induced current in rat pheochromocytoma cells] [Shen Li Xue Bao. 1998]
- Nicotinic acetylcholine receptors of the neuronal type occur in the plasma membrane of sea urchin eggs [Zygote. 1997]

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Nicotinic receptors, smoking and schizophrenia.

Leonard S, Gault J, Adams C, Breese CR, Rollins Y, Adler LE, Olincy A, Freedman R.

Department of Psychiatry, University of Colorado Health Sciences Center, Denver 80262, USA. Sherry.Leonard@UCHSC.edu

Neuronal nicotinic acetylcholine receptor expression was examined in schizophrenia. The incidence of smoking in schizophrenia is remarkably high and nicotine has been found to normalize an auditory evoked potential deficit seen in most subjects who suffer from this disease. Antagonists and agonists of a specific subset of this receptor family, the alpha7 nicotinic receptor, were found to regulate the gating of filtering of auditory information in both humans and in an animal model. The alpha7 gene has been cloned and a polymorphic dinucleotide repeat near the gene was used for linkage analysis, showing the alpha7 locus to be linked to the P50 deficit. Expression of the alpha7 receptor, which binds nicotine with low affinity, is reduced in the hippocampus of schizophrenics. [3H]-nicotine binding, a measure of the high affinity nicotinic receptors, was also decreased in schizophrenics and does not increase in response to tobacco use, as is seen in control subjects. The results of these studies suggest the presence of abnormal expression and function of the neuronal nicotinic receptor gene family in schizophrenia.

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- Smoking and schizophrenia: abnormal nicotinic receptor expression. *Psychopharmacol.* 2000
- Nicotinic receptor function in schizophrenia. *[Schizophr Bull.* 1996]
- Schizophrenia and the alpha7 Nicotinic Acetylcholine Receptor. *Neurosci Biobehav Rev Neurobiol.* 2007
- The alpha7-nicotinic acetylcholine receptor and the pathology of hippocampal interneurons in schizophrenia. *Neurosci Biobehav Rev Neuroanat.* 2000
- Abnormal regulation of high affinity nicotinic receptors in schizophrenia. *Neurosci Biobehav Rev Neuropharmacol.* 2000

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Interaction of chlorisondamine with the neuronal nicotinic acetylcholine receptor.

Woods AS, Moyer SC, Wang HY, Wise RA.

The National Institute on Drug Abuse, Intramural Research Program, National Institutes of Health, 5500 Nathan Shock Drive, Baltimore, Maryland 21224, USA. awoods@intra.nida.nih.gov

An epitope was found on the alpha2-nicotinic isoform of the neuronal nicotinic acetylcholine receptor that would likely form salt bridges with quaternary ammonium compounds and a cation-pi interaction with the pi-cloud of an aromatic ring. Chlorisondamine, a nicotinic antagonist, exerts a long-lasting, if not permanent, blockade of the ion channel gated by acetylcholine. Blocking of the ion channel prevents nicotine from exerting its rewarding effect on the CNS. Chlorisondamine contains two quaternary ammonium groups and a tetrachloroisindoline ring. We propose that chlorisondamine interacts with an epitope on the alpha2 isoform of the rat neuronal nicotinic receptor (residues 388-402, GEREETEEEEEEDE), where one or both of the quaternary ammonium groups of chlorisondamine form a salt bridge with either a glutamic acid side chain or a phosphate group, whereas the tetrachlorobenzene portion of the tetrachloroisindoline ring interacts with the guanidinium group of arginine in a cation-pi association: In this work, a new way of probing the interaction of a receptor epitope (alpha2) with organic molecules (chlorisondamine and hexachlorobenzene) was undertaken using matrix assisted laser desorption/ionization mass spectrometry.

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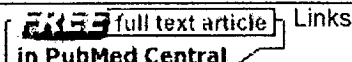
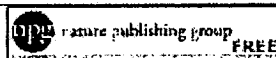
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Effect of galantamine on the human alpha7 neuronal nicotinic acetylcholine receptor, the Torpedo nicotinic acetylcholine receptor and spontaneous cholinergic synaptic activity.

Texidó L, Ros E, Martín-Satué M, López S, Aleu J, Marsal J, Solsona C.

Laboratory of Molecular and Cellular Neurobiology, Department of Cell Biology and Pathology, Medical School-Bellvitge Campus, IDIBELL-Universitat de Barcelona, Feixa Llarga s/n, L'Hospitalet de Llobregat, E-08907, Spain.

1. Various types of anticholinesterasic agents have been used to improve the daily activities of Alzheimer's disease patients. It was recently demonstrated that Galantamine, described as a molecule with anticholinesterasic properties, is also an allosteric enhancer of human alpha4beta2 neuronal nicotinic receptor activity. We explored its effect on the human alpha7 neuronal nicotinic acetylcholine receptor (nAChR) expressed in *Xenopus* oocytes. 2. Galantamine, at a concentration of 0.1 microM, increased the amplitude of acetylcholine (ACh)-induced ion currents in the human alpha7 nAChR expressed in *Xenopus* oocytes, but caused inhibition at higher concentrations. The maximum effect of galantamine, an increase of 22% in the amplitude of ACh-induced currents, was observed at a concentration of 250 microM ACh. 3. The same enhancing effect was obtained in oocytes transplanted with Torpedo nicotinic acetylcholine receptor (AChR) isolated from the electric organ, but in this case the optimal concentration of galantamine was 1 microM. In this case, the maximum effect of galantamine, an increase of 35% in the amplitude of ACh-induced currents, occurred at a concentration of 50 microM ACh. 4. Galantamine affects not only the activity of post-synaptic receptors but also the activity of nerve terminals. At a concentration of 1 microM, quantal spontaneous events, recorded in a cholinergic synapse, increased their amplitude, an effect which was independent of the anticholinesterasic activity associated with this compound. The anticholinesterasic effect was recorded in preparations treated with a galantamine concentration of 10 microM. 5. In conclusion, our results show that galantamine enhances human alpha7 neuronal nicotinic ACh receptor activity. It also enhances muscular AChRs and the size of spontaneous cholinergic synaptic events. However, only a very narrow range of galantamine concentrations can be used for enhancing effects.

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Effects of bis(7)-tacrine on spontaneous synaptic activity and on the nicotinic ACh receptor of Torpedo *electric organ*. [Neurophysiol. 2001]

The acetylcholinesterase inhibitor BW284c51 is a potent blocker of Torpedo nicotinic AChRs incorporated into the *Xenopus* oocyte membrane. [Br J Pharmacol. 2005]

Effects of CI-1002 and CI-1017 on spontaneous synaptic activity and on the nicotinic acetylcholine receptor of Torpedo electric organ. [Eur J Pharmacol. 2000]

The nicotinic allosteric potentiating ligand galantamine facilitates synaptic transmission in the mammalian *oesophagus*. [Mol Pharmacol. 2002]

Ketamine and its preservative, benzethonium chloride, both inhibit human recombinant alpha7 and alpha4beta2 neuronal nicotinic acetylcholine receptors in *Xenopus* oocytes. [Br J Pharmacol. 2001]

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Galantamine (Razadyne® (formerly available as Reminyl®), Razadyne® ER) Galantamine is used to treat the symptoms of Alzheimer's disease (AD; a brain disease that slowly destroys the memory and the ability to think, learn, communicate and handle daily activities). Galantamine is in a class o...

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Increased sensitivity of the neuronal nicotinic receptor alpha 2 subunit causes familial epilepsy with nocturnal wandering and ictal fear.

Aridon P, Marini C, Di Resta C, Brilli E, De Fusco M, Politi F, Parrini E, Manfredi I, Pisano T, Pruna D, Curia G, Cianchetti C, Pasqualetti M, Becchetti A, Guerrini R, Casari G.

Human Molecular Genetics Unit, Dibril San Raffaele Scientific Institute, Milan, Italy.

Sleep has traditionally been recognized as a precipitating factor for some forms of epilepsy, although differential diagnosis between some seizure types and parasomnias may be difficult. Autosomal dominant frontal lobe epilepsy is characterized by nocturnal seizures with hyperkinetic automatisms and poorly organized stereotyped movements and has been associated with mutations of the alpha 4 and beta 2 subunits of the neuronal nicotinic acetylcholine receptor. We performed a clinical and molecular genetic study of a large pedigree segregating sleep-related epilepsy in which seizures are associated with fear sensation, tongue movements, and nocturnal wandering, closely resembling nightmares and sleep walking. We identified a new genetic locus for familial sleep-related focal epilepsy on chromosome 8p12.3-8q12.3. By sequencing the positional candidate neuronal cholinergic receptor alpha 2 subunit gene (CHRNA2), we detected a heterozygous missense mutation, I279N, in the first transmembrane domain that is crucial for receptor function. Whole-cell recordings of transiently transfected HEK293 cells expressing either the mutant or the wild-type receptor showed that the new CHRNA2 mutation markedly increases the receptor sensitivity to acetylcholine, therefore indicating that the nicotinic alpha 2 subunit alteration is the underlying cause. CHRNA2 is the third neuronal cholinergic receptor gene to be associated with familial sleep-related epilepsies. Compared with the CHRNA4 and CHRNB2 mutations reported elsewhere, CHRNA2 mutations cause a more complex and finalized ictal behavior.

PMID: 16826524 [PubMed - indexed for MEDLINE]

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A major role of the nicotinic acetylcholine receptor gene CHRNA2 in autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) is unlikely. [Neurosci Lett. 2007]

Autosomal dominant nocturnal frontal lobe epilepsy. A video-polysomnographic and genetic appraisal of 40 patients and delineation of the epileptic syndrome. [Brain. 1998]

A missense mutation in the neuronal nicotinic acetylcholine receptor alpha 4 subunit is associated with autosomal dominant nocturnal frontal lobe epilepsy. [Neurology. 1995]

Autosomal dominant nocturnal frontal lobe epilepsy with a mutation in the CHRNB2 gene. [Epilepsia. 2007]

The nicotinic receptor beta 2 subunit is mutant in nocturnal frontal lobe epilepsy. [Neurology. 2000]

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Neuronal nicotinic receptor agonists for the treatment of attention-deficit/hyperactivity disorder: focus on cognition.

Wilens TE, Decker MW.

Massachusetts General Hospital, Pediatric Psychopharmacology Research Unit, Yawkey Center for Outpatient Care-YAW 6A, Boston, MA 02114, USA. twilens@partners.org

Attention deficit/hyperactivity disorder (ADHD) is the most commonly diagnosed neurobehavioral disorder in children and adolescents, and in about half of these patients, significant symptomology continues into adulthood. Although impulsivity and hyperactivity are the most salient features of ADHD, cognitive deficits, particularly impairments in attention and executive function, are an important component, particularly in adolescents and adults, with over 90% of adults seeking treatment for ADHD manifesting cognitive dysfunction. Currently available medications treat the core ADHD symptoms but typically do not adequately address cognitive aspects of ADHD, underscoring the need for new therapeutics. Dopamine and norepinephrine are hypothesized to be particularly important in ADHD, but there is emerging evidence that cholinergic neurotransmission, particularly involving neuronal nicotinic acetylcholine receptors (nAChRs), may play a role in the pathophysiology of ADHD. Nicotine has demonstrated procognitive effects in both humans and experimental animals and has produced signals of efficacy in small proof-of-concept adult ADHD trials. Although adverse effects associated with nicotine preclude its development as a therapeutic, a number of novel nAChR agonists with improved safety/tolerability profiles have been discovered. Of these, ABT-418 and ABT-089 have both demonstrated signals of efficacy in adults with ADHD. Notably, tolerability issues that might be expected of a nAChR agonist, such as nausea and emesis, were not observed at efficacious doses of ABT-089. Further understanding of the effects of novel neuronal nAChR agonists on specific aspects of cognitive functioning in ADHD is required to assess the full potential of this approach.

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ABT-089, a neuronal nicotinic receptor partial agonist, for the treatment of attention-deficit/hyperactivity disorder in adults: results of a pilot study. [Biol Psychiatry. 2006]

A pilot controlled clinical trial of ABT-418, a cholinergic agonist, in the treatment of adults with attention deficit hyperactivity disorder. [Am J Psychiatry. 2009]

Cognitive enhancing properties and tolerability of cholinergic agents in mice: a comparative study of nicotine, donepezil, and SIB-1553A, a subtype-selective ligand for nicotinic receptors. [Neuropharmacology. 2003]

Central nicotinic receptor agonists ABT-418, ABT-089, and (-)-nicotine reduce distractibility. [Psychopharmacology (Berl). 1998]

Nicotinic acetylcholine involvement in cognitive function. [Psychopharmacology (Berl). 1998]

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Structure-guided drug design: conferring selectivity among neuronal nicotinic receptor and acetylcholine-binding protein subtypes.

Taylor P, Talley TT, Radic' Z, Hansen SB, Hibbs RE, Shi J.

Department of Pharmacology, Skaggs School of Pharmacy & Pharmaceutical Sciences, University of California, San Diego, La Jolla, CA 92093-0657, USA. pwtaylor@ucsd.edu

Neuronal nicotinic receptors, encoded by nine genes of the alpha and three of the beta type of subunits, and whose gene products assemble in distinct permutations as pentameric molecules, constitute a fertile area for structure-guided drug design. Design strategies are augmented by a wide variety of peptide, alkaloid and terpenoid toxins from various marine and terrestrial species that interact with nicotinic receptors. Also, acetylcholine-binding proteins from mollusks, as structural surrogates of the receptor that mimic its extracellular domain, provide atomic resolution templates for analysis of structure and response. Herein, we describe a structure-guided approach to nicotinic ligand design that employs crystallography of this protein as the basic template, but also takes into consideration the dynamic properties of the receptor molecules in their biological media. We present the crystallographic structures of several complexes of various agonists and antagonists that associate with the agonist site and can competitively block the action of acetylcholine. In so far as the extracellular domain is involved, we identify additional non-competitive sites at those subunit interfaces where agonists do not preferentially bind. Ligand association at these interface sites may modulate receptor function. Ligand binding is also shown by solution-based spectroscopic and spectrometric methods to affect the dynamics of discrete domains of the receptor molecule. The surrogate receptor molecules can then be employed to design ligands selective for receptor subtype through the novel methods of freeze-frame, click chemistry that uses the very structure of the target molecule as a template for synthesis of the inhibitor.

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Carrier-mediated transport of the quaternary ammonium neuronal nicotinic receptor antagonist n,n'-dodecylbispicolinium dibromide at the blood-brain barrier.

Lockman PR, Manda VK, Geldenhuys WJ, Mittapalli RK, Thomas F, Albayati ZF, Crooks PA, Dwoskin LP, Allen DD.

Department of Pharmaceutical Sciences, Texas Tech University Health Sciences Center, 1300 S. Coulter Dr., Amarillo, TX 79106-1712, USA.
paul.lockman@ttuhsc.edu

The quaternary ammonium compound N,N'-dodecyl-bispicolinium dibromide (bPiDDB) potently and selectively inhibits nicotinic receptors (nAChRs) mediating nicotine-evoked [(3)H]dopamine release and decreases nicotine self-administration, suggesting that this polar, charged molecule penetrates the blood-brain barrier (BBB). This report focuses on 1) BBB penetration of bPiDDB; 2) the mechanism of permeation; and 3) comparison of bPiDDB to the cations choline and N-octylnicotinium iodide (NONI), both of which are polar, charged molecules that undergo facilitated BBB transport. The BBB permeation of [(3)H]choline, [(3)H]NONI, and [(14)C]bPiDDB was evaluated using in situ rat brain perfusion methods. Cerebrovascular permeability surface-area product (PS) values for [(3)H]choline, [(3)H]NONI, and [(14)C]bPiDDB were comparable (1.33 +/- 0.1, 1.64 +/- 0.15, and 1.3 +/- 0.3 ml/s/g, respectively). To ascertain whether penetration was saturable, unlabeled substrate was added to the perfusion fluid. Unlabeled choline (500 microM) reduced the PS of [(3)H]choline to 0.15 +/- 0.06 microl/s/g (p < 0.01). Likewise, unlabeled bPiDDB (500 microM) reduced the PS of [(14)C]bPiDDB to 0.046 +/- 0.005 microl/s/g (p < 0.01), whereas unlabeled NONI reduced the PS for [(3)H]NONI by approximately 50% to 0.73 +/- 0.31 microl/s/g. The PS of [(14)C]bPiDDB was reduced (p < 0.05) in the presence of 500 microM choline, indicating that the BBB choline transporter may be responsible for the transport of bPiDDB into brain. Saturable kinetic parameters for [(14)C]bPiDDB were similar to those for [(3)H]choline. The current results suggest that bPiDDB uses the BBB choline transporter for approximately 90% of its permeation into brain, and they demonstrate the carrier-mediated BBB penetration of a novel bisquaternary ammonium nAChR antagonist.

PMID: 17921191 [PubMed - indexed for MEDLINE]

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Active transport of high-affinity choline and nicotine analogs into the central nervous system by the blood-brain barrier choline transporter. [J Pharmacol Exp Ther. 2003]

Discovery of a novel nicotinic receptor antagonist for the treatment of nicotine addiction: 1-(3-Picolinium)-12-triethylammonium-dodecane dibromide (TMPD). [Biochem Pharmacol. 2007]

N-n-alkylnicotinium analogs, a novel class of nicotinic receptor antagonist: inhibition of S(-)-nicotine-evoked [(3)H]dopamine overflow from superfused rat striatal slices. [J Pharmacol Exp Ther. 2002]

Introduction of unsaturation into the N-n-alkyl chain of the nicotinic receptor antagonists, NONI and NDNI: effect on affinity and selectivity. [AAPS J. 2005]

The effects of a novel nicotinic receptor antagonist N,N-dodecane-1,12-diyl-bis-3-picolinium dibromide (bPiDDB) on acute and repeated nicotine-induced increases in extracellular dopamine in rat nucleus accumbens. [Neuropharmacology. 2007]

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7-Azaindole derivatives as potential partial nicotinic agonists.

Stoit AR, den Hartog AP, Mons H, van Schaik S, Barkhuijsen N, Stroomer C, Coolen HK, Reinders JH, Adolfs TJ, van der Neut M, Keizer H, Kruse CG.

Solvay Pharmaceuticals, Research Laboratories, C.J. van Houtenlaan 36, 1381 CP Weesp, The Netherlands. axel.stoit@solvay.com

We have investigated a series of 7-azaindoles as potential partial agonists of the alpha4beta2 nicotinic acetylcholine receptor (nAChR). Three series of 7-azaindole derivatives have been synthesized and evaluated for rat brain neuronal nicotinic receptor affinity and functional activity. Compound (+)-51 exhibited the most potent nAChR binding ($K_i = 10$ nM). Compound 30A demonstrated both moderate binding affinity and partial agonist potency, thus representing a promising lead for the indications of cognition and smoking cessation.

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In pursuit of alpha4beta2 nicotinic receptor partial agonists for smoking cessation: carbon analogues. [Bioorg Med Chem Lett. 2005](#)

ABT-594 [(R)-5-(2-azetidylmethoxy)-2-chloropyridine]: a novel, orally effective analgesic acting via neuronal nicotinic acetylcholine receptors: I. In vitro characterization. [Pharmacol Exp Ther. 1998](#)

Novel 3-Pyridyl ethers with subnanomolar affinity for central neuronal nicotinic acetylcholine receptors. [J Med Chem. 1996](#)

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The neuronal nicotinic receptor subunit genes (CHRNA6 and CHRNB3) are associated with subjective responses to tobacco.

Zeiger JS, Haberstick BC, Schlaepfer I, Collins AC, Corley RP, Crowley TJ, Hewitt JK, Hopfer CJ, Lessem J, McQueen MB, Rhee SH, Ehringer MA.

Institute for Behavioral Genetics, University of Colorado, Boulder, CO 80309, USA.

Neuronal nicotinic acetylcholine receptors have been implicated in various measures of nicotine dependence. In this paper, we present findings from an exploratory study of single nucleotide polymorphisms (SNPs) in the CHRNB3 and CHRNA6 genes with tobacco and alcohol phenotypes, including frequency of use and three subjective response factors occurring shortly after initiation of use. Subjects were 1056 ethnically diverse adolescents ascertained from clinical and community settings. The most significant associations were found between two CHRNB3 SNPs (rs4950 and rs13280604) and the three subjective response factors to initial tobacco use. These findings were replicated in a separate community sample of 1524 families participating in the National Longitudinal Study of Adolescent Health. Both CHRNB3 SNPs were found to be associated with similar measures of subjective response to tobacco. These results indicate that early subjective response to nicotine may be a valuable endophenotype for genetic studies aimed at uncovering genes contributing to nicotine use and addiction.

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Cholinergic nicotinic receptor genes implicated in a nicotine dependence association study targeting 348 candidate genes with 3743 SNPs [Hum Mol Genet. 2007]

Gene-based analysis suggests association of the nicotinic acetylcholine receptor beta1 subunit (CHRNB1) and M1 muscarinic acetylcholine receptor (CHRM1) with vulnerability for nicotine dependence. [Hum Mol Genet. 2006]

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Neuronal nicotinic alpha7 receptors modulate inflammatory cytokine production in the skin following ultraviolet radiation.

Osborne-Hereford AV, Rogers SW, Gahring LC.

Department of Pathology, University of Utah School of Medicine, Salt Lake City, Utah 84132, United States.

The anti-inflammatory effects of the neuronal nicotinic receptor alpha7 (nAChRalpha7) are proposed to require acetylcholine release from vagal efferents. The necessity for vagal innervation in this anti-inflammatory pathway was tested in the skin, which lacks parasympathetic innervation, using ultraviolet radiation (UVB) to induce a local pro-inflammatory response. Cytokine responses to UV in mice administered chronic oral nicotine, a nAChR agonist, were reduced. Conversely, nAChRalpha7 knock-out mice exposed to UVB elicit an enhanced pro-inflammatory cytokine response in the skin. Altered pro-inflammatory responses correlated with changes in SOCS3 protein. These results demonstrate that nAChRalpha7 can participate in modulating a local pro-inflammatory response in the absence of parasympathetic innervation.

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T cells express alpha7-nicotinic acetylcholine receptor subunits that require a functional TCR and leukocyte-specific protein tyrosine kinase for nicotine-induced Ca²⁺ response. [J Immunol. 2007]

Activation of alpha7 nicotinic acetylcholine receptor by nicotine selectively up-regulates cyclooxygenase-2 and prostaglandin E2 in rat microglial cells. [Neuroinflammation. 2005]

Indirect modulation by alpha7 nicotinic acetylcholine receptors of noradrenaline release in rat hippocampal slices: interaction with glutamate and GABA systems and effect of nicotine with UVB. [Pharmacol. 2006]

Nicotine-induced neuroprotection against N-methyl-D-aspartic acid or beta-amyloid peptide occur through independent mechanisms distinguished by pro-inflammatory cytokines. [J Neurochem. 2003]

Activation of the cholinergic anti-inflammatory pathway ameliorates postoperative ileus. [Gastroenterology. 2007]

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CCCP enhances catecholamine release from the perfused rat adrenal medulla.

Lim DY, Park HG, Miwa S.

Department of Pharmacology, College of Medicine, Chosun University, Gwangju 501-759, Korea. dylim@chosun.ac.kr

The present study was designed to investigate the effect of carbonyl cyanide m-chlorophenylhydrazone (CCCP), a mitochondrial uncoupler, on secretion of catecholamines from the isolated perfused model of the rat adrenal gland and to establish the mechanism of its adrenomedullary secretion. The perfusion of CCCP (3×10^{-5} M) into an adrenal vein of for 90 min caused a great increase in catecholamine secretion. Tachyphylaxis to catecholamine-releasing effect of CCCP was not observed by repeated perfusion of it. The net catecholamine-releasing effects of CCCP were depressed by pretreatment with pirenzepine (a selective muscarinic M(1)-receptor antagonist), chlorisondamine (a selective neuronal nicotinic receptor antagonist), nicardipine (an L-type Ca^{2+} -channel antagonist), TMB-8 (an intracellular Ca^{2+} -antagonist), and the perfusion of EGTA plus Ca^{2+} -free medium, respectively. In the presence of CCCP (3×10^{-5} M), catecholamine secretory responses induced by ACh (5.32×10^{-3} M), high K^+ (5.6×10^{-2} M, a direct membrane depolarizer), DMPP (10^{-4} M, (a selective neuronal nicotinic receptor agonist), and McN-A-343 (10^{-4} M, (a selective muscarinic M1-receptor agonist) were significantly enhanced. CCCP also significantly enhanced the catecholamine secretory responses evoked by Bay-K-8644 (10^{-5} M), L-type Ca^{2+} channel activator, and cyclopiazonic acid (10^{-5} M), an inhibitor of Ca^{2+} -ATPase. Furthermore, the perfusion of FCCP (3×10^{-5} M), a similar mitochondrial uncoupler, into an adrenal vein of for 90 min also caused a great increase in catecholamine secretion in a similar pattern with CCCP. Taken together, the results demonstrate that CCCP causes the catecholamine secretion from the perfused rat adrenal medulla in a calcium-dependent fashion. It is thought that this catecholamine secretory enhancement of CCCP may be mediated by both cholinergic receptor stimulation and membrane depolarization, which are relevant to the cytoplasmic Ca^{2+} increase by stimulation of the Ca^{2+} influx as well as by the inhibition of Ca^{2+} uptake into the cytoplasmic Ca^{2+} stores (both endoplasmic reticulum and mitochondria in chromaffin cells). It also seems that protonophores, such as CCCP, suppress mitochondrial Ca^{2+} uptake and increase the stimulated secretion

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of catecholamine by the secretagogues. These results indicate that mitochondria modulate catecholamine secretion by regulating the Ca²⁺ mobilization for exocytosis.

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FULL-TEXT ARTICLE

ABT-089, a neuronal nicotinic receptor partial agonist, for the treatment of attention-deficit/hyperactivity disorder in adults: results of a pilot study.

Wilens TE, Verlinden MH, Adler LA, Wozniak PJ, West SA.

Department of Psychiatry, Massachusetts General Hospital, Boston, Massachusetts 02114, USA. twilens@partners.org

BACKGROUND: This pilot study was designed to evaluate ABT-089, a neuronal nicotinic receptor partial agonist, as treatment for adult attention-deficit/hyperactivity disorder (ADHD).
METHODS: Adults with ADHD received placebo, 2 mg, 4 mg, or 20 mg of ABT-089 for 2 weeks each in a randomized, double-blind, placebo-controlled, 4 x 4 Latin square design for a total of 8 weeks. In addition to the primary outcome, the Conner's Adult ADHD Rating Scale (CAARS), secondary rating scales, and neuropsychological and safety assessments were completed.
RESULTS: A total of 11 adults with well-characterized ADHD completed this crossover study. ABT-089 b.i.d. was superior to placebo for the CAARS Total Symptom Score, which was the primary endpoint (placebo: 38.0 +/- 1.9; 2 mg b.i.d.: 32.2 +/- 1.9, one-tail p = .021; 4 mg b.i.d.: 33.2 +/- 1.9, p = .047; 20 mg b.i.d.: 33.5 +/- 1.9, p = .056). ABT-089 was also superior to placebo for the CAARS ADHD Index and Hyperactive/Impulsive scores and the Clinical Global Impression-ADHD Severity score. On the clinical efficacy endpoints, CAARS Total Symptom Score and CAARS Hyperactive/Impulsive score, a shallow inverted U-shaped dose-response curve was observed; however, the dose-response curve for attention and memory effects as measured by computerized cognitive testing seemed dose-linear. No clinically meaningful findings in safety assessments or side effect profile were observed. **CONCLUSIONS:** Data from this pilot study suggest that ABT-089 might be effective in treating adult ADHD and that it is well tolerated. On the basis of these promising results, larger, parallel-group ABT-089 studies of longer duration are warranted.

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Does DRQS-methylphenidate improve core symptoms and deficits in executive function? Results of an open-label trial in adults with attention deficit hyperactivity disorder. *Ann Clin Psychiatry.* 2006

Once-daily atomoxetine treatment for children with attention-deficit/hyperactivity disorder, including an assessment of evening and morning behavior: a double-blind, placebo-controlled trial. *Pediatrics.* 2004

Efficacy of a novel biphasic controlled-release methylphenidate formula in adults with attention-deficit/hyperactivity disorder: results of a double-blind, placebo-controlled crossover study. *J Clin Psychiatry.* 2007

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Alpha-selenoconotoxins, a new class of potent alpha7 neuronal nicotinic receptor antagonists.

Armishaw CJ, Daly NL, Nevin ST, Adams DJ, Craik DJ, Alewood PF.

Institute for Molecular Bioscience, University of Queensland, Brisbane, Queensland 4072, Australia.

Disulfide bonds are important structural motifs that play an essential role in maintaining the conformational stability of many bioactive peptides. Of particular importance are the conotoxins, which selectively target a wide range of ion channels that are implicated in numerous disease states. Despite the enormous potential of conotoxins as therapeutics, their multiple disulfide bond frameworks are inherently unstable under reducing conditions. Reduction or scrambling by thiol-containing molecules such as glutathione or serum albumin in intracellular or extracellular environments such as blood plasma can decrease their effectiveness as drugs. To address this issue, we describe a new class of selenoconotoxins where cysteine residues are replaced by selenocysteine to form isosteric and nonreducible diselenide bonds. Three isoforms of alpha-conotoxin ImI were synthesized by t-butoxycarbonyl chemistry with systematic replacement of one ([Sec(2,8)]ImI or [Sec(3,12)]ImI), or both ([Sec(2,3,8,12)]ImI) disulfide bonds with a diselenide bond. Each analogue demonstrated remarkable stability to reduction or scrambling under a range of chemical and biological reducing conditions. Three-dimensional structural characterization by NMR and CD spectroscopy indicates conformational preferences that are very similar to those of native ImI, suggesting fully isomorphous structures. Additionally, full bioactivity was retained at the alpha7 nicotinic acetylcholine receptor, with each selenoanalogue exhibiting a dose-response curve that overlaps with wild-type ImI, thus further supporting an isomorphous structure. These results demonstrate that selenoconotoxins can be used as highly stable scaffolds for the design of new drugs.

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Novel alpha-conotoxins from *Conus spurius* and the alpha-conotoxin EI share high-affinity potentiation and low-affinity inhibition of nicotinic acetylcholine receptors. [PLoS J. 2007]

Minimal conformation of the alpha-conotoxin ImI for the alpha7 neuronal nicotinic acetylcholine receptor recognition: correlated CD, NMR and X-ray crystallography. [FEBS Lett. 1999]

NMR solution structure of alpha-conotoxin ImI and comparison to other conotoxins specific for neuronal nicotinic acetylcholine receptors. [Biochemistry. 1999]

Structure of alpha-conotoxin BnA: influences of disulfide connectivity on structural dynamics. [BMC Struct Biol. 2007]

Structure-activity relationships in a peptidic alpha7 nicotinic acetylcholine receptor antagonist. [J Mol Biol. 2000]

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Population-based and family-based association studies of an (AC)_n dinucleotide repeat in alpha-7 nicotinic receptor subunit gene and schizophrenia.

Fan JB, Ma J, Li XW, Zhang CS, Sun WW, He G, Gu NF, Feng GY, St Clair D, He L.

Institute for Nutritional Sciences, Shanghai Institute of Biological Sciences, Chinese Academy of Sciences, 200031, China.

The human alpha-7 neuronal nicotinic receptor subunit (CHRNA7) gene, located at chromosome 15q13.2, represents a strong candidate gene for schizophrenia. We have examined an (AC)_n dinucleotide repeat in intron 2 of the CHRNA7 gene, which was previously shown to be strongly linked with schizophrenia, using both population-based and family-based association studies. In the population-based study, no significant differences between the genotype and allele frequency distributions in schizophrenia patients and control subjects were observed after correction for multiple testing, although a nominally significant association between the most common allele and schizophrenia was observed (P = 0.023, uncorrected for multiple testing). In the family-based study, there is no significant over-transmission (Transmitted/Non-transmitted: 61/50) of the same allele in 160 family trios. Overall, our results do not support a major role for the (AC)_n dinucleotide repeat in schizophrenia susceptibility in Han Chinese. Further large-scale genetic studies based on a set of single nucleotide polymorphisms (SNPs) that fully characterize the linkage disequilibrium patterns at the CHRNA7 gene are necessary to determine the relevance of this gene as a risk factor for schizophrenia susceptibility.

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Linkage disequilibrium for schizophrenia at the chromosome 15q13-14 locus of the alpha7-nicotinic acetylcholine receptor subunit gene (CHRNA7) [Am J Med Genet. 2001]

Association study of neuregulin 1 gene with schizophrenia. [Mol Psychiatry. 2003]

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Signaling mechanisms underlying Abeta toxicity: potential therapeutic targets for Alzheimer's disease.

Smith WW, Gorospe M, Kusiak JW.

Division of Neurobiology, Department of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA. wsmith60@jhmi.edu

The accumulation of amyloid beta peptide (Abeta) is believed to be an early and critical event leading to synapse and neuronal cell loss in Alzheimer's Disease (AD). Abeta itself is toxic to neurons in vitro and the load of Abeta in vivo causes the loss of synapses and neurons in brain in animal models. Therefore, there has been considerable interest in elucidating the mechanism(s) of Abeta neurotoxicity. Here, we review the molecular signaling pathways involved in Abeta-induced cell death, including signaling through the neuronal nicotinic receptor and the Abeta-triggered generation of reactive oxygen species (ROS) leading to the activation of the c-jun N-terminal kinase (JNK), and the ensuing phosphorylation of p66Shc and inactivation of the Forkhead transcription factors. This focused review not only provides a better understanding of the signaling mechanisms involved in Abeta-induced cell death, but also underscores the potential of JNK, p66Shc, Forkhead proteins, p25/cdk5, and neuronal nicotinic receptor, as therapeutic targets for AD.

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- Phosphorylation of p66Shc and forkhead proteins mediates Abeta toxicity. *Cereb Biol.* 2005
- Signaling events in amyloid beta-peptide-induced neuronal death and insulin-like growth factor I protection. *J Biol Chem.* 2002
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Enhancement of insulin-induced PI3K/Akt/GSK-3beta and ERK signaling by neuronal nicotinic receptor/PKC-alpha/ERK pathway: up-regulation of IRS-1/2 mRNA and protein in adrenal chromaffin cells.

Sugano T, Yanagita T, Yokoo H, Satoh S, Kobayashi H, Wada A.

Department of Pharmacology, Miyazaki Medical College, University of Miyazaki, Miyazaki, Japan.

In cultured bovine adrenal chromaffin cells treated with nicotine (10 microm for 24 h), phosphorylation of Akt, glycogen synthase kinase-3beta (GSK-3beta) and extracellular signal-regulated kinase (ERK)1/2 induced by insulin (100 nm for 10 min) was enhanced by approximately 62%, without altering levels of these protein kinases. Nicotine produced time (> 12 h)- and concentration (EC(50) 3.6 and 13 microm)-dependent increases in insulin receptor substrate (IRS)-1 and IRS-2 levels by approximately 125 and 105%, without altering cell surface density of insulin receptors. In these cells, insulin-induced tyrosine phosphorylation of IRS-1/IRS-2 and recruitment of phosphoinositide 3-kinase (PI3K) to IRS-1/IRS-2 were augmented by approximately 63%. The increase in IRS-1/IRS-2 levels induced by nicotine was prevented by nicotinic acetylcholine receptor (nAChR) antagonists, the Ca(2+) chelator 1,2-bis(2-aminophenoxy)-ethane-N,N',N'-tetra-acetic acid tetrakis-acetoxymethyl ester, cycloheximide or actinomycin D. Nicotine increased IRS-1 and IRS-2 mRNA levels by approximately 57 and approximately 50%, and this was prevented by conventional protein kinase C (cPKC) inhibitor Gö6976, or ERK kinase inhibitors PD98059 and U0126. Nicotine phosphorylated cPKC-alpha, thereby increasing phosphorylation of ERK1/ERK2, as demonstrated by using Gö6976, PD98059 or U0126. Selective activation of cPKC-alpha by thymeleatoxin mimicked these effects of nicotine. Thus, stimulation of nAChRs up-regulated expression of IRS-1/IRS-2 via Ca(2+)-dependent sequential activation of cPKC-alpha and ERK, and enhanced insulin-induced PI3K/Akt/GSK-3beta and ERK signaling pathways.

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Insulin-like growth factor 1 inhibits extracellular signal-regulated kinase to promote neuronal survival via the phosphatidylinositol 3-kinase/protein kinase A/c-Raf pathway. [\[J Neurosci. 2005\]](#)

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Effects of TC-1734 (AZD3480), a selective neuronal nicotinic receptor agonist, on cognitive performance and the EEG of young healthy male volunteers.

Dunbar G, Boeijinga PH, Demazières A, Cisterni C, Kuchibhatla R, Wesnes K, Luthringer R.

TARGACEPT Inc., 200 East First Street Suite 300, Winston-Salem, NC 27101-4165, USA.

OBJECTIVES: The aim of this study was to get insight into the central effects of TC-1734 (renamed AZD3480), a selective agonist at the neuronal nicotinic receptor of the alpha4beta2 subtype. MATERIALS AND METHODS: Electroencephalography (EEG) techniques and computerized cognitive tests were performed in young, healthy male volunteers during two double-blind and placebo-controlled studies: a rising single dose crossover study (from 2 to 320 mg) and a rising repeated dose study with a parallel group design (50, 100, and 200 mg). RESULTS: In contrast to acute administration, administration of AZD3480 over 10 days produced statistically significant enhancement of several cognitive measures (attention and episodic memory) compared to placebo. Regarding EEG data, AZD3480 showed acceleration of the alpha centroid and of the alpha peak in the single-dose study. This EEG profile of the acceleration type was confirmed in the repeated dose study on both day 1 and day 10, with the greatest effect observed with the highest dose. The EEG pattern shown for AZD3480 was consistent with that previously described with other drugs known to improve attention and vigilance (including nicotine). In addition, subjects dosed with AZD3480 showed a statistically significant increase in mismatch negativity (MMN) amplitude at 50 and 200 mg while reducing MMN latency (200 mg only), suggesting an improvement of pre-attentional mechanisms. CONCLUSION: These early data in healthy subjects provide encouragement to consider development of AZD3480 as a novel agent for the treatment of cognitive decline in the elderly, including age-associated memory impairment and/or dementia of the Alzheimer's type.

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Cognitive enhancement in man with ispronicline, a nicotinic partial agonist. [Int J Neuropsychopharmacol. 2006]

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Synthesis of bicyclic tertiary alpha-amino acids.

Strachan JP, Whitaker RC, Miller CH, Bhatti BS.

Targacept, Inc., Winston-Salem, North Carolina 27101-4165, USA.

Novel bicyclic alpha-amino acids, exo and endo-1-azabicyclo[2.2.1]heptane-2-carboxylic acid, 1-azabicyclo[2.2.1]heptane-7-carboxylic acid, and 1-azabicyclo[3.2.2]nonane-2-carboxylic acid have been readily synthesized for the generation of neuronal nicotinic receptor ligands. Alkylation of glycine-derived Schiff bases or nitroacetates with cyclic ether electrophiles, followed by acid-induced ring opening and cyclization in NH₄OH, allowed for the preparation of substantial quantities of the three tertiary bicyclic alpha-amino acids.

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Enantioselective synthesis of bicyclo[3.1.0]nonane-9-carboxylic acids via Me₂AlOTf-promoted intramolecular Friedel-Crafts alkylation of arenes with the gamma-lactone moiety of 3-oxabicyclo[3.1.0]hexane-2-one. [J Org Chem. 2003]

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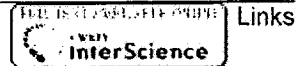
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Association of the neuronal nicotinic receptor beta2 subunit gene (CHRNA4) with subjective responses to alcohol and nicotine.

Ehringer MA, Clegg HV, Collins AC, Corley RP, Crowley T, Hewitt JK, Hopfer CJ, Krauter K, Lessem J, Rhee SH, Schlaepfer I, Smolen A, Stallings MC, Young SE, Zeiger JS.

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Nicotine addiction and alcohol dependence are highly comorbid disorders that are likely to share overlapping genetic components. We have examined two neuronal nicotinic receptor subunit genes (CHRNA4 and CHRN2) for possible associations with nicotine and alcohol phenotypes, including measures of frequency of use and measures of initial subjective response in the period shortly after first using the drugs. The subjects were 1,068 ethnically diverse young adults participating in ongoing longitudinal studies of adolescent drug behaviors at the University of Colorado, representing both clinical and community samples. Analysis of six SNPs in the CHRNA4 gene provided modest support for an association with past 6 month use of alcohol in Caucasians (three SNPs with $P < 0.08$), but no evidence for an association with tobacco and CHRNA4 was detected. However, a SNP (rs2072658) located immediately upstream of CHRN2 was associated with the initial subjective response to both alcohol and tobacco. This study provides the first evidence for association between the CHRN2 gene and nicotine- and alcohol-related phenotypes, and suggests that polymorphisms in CHRN2 may be important in mediating early responses to nicotine and alcohol.

PMID: 17226798 [PubMed - indexed for MEDLINE]

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Haplotypes of four novel single nucleotide polymorphisms in the nicotinic acetylcholine receptor beta2-subunit (CHRN2) gene show no association with smoking initiation or nicotine dependence. [Am J Med Genet. 2000]

Genetic and functional analysis of single nucleotide polymorphisms in the beta2-neuronal nicotinic acetylcholine receptor gene (CHRN2). [Nicotine Tob Res. 2002]

CHRNA4 and tobacco dependence: from gene regulation to behavior. [Arch Gen Psychiatry. 2007]

The neuronal nicotinic receptor subunit genes (CHRNA6 and CHRN3) are associated with subjective responses to tobacco. [Hum Mol Genet. 2008]

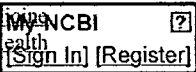
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Attention-deficit/hyperactivity disorder: a plausible mouse model?

Granon S, Changeux JP.

URA CNRS Récepteur et Cognition, Institut Pasteur, Paris, France. granon@pasteur.fr

Attention-deficit/hyperactivity disorder (ADHD) is a multifactorial and heterogeneous disorder, highly prevalent in children and characterized by three main components: inattention, lack of inhibitory control and hyperactivity. Epidemiological evidence reveals that ADHD is associated with nicotine exposure, mostly, with prenatal cigarette smoking. Mice deleted for the beta2-subunit gene of the neuronal nicotinic receptor are proposed as a simple and reliable animal model for ADHD. CONCLUSION: Nicotinic agonists targeting the alpha4beta2 nicotinic receptors alleviate ADHD symptoms and may possibly contribute to an efficient therapy of ADHD children.

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Neuronal nicotinic receptor agonists for the treatment of attention-deficit/hyperactivity disorder: focus on the alpha4beta2 receptor. [Biol Psychiatry. 2007](#)

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Regulation of neuronal nicotinic receptor traffic and expression.

Gaimarri A, Moretti M, Riganti L, Zanardi A, Clementi F, Gotti C.

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Neuronal nicotinic acetylcholine receptors (nAChRs) are a family of cation channels widely distributed in the brain, whose subunit composition and biophysical properties vary depending on the subtype and the area of the brain in which they are found. Brain nAChRs are also the target of nicotine, the most widespread drug of abuse. Chronic nicotine exposure differentially affects the number, subunit composition, stoichiometry and functional state of some nAChR subtypes, leaving others substantially unaffected. In this review, we will summarise recent data concerning the nAChR subtypes expressed in the CNS, and how they are regulated by means of chronic nicotine and/or nicotinic drugs. We will particularly focus on the possible mechanisms involved in the up-regulation of nAChRs.

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