Vareniclina (Champix®): Desde las señales de la naturaleza a la innovación en la cesación del fumado

Dr. Pedro Lovato

Basado en la presentación del

Dr. Daniel Bustos Montero

Diciembre 2013

El Tabaquismo como problema de salud pública

- **A pesar de los riesgos para la salud asociados con el tabaquismo, la prevalencia del consumo crónico del tabaco y en consecuencia la dependencia a la nicotina se mantienen altos en los Estados Unidos para el año 2004 – 44.5 millones de fumadores.[1,2]**
- **Mientras que la prevalencia de fumadores disminuyo desde 1998 cuando fue del 24,1%, esta disminución no fue suficiente para alcanzar el objetivo nacional de salud en Estados Unidos de prevalencia ≤ 12% en 2010 según el Centro para el Control y Prevención de Enfermedades (CDC) (20,9% de los estadounidenses adultos eran fumadores en 2004).[2]**

1. Fiore, M.C., Bailey, W.C., Cohen, S.J. et al. Treating tobacco use and dependence: Clinical practice guideline.US Dept of Health and Human Services, Public Health Service, Rockville, 2000.
2. 2. Centers for Disease Control and Prevention. Cigarette smoking among adults – UnitedStates, 2004. MMWR Morb Mortal Wkly Rep2005, 54: 1121-4.

El Tabaquismo como problema de salud pública

- **Actualmente, 1 de cada 10 personas morirán a causa de enfermedades relacionadas con el tabaco en todo el mundo.** [3]
- **Se estima que de no controlar el tabaquismo en la población, la mortalidad mundial relacionada con el tabaco adicionará 10 millones de personas al año en 2020 a sus cifras.** [3]
- **En los Estados Unidos, aproximadamente 438.000 muertes prematuras ocurrieron cada año debido al consumo de tabaco entre 1997 y 2001.** [5]

3. World Health Organization. Why is tobacco a public health priority? http://www.who.int/tobacco/health_priority/en/index.html.; Accessed September 8, 2006.
5. Centers for Disease Control and Prevention.Annual smoking-attributable mortality, years ofpotential life lost, and productivity losses –United States, 1997-2001. MMWR MorbMortal Wkly Rep 2005, 54: 625-8.

El Tabaquismo como problema de salud pública

- **Fumar es un factor de riesgo reconocido para el cáncer y las enfermedades cardíacas y pulmonares, sin embargo, muchos de los efectos adversos para la salud del consumo de tabaco son reversibles.** [5]
- **La mayoría de los fumadores (70%) en un informe de los Estados Unidos tiene ganas de parar y muchos (40,5%) intentan dejar de fumar cada año, pero sólo el 3-5% de los que intentan dejar de fumar por sí solos son capaces de mantenerse libre de tabaco hasta por12 meses.** [1, 2, 6]

1. Fiore, M.C., Bailey, W.C., Cohen, S.J. et al. Treating tobacco use and dependence: Clinical practice guideline.US Dept of Health and Human Services, Public Health Service, Rockville, 2000.
2. Centers for Disease Control and Prevention. Cigarette smoking among adults – UnitedStates, 2004. MMWR Morb Mortal Wkly Rep2005, 54: 1121-4.
6. Hughes, J.R., Keely, J., Naud, S. Shape of the relapse curve and long-term abstinence among untreated smokers. Addiction 2004, 99:29-38.

El Tabaquismo como problema de salud pública – CDC Review Advice to Quit

TABLE 1. Percentage of current tobacco smokers* aged ≥15 years who visited a health-care provider during the preceding 12 months and were asked about smoking and advised to quit, by selected characteristics — Global Adult Tobacco Survey, 17 countries, 2008–2011

	Bangladesh (2009†)		Brazil (2008)		China (2010)		Egypt (2009)		India (2009–2010)		Indonesia (2011)	
Characteristic	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)
Percentage of current smokers	23.0	(21.9–24.2)	17.2	(16.7–17.7)	28.1	(26.7–29.7)	19.4	(18.8–20.1)	14.0	(13.4–14.6)	34.8	(33.2–36.4)
Percentage of current smokers who visited a health-care provider§	38.3	(35.0–41.7)	58.8	(57.3–60.3)	30.0	(26.7–33.5)	21.6	(19.9–23.5)	47.3	(45.3–49.4)	30.2	(26.5–34.2)
Percentage asked by a health-care provider if they smoked¶	56.0	(49.9–62.0)	71.0	(69.3–72.6)	40.8	(35.3–46.5)	74.1	(70.7–77.2)	53.0	(50.3–55.7)	40.5	(34.6–46.6)
Sex												
Male	55.9	(49.7–61.9)	70.2	(67.7–72.5)	41.7	(36.1–47.6)	75.3	(71.8–78.6)	54.0	(51.2–56.8)	41.6	(35.7–47.8)
Female	64.6	(40.4–83.0)	71.8	(69.5–74.0)	25.5	(18.2–34.5)	35.8	(19.8–55.8)	45.5	(37.6–53.7)	17.9	(9.0–32.4)
Age group (yrs)												
15–24	31.3	(20.4–44.9)	54.9	(49.3–60.4)	22.8	(12.2–38.6)	60.9	(46.0–74.0)	31.3	(23.6–40.2)	31.6	(21.6–43.5)
25–44	54.2	(44.1–63.9)	70.2	(67.8–72.5)	34.2	(26.6–42.6)	74.1	(68.8–78.8)	51.3	(47.6–55.0)	38.8	(30.9–47.4)
45–64	69.2	(61.8–75.8)	74.6	(71.9–77.2)	45.9	(39.6–52.4)	76.5	(70.7–81.4)	58.5	(54.1–62.8)	44.2	(37.1–51.4)
≥65	60.1	(45.7–73.0)	81.6	(76.9–85.5)	54.7	(45.9–63.2)	82.7	(71.5–90.1)	63.8	(57.0–70.1)	49.1	(38.3–59.9)
Residence												
Urban	52.3	(37.6–66.5)	71.5	(69.7–73.3)	39.4	(33.4–45.8)	74.3	(69.6–78.6)	57.9	(53.8–62.0)	42.1	(34.4–50.2)
Rural	57.4	(51.4–63.2)	67.8	(63.5–71.8)	41.7	(33.8–50.1)	73.9	(69.0–78.2)	51.5	(48.1–54.8)	39.2	(30.9–48.1)
Education level**												
Less than primary	56.9	(48.4–65.1)	NA	NA	47.6	(38.9–56.5)	78.2	(73.6–82.2)	54.6	(50.9–58.3)	42.3	(34.2–51.0)
Primary	51.9	(42.6–61.1)	NA	NA	41.0	(31.0–51.7)	72.8	(60.7–82.3)	52.3	(47.4–57.3)	35.4	(25.0–47.3)
Secondary	63.7	(47.3–77.4)	NA	NA	40.0	(33.9–46.5)	69.4	(62.2–75.7)	48.1	(41.9–54.3)	41.3	(33.7–49.2)
University	57.6	(34.6–77.8)	NA	NA	30.0	(20.2–42.1)	67.2	(53.9–78.2)	54.3	(45.0–63.2)	48.6	(36.2–61.2)

4. Centers for Disease Control and Prevention - MMWR. Health-Care Provider Screening for Tobacco Smoking and Advice to Quit — 17 Countries, November 22, 2013 / Vol. 62 / No. 46

Adicción a la nicotina

- La nicotina durante mucho tiempo ha sido reconocida como un factor primordial en el fortalecimiento de la conducta de fumar. El consumo de nicotina resulta en cambios significativos en el cerebro que crean el deseo de fumar. [7, 8]
- La combinación de consumo de nicotina con rituales de comportamiento y aspectos sensoriales de fumar refuerza la conducta y el deseo de fumar. [7,8]
- El Informe del Instituto Nacional de Salud de Estados Unidos hizo hincapié en que el perfil farmacológico y conductual asociadas con el tabaquismo son similares a las de sustancias adictivas como la cocaína y la heroína . [8]

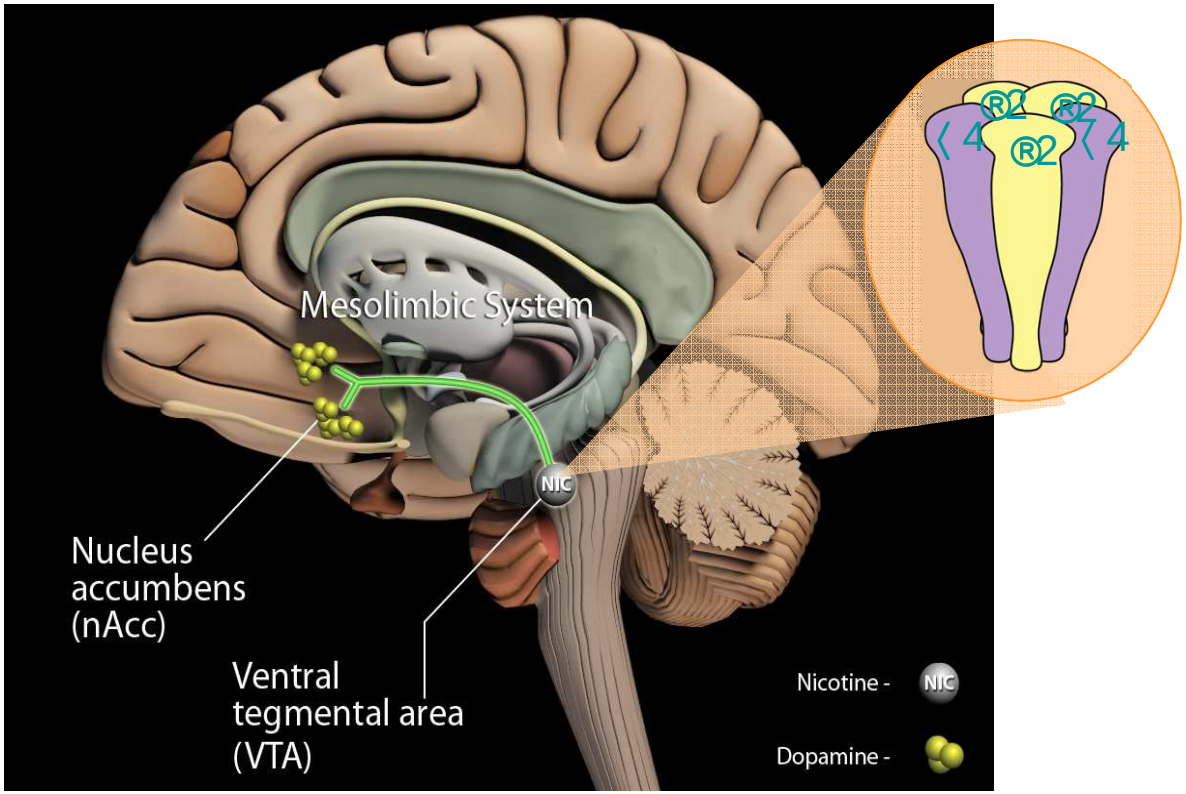
7. Jarvis, M.J. Why people smoke. BMJ 2004,328: 277-9.12. The Health Consequences of Smoking: Nicotine Addiction. Office of the Surgeon General, US Dept of Health and Human Services, Washington, DC, 1988.
8. The Health Consequences of Smoking:Nicotine Addiction. Office of the Surgeon General, US Dept of Health and HumanServices, Washington, DC, 1988.

Sustrato neurobiológico de la adicción a la nicotina

- La estimulación de las neuronas dopaminérgicas mesolímbicas está implicado en el efecto adictivo de varias drogas, incluyendo la nicotina. [9]
- Estas neuronas dopaminérgicas proyectan impulsos desde el área tegmental ventral a varias estructuras del cerebro, incluyendo el núcleo accumbens y la corteza prefrontal. [10]
- Aunque los receptores de acetilcolina nicotínicos (nAChR) se expresan en todo el sistema nervioso central, se ha demostrado que la estimulación de nicotina da como resultado la liberación de dopamina a la activación directa de los nAChR en el área tegmental ventral. [11]

9. Di Chiara, G. Role of dopamine in the behav-ioural actions of nicotine related to addiction.Eur J Pharmacol 2000, 393: 295-314.14. Mameli-Engvall, M., Evrard, A., Pons, S. et al. Hierarchical control of dopamine neuron-firing patterns by nicotinic receptors. Neuron 2006,50: 911-21.
10. Mameli-Engvall, M., Evrard, A., Pons, S. et al.Hierarchical control of dopamine neuron-firing patterns by nicotinic receptors. Neuron 2006,50: 911-21.
11. Jarvis, M.J. Why people smoke. BMJ 2004,328: 277-9.

Evidencias de que la nicotina es una sustancia psicoactiva que modifica el funcionamiento del Sistema Nervioso Central del fumador

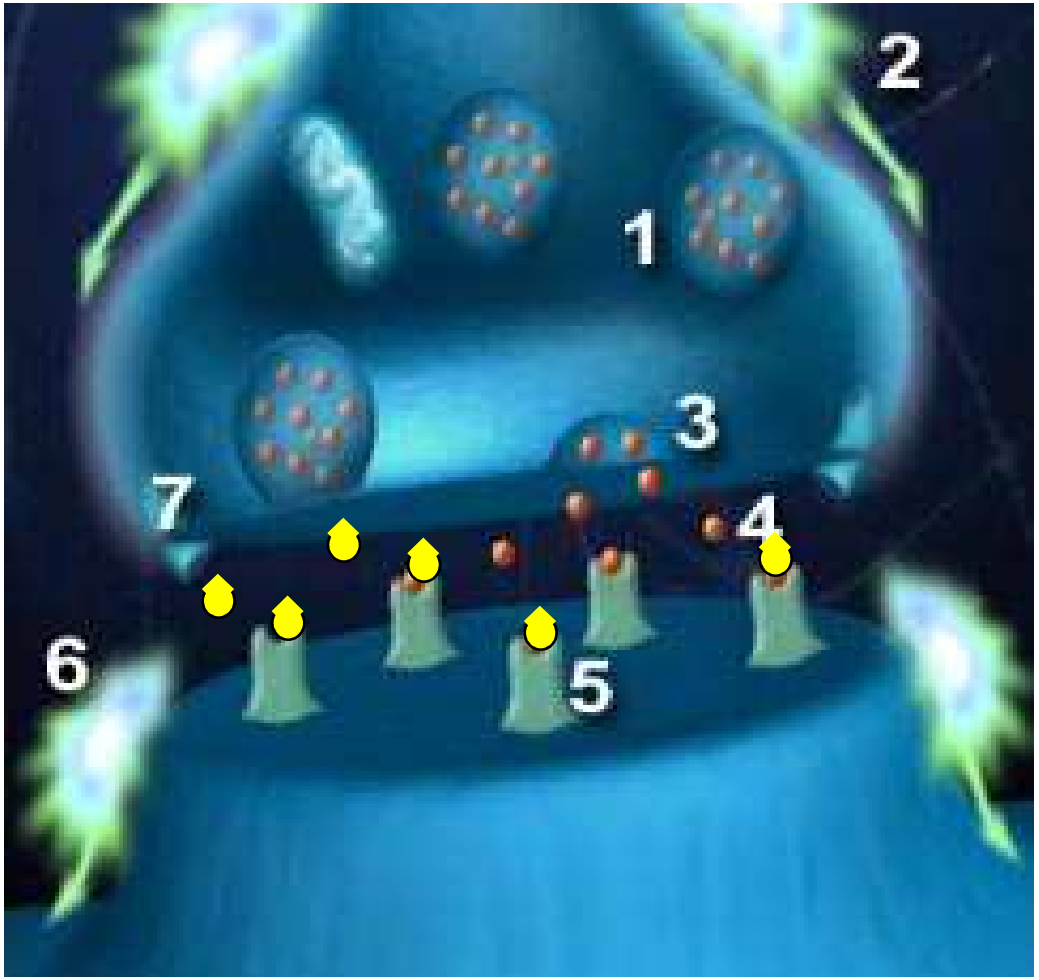


Sustrato neurobiológico de la adicción a la nicotina

- **Una mejor comprensión de la neurofisiología ha perfeccionado el foco de las conductas adictivas a la nicotina y su relacion con ciertos nAChRs específicos.** [12-18]
- **Los nAChR neuronales se expresan diferencialmente en todo el sistema nervioso, pero el receptor α4β2 es el más abundante subtipo nAChR en cerebro. Este ha sido identificado como central para la adicción a la nicotina.** [12-18]

12. Maskos, U., Molles, B.E., Pons, S. et al. Nico-tine reinforcement and cognition restored bytargeted expression of nicotinic receptors.Nature 2005, 436: 103-7.16.
13. Buccafusco, J.J. Neuronal nicotinic receptorsubtypes: Defining therapeutic targets. MolInterv 2004, 4: 285-95.17.
14. Cassels, B.K., Bermudez, I., Dajas, F., Abin-Carriquiry, J.A., Wonnacott, S. From ligand design to therapeutic efficacy: The challenge fornicotinic receptor research. Drug Discov Today2005, 10: 1657-65.18.
15. Dajas-Bailador, F., Wonnacott, S. Nicotinicacetylcholine receptors and the regulation ofneuronal signalling. Trends Pharmacol Sci2004, 25: 317-24.
16. Coe, J.W., Brooks, P.R., Wirtz, M.C. et al. 3,5-Bicyclic aryl piperidines: A novel class of alpha4beta2 neuronal nicotinic receptor partialagonists for smoking cessation. Bioorg MedChem Lett 2005, 15: 4889-97.
17. Tapper, A.R., McKinney, S.L., Nashmi, R. et al.Nicotine activation of alpha4* receptors: Sufficient for reward, tolerance, and sensitization. Science 2004, 306: 1029-32.
18. Picciotto, M.R., Zoli, M., Rimondini, R. et al.Acetylcholine receptors containing the beta2subunit are involved in the reinforcing proper-ties of nicotine. Nature 1998, 391: 173-7.

Adicción: el cerebro secuestrado



Conexión entre 2 neuronas

Rojo: Transmisor (ACh, DA)

Amarillo: Droga (Nicotina, Cocaina)

Una droga puede producir sistemas naturales de motivación y recompensa

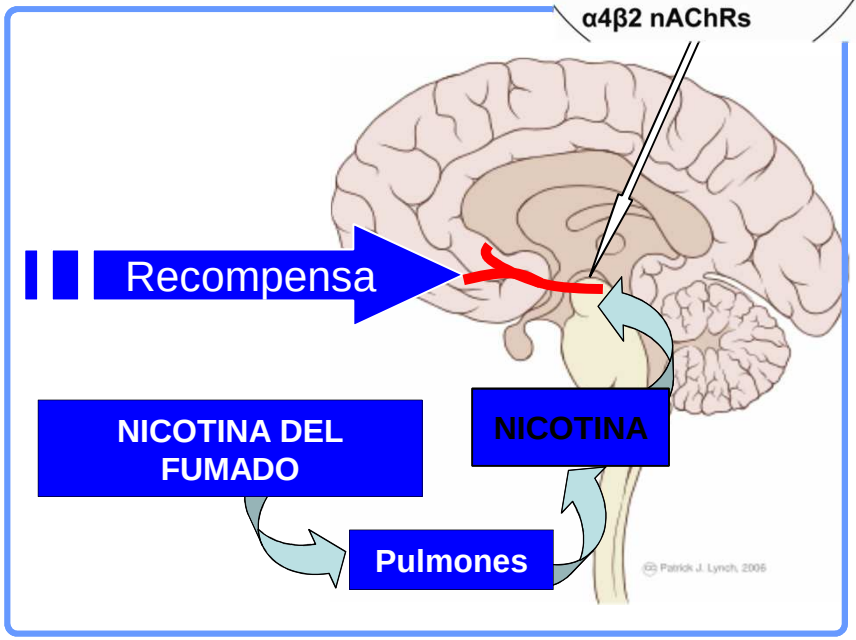
Esto causa cambios en las funciones cognitivas y emocionales, tales como compulsión para usar dichas drogas, conviertiéndose en una prioridad

Sustrato neurobiológico de la adicción a la nicotina

- La actividad agonista de la nicotina en el receptor α4β2 nAChR en el área tegmental ventral afecta tanto a los mecanismos sinápticos anteriores y posteriores que implican interacciones funcionales entre los sistemas dopaminérgicos y neurales γ-amino-butírico ácido-dependientes. [22-24]
- La exposición crónica a la nicotina provoca una desensibilización de los receptores nAChR y regulación superior. [22-24]

22. Brody, A.L., Mandelkern, M.A., London, E.D. et al. Cigarette smoking saturates brain alpha4beta2 nicotinic acetylcholine receptors. Arch Gen Psychiatry 2006, 63: 907-15.
23. Laviolette, S.R., van der Kooy, D. The neuro-biology of nicotine addiction: Bridging the gap from molecules to behaviour. Nat RevNeurosci 2004, 5: 55-65.27.
24. Coe, J.W., Brooks, P.R., Vetelino, M.G. et al. Varenicline: An alpha4beta2 nicotinic receptor partial agonist for smoking cessation. J MedChem 2005, 48: 3474-7.

Mecanismo de adicción a la nicotina



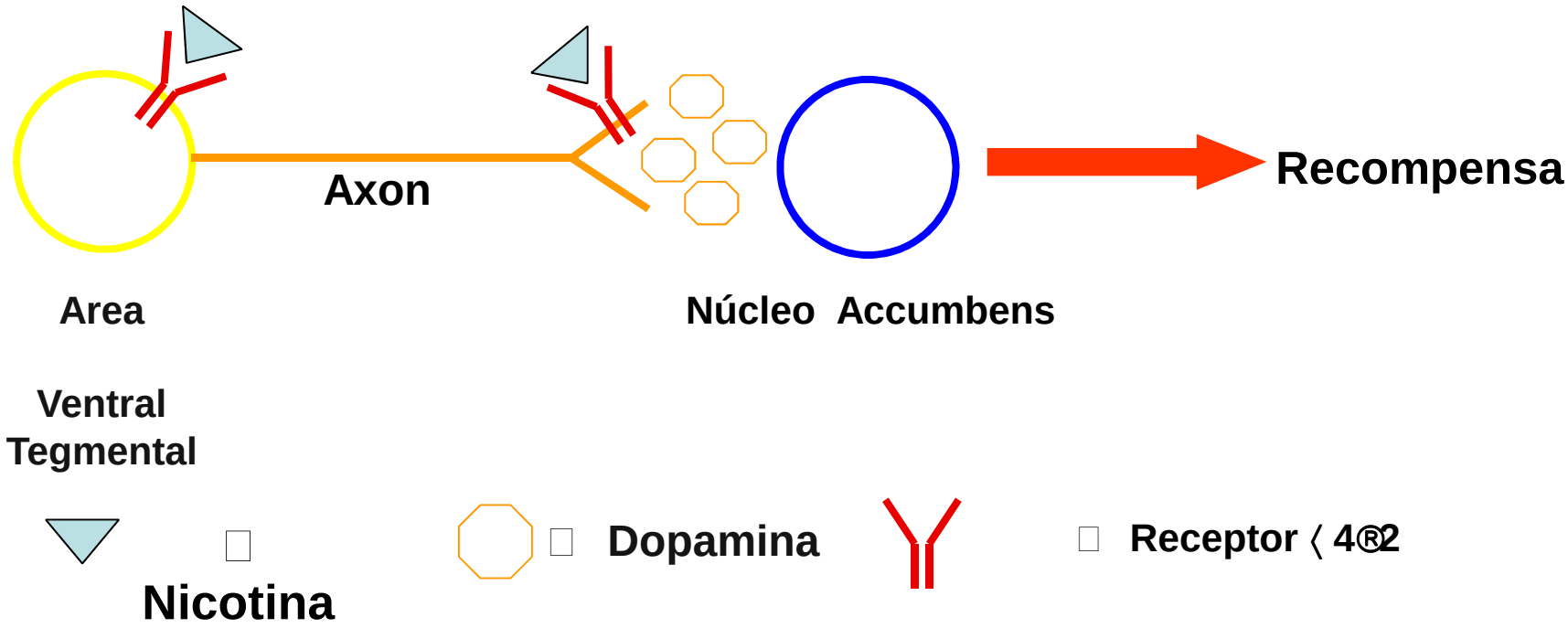
Después de inhalar, la nicotina entra rápidamente al cerebro (6 seg)

Se une a los receptores nicotínicos α4β2 nAChRs

Da efecto de recompensa en el cerebro por la liberación de dopamina

Mecanismo de acción de la nicotina

La nicotina activa a los receptores α4β2 en el área ventral tegmental lo que resulta en la liberación de dopamina en el núcleo accumbens. Esto determina el efecto de recompensa/sastisfacción de corto plazo que se asocia con fumar.



Vareniclina: Una opción para dejar de fumar

Farmacología

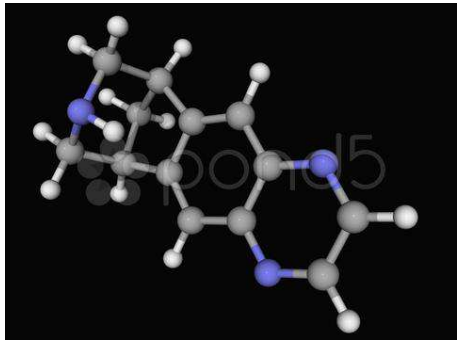
- **Se ha sugerido que una ayuda eficaz para dejar de fumar sería una opción que reduzca el stress y los síntomas de abstinencia, mientras que la atenúe los efectos inducidos por la nicotina.** [25, 26]
- **Este efecto podría conseguirse mediante un agente agonista parcial que tenga la capacidad de inhibir simultáneamente la acción provocada por la nicotina y la liberación de dopamina, reduciendo de esta manera la recompensa mientras que aumente el tono dopaminérgico para reducir la sintomatología de abstinencia.** [25, 26]

25. Coe, J.W., Brooks, P.R., Vetelino, M.G. et al.Varenicline: An alpha4beta2 nicotinic receptorpartial agonist for smoking cessation. J MedChem 2005, 48: 3474-7.
26. Mihalak, K.B., Carroll, F.I., Luetje, C.W.Varenicline is a partial agonist at alpha4beta2and a full agonist at alpha7 neuronal nicotinicreceptors. Mol Pharmacol 2006, 70: 801-5.

Vareniclina: Una opción para dejar de fumar

Farmacología

- La vareniclina es un agonista parcial selectivo nAChR con gran afinidad y un sitio específico de unión al receptor subtipo α4β2, es decir muestra selectividad por el receptor α4β2 con una afinidad de más de 500 veces mayor que para el subtipo α3β4 y más de 5000 veces mayor que para el subtipo α7. [27, 28]

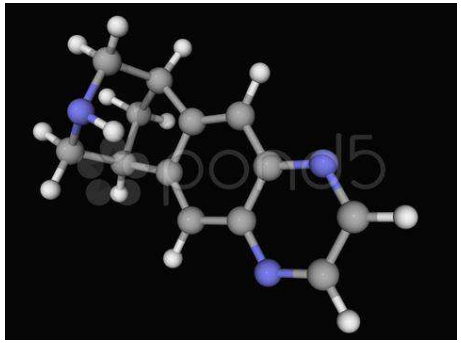


27. Mihalak, K.B., Carroll, F.I., Luetje, C.W.Varenicline is a partial agonist at alpha 4beta 2 and a full agonist at alpha7 neuronal nicotinic receptors. Mol Pharmacol 2006, 70: 801-5.29.
28. Rollema, H., Chambers, L.K., Coe, J.W. et al.Pharmacological profile of the alpha4beta2nicotinic acetylcholine receptor partial agonist varenicline, an effective smoking cessation aid.Neuropharmacology 2006, in press.

Vareniclina: Una opción para dejar de fumar

Farmacología

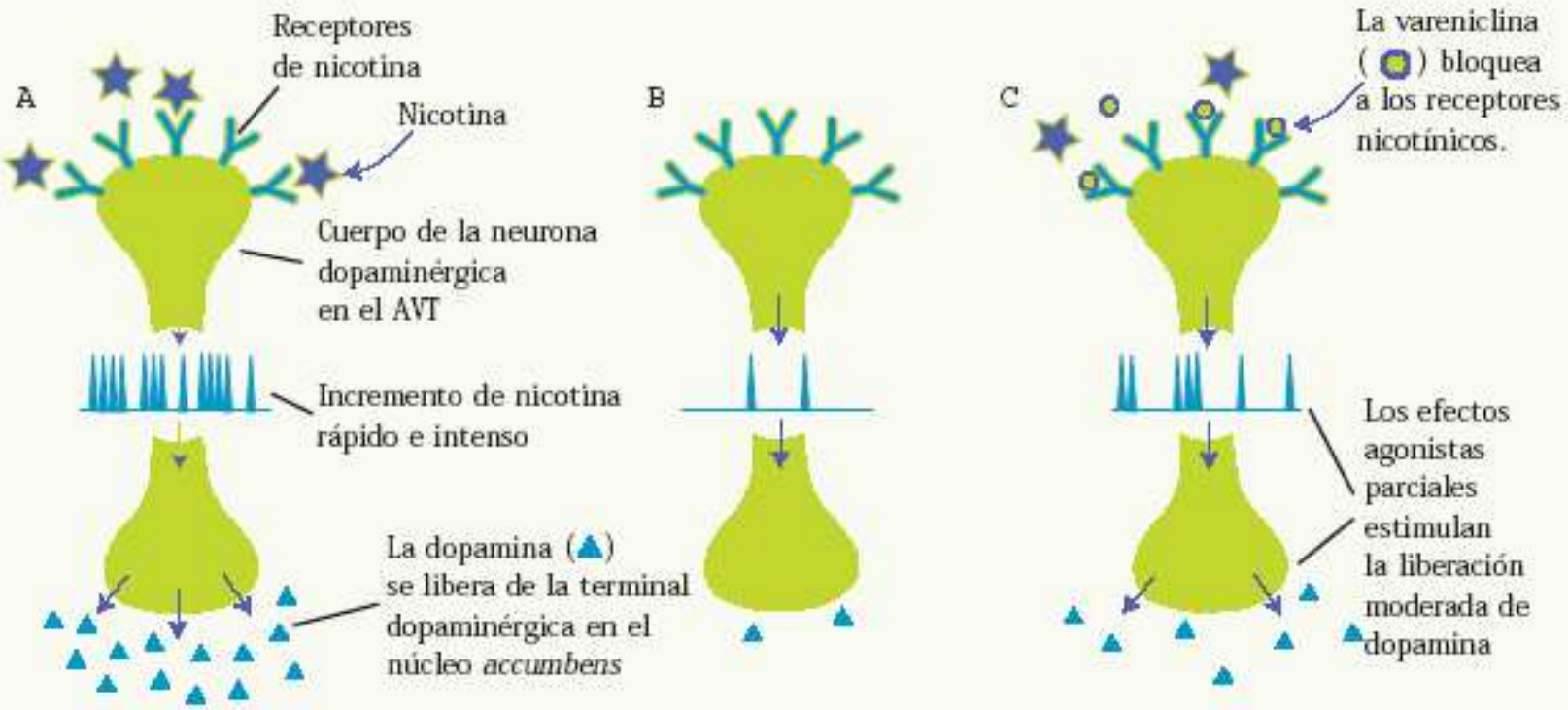
- **Con aproximadamente un 40-60% de la actividad agonista de la nicotina la actividad agonista parcial de la vareniclina para estimular la liberación de dopamina parece suficiente para reducir el ansia del tabaco y su retirada in vivo.** [27, 29]



28. Rollema, H., Chambers, L.K., Coe, J.W. et al.Pharmacological profile of the alpha4beta2nicotinic acetylcholine receptor partial agonist varenicline, an effective smoking cessation aid.Neuropharmacology 2006, in press.
29. Coe, J.W., Brooks, P.R., Vetelino, M.G. et al.Varenicline: An alpha4beta2 nicotinic receptorpartial agonist for smoking cessation. J MedChem 2005, 48: 3474-7.

Vareniclina: Mecanismo de acción

Figura 4. Esquema simplificado que muestra los efectos de: a) la nicotina de los cigarrillos; b) durante la abstinencia y c) el tartrato de vareniclina sobre los receptores nicotínicos y en la liberación de dopamina.



Modificado de: J. Foulds. The neurobiological basis for partial agonist treatment of nicotine dependence: varenicline. Int J Clin Pract. 2006;60(5):571-6.

Vareniclina: Una opción para dejar de fumar

Farmacocinética

- La vareniclina posee farmacocinética lineal después de una administración de dosis única (0,1-3,0 mg) y dosis múltiples (1, 2, y 3 mg por día) administración. [33,34]
- En un estudio clínico, la excreción total de vareniclina administrada fue del 88%, con la gran mayoría excreta sin cambios en la orina, lo que indica que la absorción de la vareniclina es prácticamente completa y la disponibilidad sistémica es alta después de la administración oral. [33,34]
- La unión a proteínas plasmáticas es baja (≤ 20%) [35]

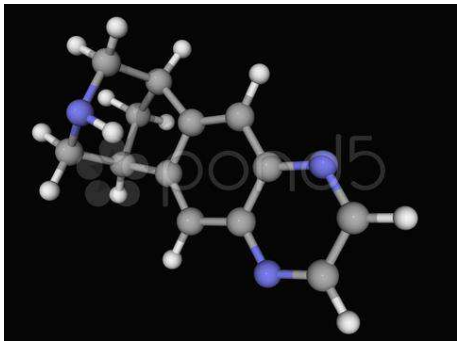
34 Faessel, H.M., Gibbs, M.A., Clark, D.J.,Rohrbacher, K., Stolar, M., Burstein, A.H.Multiple-dose pharmacokinetics of the selec-tive nicotinic receptor partial agonist, vareni-cline, in healthy smokers. J Clin Pharmacol2006, 46: 1439-48.

35 Obach, R.S., Reed-Hagen, A.E., Krueger, S.S.et al. Metabolism and disposition of vareni-cline, a selective alpha4beta2 acetylcholine re-ceptor partial agonist, in vivo and in vitro. DrugMetab Dispos 2006, 34: 121-30.

Vareniclina: Una opción para dejar de fumar

Farmacocinética

- La vareniclina se metaboliza mínimamente a nivel del hígado, con> 90% se excreta sin cambios en la orina, lo que indica que la excreción renal es la principal vía de eliminación del fármaco. [34, 35]



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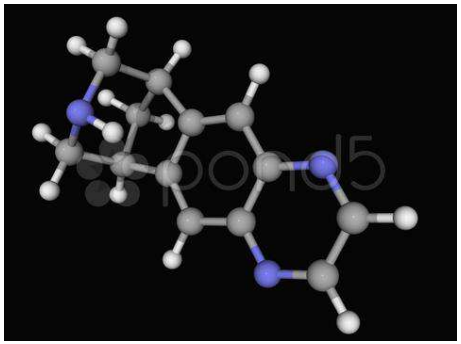
Vareniclina: Una opción para dejar de fumar

Farmacocinética

- **No se han reportado diferencias clínicamente significativas en la farmacocinética debido a la edad, la raza, el género, el consumo de tabaco o el uso de ciertos medicamentos concomitantes.** [34, 35]



34 Faessel, H.M., Gibbs, M.A., Clark, D.J.,Rohrbacher, K., Stolar, M., Burstein, A.H.Multiple-dose pharmacokinetics of the selec-tive nicotinic receptor partial agonist, vareni-cline, in healthy smokers. J Clin Pharmacol2006, 46: 1439-48.

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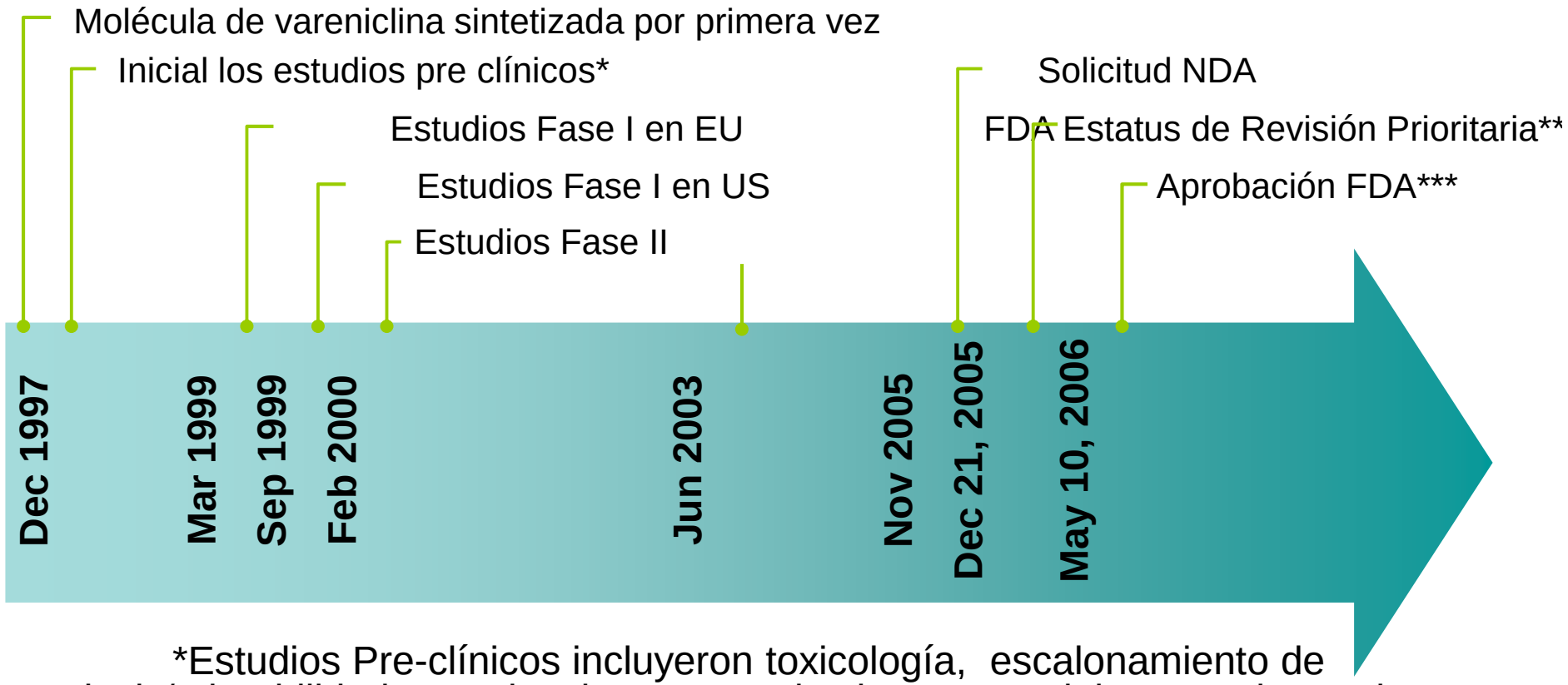
CHAMPIX® (vareniclina): Puntos angulares en el proceso de desarrollo



*Estudios Pre-clínicos incluyeron toxicología, escalonamiento de dosis/tolerabilidad, y evaluaciones reproductivas en modelos experimentales

**El estatus de revisión prioritaria fue otorgado porque la información previa sugería beneficios significativos sobre las terapias disponibles

***CHAMPIX es la primera ayuda farmacológica para la cesación de fumado aprobada en más de una década

CHAMPIX® (vareniclina): Evidencia 2013

Relapse prevention interventions for smoking cessation (Review)

Hajek P, Stead LF, West R, Jarvis M, Hartmann-Boyce J, Lancaster T

THE COCHRANE COLLABORATION®

"For pharmacological interventions,e xtended treatment with varenicline signifcantly reduced relapse in one trial (riskratio (RR)1.18,95% confdence interval (CI)1.03to1.36)."

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2013, Issue 8

http://www.thecochranelibrary.com

CHAMPIX® (vareniclina): Evidencia 2013

Review

EXPERT OPINION

1. Introduction
2. Current pharmacotherapies
3. Future treatments
4. Harm reduction
5. Conclusion

Pharmacotherapies and harm-reduction options for the treatment of tobacco dependence

Jacques Le Houezec† & Henri-Jean Aubin
†*Amzer Glas, Rennes, France*

Introduction: Tobacco dependence, a chronic relapsing condition, requires repeated interventions and multiple attempts to quit.

Expert Opin. Pharmacother. (2013) 14(14):1959-1967

"Three drugs are currently used as first line pharmacotherapy: nicotine replacement therapy(NRT), bupropion and varenicline. Compared to placebo, the drug effect varies from RR=2.27 for varenicline, to1.69 for bupropion, and 1.60 for any form of NRT."

CHAMPIX® (vareniclina): Evidencia 2013

CNS Drugs (2013) 27:921–941
DOI 10.1007/s40263-013-0092-8

SYSTEMATIC REVIEW

Neural Bases of Pharmacological Treatment of Nicotine Dependence - Insights from Functional Brain Imaging: A Systematic Review

Henrique Soila Menossi · Anna E. Goudriaan · Cintia de Azevedo-Marques Périco · Sérgio Nicastri · Arthur Guerra de Andrade · Gilberto D'Elia · Chiang-Shan R. Li · João Mauricio Castaldelli-Maia

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CHAMPIX® (vareniclina): Evidencia 2013

Neural Bases of Pharmacological Treatment of Nicotine Dependence - Insights from Functional Brain Imaging: A Systematic Review

Henrique Soila Menossi · Anna E. Goudriaan · Cintia de Azevedo-Marques Périco · Sérgio Nicastri · Arthur Guerra de Andrade · Gilberto D'Elia · Chiang-Shan R. Li · João Mauricio Castaldelli-Maia

Table 1 Main findings from a systematic review on non-nicotinic pharmacological functional magnetic resonance imaging (fMRI) studies in smokers; the search went up to May 2012 in Pubmed, PsycINFO and Web of Science

Reference	Challenge	Mean age in years, (*n*)	Main sample characteristics	Smoking status	Study type and methodology	Main findings
Loughead et al. [12]	Varenicline vs placebo	41 ± 13, (22)	- 12 men and 10 women - Smokers looking for treatment, without any other psychiatric disorders - Recruited by media ads - 77 % Caucasian - 45 % had finished high school	- Use of 10 cigarettes/day or more for 6 months or more with the DSM-IV criteria for nicotine dependence - Average use 18.5 ± 5.3 cigarettes/day - FTND 4.5 ± 1.7 - Expired carbon monoxide 26 ± 9.0 ppm	- Double-blind trial, crossover, controlled - 10 participants in the varenicline group and 12 in the placebo group - Beginning on the 9th day of treatment abstinence mandatory - BOLD fMRI on the 13th day as they performed the N-back visual memory test	- Varenicline correlated with BOLD signal change in dorsal anterior cingulate cortex/medial frontal cortex, dorsolateral prefrontal cortex right and left - Varenicline was associated with shorter correct response in participants with FTND score of 6–10 points
Loughead et al. [13]	Varenicline vs placebo	41 ± 13, (22)	- 12 men and 10 women - Smokers looking for treatment, without any other psychiatric disorders - Recruited by media ads - 77 % Caucasian - 45 % had finished high school	- Use of 10 cigarettes/day or more for 6 months or more, DSM-IV criteria for nicotine dependence - Average use 18.5 ± 5.3 cigarettes/day - FTND 4.5 ± 1.7 - CES-D score 3.32 ± 3.13 - PANAS score: positive affect 36.27 ± 5.75 and negative 12.95 ± 3.47	- Double-blind trial, crossover, controlled - 10 participants in the varenicline group and 12 participants in the placebo group - Home on the 9th day of treatment abstinence mandatory - BOLD fMRI on the 13th day as they performed the face emotion identification test. Filled new PANAS	- Varenicline correlated with a decrease in BOLD signal in dorsal anterior cingulate cortex/medial frontal cortex, occipital cortex and thalamus, and an increase in average temporal gyrus - Results suggest that drug effects on BOLD signal do not reflect affective changes - Varenicline improved response time correct
Franklin et al. [11]	Varenicline vs placebo	36 ± 2.2, (22)	- 16 men and 6 women - Smokers who were not seeking treatment, without other psychiatric disorders - Recruited by radio and internet ads - 7 African–American, 14 European American, 1 mixed	- DSM-IV criteria for nicotine dependence - Average use 17.5 ± 1.6 cigarettes/day - FTND 4.7 ± 0.4 - Desire to quit: 86.3 % of the individuals included	- Double-blind randomized controlled trial - 11 participants in the varenicline group and 11 participants in the placebo group - CASL perfusion fMRI before medication and on 21st day of treatment, after smoking, with stimulation of videos related to smoking and neutral videos, and resting - The Shiffman-Jarvik withdrawal scale was applied before and after exposure	- Exposure to videos related to smoking before treatment and after placebo was related to activation in large region of ventral striatum and medial orbitofrontal cortex - Varenicline exposure was associated with increased flow in anterior cingulate and posterior inferior frontal gyrus, middle and upper lateral orbitofrontal cortex, dorsolateral prefrontal cortex - Varenicline, at rest, was associated with increased flow in right left lateral orbitofrontal cortex and decreased activity in right amygdala

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Addiction

COCHRANE UPDATES

doi:10.1111/add.12291

Efficacy of interventions to combat tobacco addiction: Cochrane update of 2012 reviews

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Submitted 9 April 2013; initial review completed 29 April 2013; final version accepted 1 July 2013

"The updated reviews confimed the benefit of nicotine replacement therapy, standard dose varenicline and providing cessation treatment free of charge.."

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Substance Abuse: Research and Treatment

Libertas Academica
FREEDOM TO RESEARCH

REVIEW

Current and Emerging Pharmacotherapeutic Options for Smoking Cessation

Kristin V. Carson[1–3], Malcolm P. Brinn[1,3], Thomas A. Robertson[4], Rachada To-A-Nan[4], Adrian J. Esterman[5], Matthew Peters[6] and Brian J. Smith[1,3]

[1]The Clinical Practice Unit, The Basil Hetzel Institute for Translational Health Research, Adelaide, Australia. [2]School of Medicine, The University of Adelaide, Adelaide, Australia. [3]Respiratory Medicine, The Queen Elizabeth Hospital, Adelaide, Australia. [4]Therapeutics Research Centre, School of Pharmacy and Medical Sciences, University of South Australia and The Basil Hetzel Institute for Translational Health Research, Adelaide, Australia. [5]School of Nursing and Midwifery, The University of South Australia, Adelaide, Australia. [6]Thoracic Medicine, The Concord Hospital, Sydney, Australia.
Corresponding author email: kristin.carson@health.sa.gov.au

Substance Abuse: Research and Treatment 2013:7 85–105

doi: 10.4137/SART.S8108

"Clinical practice guidelines report that varenicline is the most effective form of single pharmacotherapy for smoking cessation based on available evidence."

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Varenicline, an $\alpha 4\beta 2$ nicotinic acetylcholine receptor partial agonist, selectively decreases ethanol consumption and seeking

Pia Steensland, Jeffrey A. Simms, Joan Holgate, Jemma K. Richards, and Selena E. Bartlett*

Ernest Gallo Clinic and Research Center, University of California, San Francisco, 5858 Horton Street, Suite 200, Emeryville, CA 94608

Communicated by Raymond L. White, University of California, San Francisco, Emeryville, CA, June 7, 2007 (received for review May 4, 2007)

"The data suggest that the 4ή 2nAChRs may play a role in ethanol-seeking behaviors in animals chronically exposed to ethanol. The selectivity of varenicline in decreasing ethanol consumption combined with its reported safety profile and mild side effects in humans suggest that varenicline may prove to be a treatment for alcohol dependence."

Tabaquismo e Infección

Review

Journal of INTERNAL MEDICINE

doi: 10.1111/j.1365-2796.2010.02332.x

Smoking and the outcome of infection

R. Huttunen[1,2], T. Heikkinen[3] & J. Syrjänen[1,2]

From the [1]Department of Internal Medicine, Tampere University Hospital, Tampere; [2]University of Tampere Medical School, Tampere; and [3]Department of Pediatrics, Turku University Hospital, Turku; Finland[1]

 Journal of Internal Medicine 269; 258–269

"Smokers are at increased risk of invasive pneumococcal disease, pneumonia, periodontitis, surgical infections, tuberculosis, inflenza and meningococcal disease."

Tabaquismo y Neumococo

The Influence of Chronic Illnesses on the Incidence of Invasive Pneumococcal Disease in Adults

Moe H. Kyaw,[1] Charles E. Rose, Jr.,[1,a] Alicia M. Fry,[1,a] James A. Singleton,[2] Zack Moore,[1,a] Elizabeth R. Zell,[1] and Cynthia G. Whitney,[1] for the Active Bacterial Core Surveillance Program of the Emerging Infections Program Network[b]

[1]Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, and [2]Epidemiology and Surveillance Division, National Immunization Program, Centers for Disease Control and Prevention, Atlanta, Georgia

The Journal of Infectious Diseases 2005; 192:377–86

0022-1899/2005/19203-0004

“The risk of developing invasive pneumococcal disease is higher in persons with certain underlying medical conditions, who are of low socioeconomic status, or who engage in high-risk behaviors, such as smoking and alcohol abuse”

Tabaquismo y Vacunación

Preventive Medicine 48 (2009) 180–183

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Influenza and pneumococcal vaccination rates among smokers: Data from the 2006 Behavioral Risk Factor Surveillance System ☆

William S. Pearson [a,*], Shanta R. Dube [b], Earl S. Ford [a], Ali H. Mokdad [c]

[a] Behavioral Surveillance Branch, Division of Adult and Community Health, Centers for Disease Control and Prevention, 4770 Buford Highway, N.E. MS K-66, Atlanta, GA 30341, USA
[b] Epidemiology Branch, Office on Smoking and Health, Centers for Disease Control and Prevention, Atlanta, USA
[c] Institute for Health Metrics and Evaluation, University of Washington, Seattle, USA

Available online 8 November 2008

"It is important for current smokers to receive both influenza and pneumococcal vaccinations. Health care providers should assess and advise current smokers to quit, as well as promote receipt of vaccinations among current smokers to help prevent respiratory infections."

Tabaquismo y Vacuna Antineumococo

Early Release

Advisory Committee on Immunization Practices (ACIP) Recommended Immunization Schedule for Adults Aged 19 Years and Older — United States, 2013

ACIP Adult Immunization Work Group
Carolyn B. Bridges, MD[1]
LaDora Woods[1]
Tamera Coyne-Beasley, MD[2]
[1]*Immunization Services Division, National Center for Immunization and Respiratory Diseases, CDC*
[2]*Division of General Pediatrics and Adolescent Medicine, University of North Carolina, Chapel Hill, North Carolina*
Corresponding contributor: Carolyn B. Bridges, cbridges@cdc.gov, 404-639-8689.

MMWR / January 28, 2013 / Vol. 62

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8. Pneumococcal polysaccharide (PPSV23) vaccination

- Vaccinate all persons with the following indications:
  - —all adults aged 65 years and older;
  - —adults younger than age 65 years with chronic lung disease (including chronic obstructive pulmonary disease, emphysema, and asthma); chronic cardiovascular diseases; diabetes mellitus; chronic renal failure; nephrotic syndrome; chronic liver disease (including cirrhosis); alcoholism; cochlear implants; cerebrospinal fluid leaks; immunocompromising conditions; and functional or anatomic asplenia (e.g., sickle cell disease and other hemoglobinopathies, congenital or acquired asplenia, splenic dysfunction, or splenectomy [if elective splenectomy is planned, vaccinate at least 2 weeks before surgery]);
  - —residents of nursing homes or long-term care facilities; and
  - —adults who smoke cigarettes.

Tabaquismo y Vacuna Antineumococo

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10. Pneumococcal conjugate 13-valent vaccination (PCV13)

- Adults aged 19 years or older with immunocompromising conditions (including chronic renal failure and nephrotic syndrome), functional or anatomic asplenia, CSF leaks or cochlear implants, and who have not previously received PCV13 or PPSV23 should receive a single dose of PCV13 followed by a dose of PPSV23 at least 8 weeks later.
- Adults aged 19 years or older with the aforementioned conditions who have previously received one or more doses of PPSV23 should receive a dose of PCV13 one or more years after the last PPSV23 dose was received. For those that require additional doses of PPSV23, the first such dose should be given no sooner than 8 weeks after PCV13 and at least 5 years since the most recent dose of PPSV23.

Gracias.