[세미나]

니코틴중독의 진실

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Basic Definitions

- Drug – any substance other than food that by its chemical nature alters structure or function
- Illicit drug – drug that is unlawful to possess or use
- Drug misuse – use of prescribed drugs in greater amounts or for other purposes than prescribed

Drug Abuse(약물남용)

Use of a substance in a manner, in amounts, or in situations such that the drug causes problems or greatly increases the chances of problems occurring. Problems include:

- Social
- Occupational
- Psychological
- Physical

내성(tolerance)

- 중독성 약물의 생물학적 효과중의 하나는 내성(tolerance)를 유발시킨다.
- 이는 동일 복용양의 약물이 반복적으로 사용되었을 때 감소된 효과를 보여주는 것이다. 동일효과를 위하여 더 많은 약물 복용이 이루어져야 한다.
- 그렇다면 그들이 원하는 대로 모든 약물을 주면 되지 않을 까?
- 그러나 다른 신체기관에는 내성이 생기지 않는다. 즉 고농도의 약물 복용, 많은 양의 흡연은 폐와 심장기능에 더 나쁜 영향을 주게 된다는 것이다. 이러한 약물증가는 어떤 경우에서는 치명적인 경우가 발생할 수도 있다.

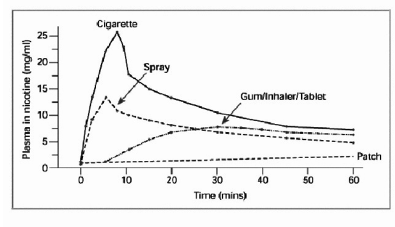
- 뇌에서의 내성이란 약물에 대한 수용체 숫자의 변화를 의

Route of Administration(투여경로)

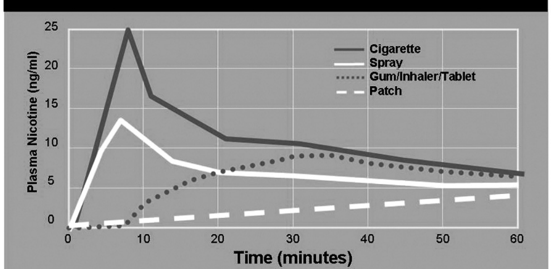
- Inhalation (흡입)→ 담배
  - Vaporized drug is inhaled through mouth and lungs
  - Reaches brain within 7 sec
- Snorting
  - Drug is absorbed by blood vessels in nasal mucous membranes
  - Reaches brain in approximately 4 min

Route of Administration

- Injection (주사)
  - IV reaches brain in 20 sec
  - IM, SQ reaches brain in 4 min
- Oral ingestion
  - Absorbed by blood vessels in intestine
  - Reaches brain in about 30 min
- Other routes: buccal, rectal, vaginal, eye drops



Nicotine blood levels achieved by smoking one cigarette compared with levels achieved with Nicotine nasal spray, gum, Inhalator, sublingual tablet and patch[21]



Note: nicotine from cigarettes is absorbed into the arterial circulation, where nicotine concentration is 6-10 times higher than in venous blood

Definition of Addiction

Progressive, chronic, primary disease characterizes by compulsion, loss of control, continued drug use despite adverse consequences and distortions in normal thinking, such as denial

중독질환(addiction)이란 만성적이고, 계속 진행하는 치명적인 질환으로 정의 할 수 있다.

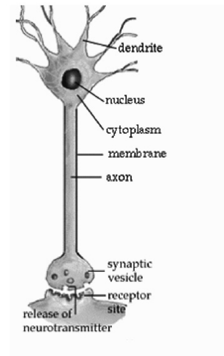
- 중독이란 크게 행동중독(behavioral addiction)과 물질중독(chemical addiction)으로 구별될 수 있다.
- 행동중독 : 도박, 경마, 인터넷중독, 섹스중독
- 물질중독 : 알코올 의존, 니코틴 의존, 히로뽕의존, 아편의존, 코카인 의존

1. 신경전달물질

- 비록 뉴론은 전기적으로 흥분 하지만 세포와 세포 사이의 신호전달은 일반적으로 화학적이지만 전기적이지 않다.
- 활동 전위의 생성을 촉진시키거나 억제시키는 물질을 통틀어 신경전달물질이라 한다.
- 흡연시 두뇌에 작용하는 신경전달 물질은 니코틴이다.

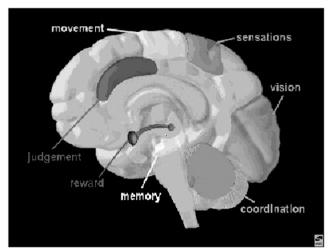
신경계와 뉴론

1. 중추신경계는 뇌와 척수를 포함한다.
2. 뇌를 포함한 신경계의 기능 : 신경충격을 전달하는 신경 세포 즉, 뉴론이라는 세포에 의해 이루어진다.
3. 뉴론의 중심부에는 세포체가 있고, 세포체로부터 뻗어 나온 잔가지를 수상돌기(dendrite)라 하며 신호의 수용에 관여한다.
4. 뉴론은 축삭(axon)이라 하는 또 다른 가지를 갖고 있는데 축삭은 신호의 발산 통로 사용된다.



Addiction

- Involves craving and compulsion
  - Overwhelming pre-occupation, desire or drive to use a drug
  - May take the form of simple drug hunger or of drug-seeking or drug hoarding behavior
- Hallmark feature is the tendency for continued use despite adverse consequences

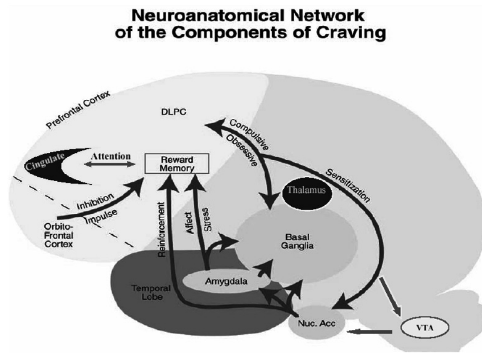


2. 뇌보상회로

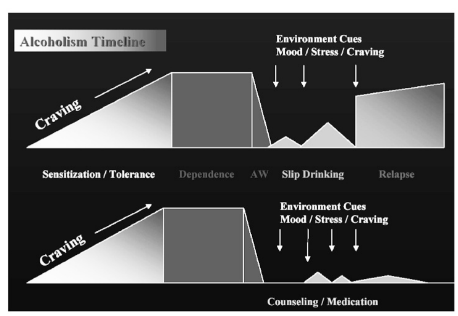
- 뇌 과학자들은 뇌 안에 존재하는 긍정적인 보상 또는 강화시스템을 발견하였다.
- 양성강화시스템에서 뇌의 자극은 행동의 반복을 유발한다. 즉 먹는 것, 성행위 등 기본적인 생물학적 기능들은 반복적으로 일어나는데 이는 이들 신경을 활성화시키기 때문이다.
- 우리는 일생을 통하여 이들 중추들을 자극하는 경험을 배우게된다. 그러나 인위적으로 이들 뇌보상회로를 활성화시킬수 있다.

1. 쉽게 주위에서 구할 수 있는 것은 알코올이나 담배 등이며 불법적인 것은 히로뽕이니 코카인 등이다.
2. 이러한 약물들은 직접적으로 뇌보상회로를 자극하며, 뇌화학적으로 긍정적인 환회를 자아낸다.
3. 이러한 뇌보상회로를 자극될 때 나오는 신경전달물질은 도파민이다. 즉 도파민이라는 물질이 우리 인체내에서 쾌감을 느끼게 해준다.

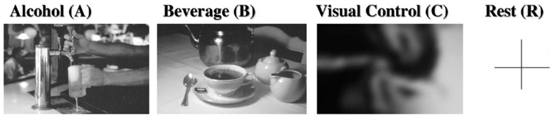
- 니코틴도 마찬가지로 뇌보상회로를 자극하여 쾌감을 느낀다. 니코틴은 nicotinic acetylcholine 수용체를 통하여 간접적으로 뇌보상회로를 자극한다.
- 뇌보상회로은 가장 중요한 요소는 복뇌 뒤판역(ventral tegmental area, VTA)와 중격의지핵(nucleus accumbens, NA) 이다. VTA에서 NA로 향하는 dopamine계 신경은 보상 감각과 관련이 되어 있다.

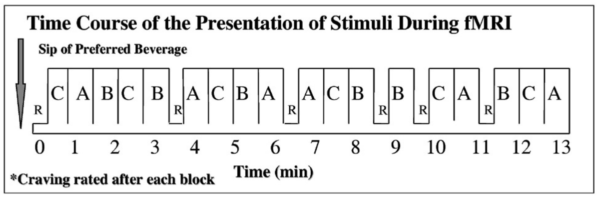


General Strategies Used to Treat Drug Addiction or Associated Physical Withdrawal



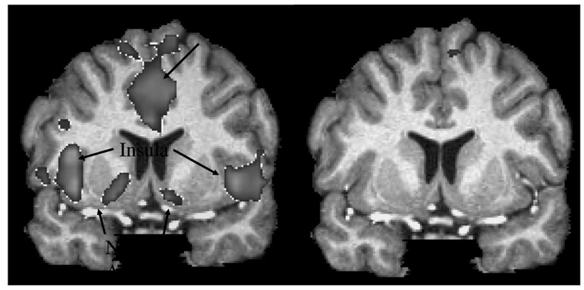
Examples of the various visual cues from Normative Appetitive Picture System (NAPS)





Comparisons: Alcohol - Beverage, Alcohol - Vis Ctrl, Vis Ctrl - Rest, Beverage - Vis Ctrl, Beverage - Rest

Alcohol - Beverage Condition



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Journal of Psychiatric Research xxx (2004) xxx–xxx

JOURNAL OF PSYCHIATRIC RESEARCH

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fMRI investigation on cue-induced smoking craving

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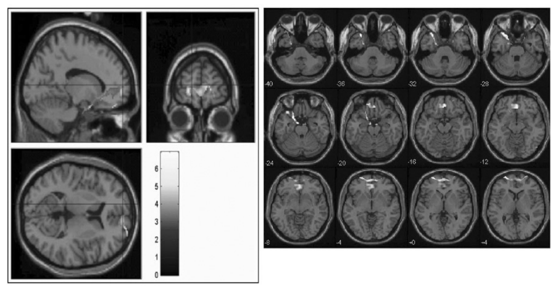
Received 11 June 2004; revised 28 July 2004; accepted 5 August 2004

Functional Brain Activation before Smoking Associated with Cue induced Nicotine Craving in Experienced Smokers



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ALCOHOLISM: CLINICAL AND EXPERIMENTAL RESEARCH
Vol. 27, No. 12
December 2003

Complexity Changes of the EEG Induced by Alcohol Cue Exposure in Alcoholics and Social Drinkers

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Background: An understanding of the neurophysiological mechanisms underlying alcohol craving is important in the effective treatment of alcohol dependence. The aim of this study was to examine the utility of the electroencephalogram (EEG) to measure the changes in electrical brain activity of alcoholics when exposed to alcohol-specific cues.

Methods: Fifteen adult alcoholic subjects (four women) with a mean age of 35 (SD = 4.5) and 10 healthy social drinking controls (three women) with a mean age of 34 (SD = 5.6) were recruited. Subjects were serially rated for alcohol craving after presentations of pictures of control nonalcoholic and alcohol beverages. After the picture presentation, the EEG was recorded (16,384 data points for each epoch) with eyes closed. The dimensional complexity (D_2) was estimated as a measure of complexity of the EEG.

Results: Alcoholic subjects exhibited a significant increase in the D_2 values of the EEG in frontal (F_3, F_4), right posterior temporal (T_6), and occipital (O_1, O_2) regions after viewing alcohol cues compared with viewing other beverage cues. These results indicate that more complex (or higher) cortical activity is induced over specific brain regions of alcoholic subjects by alcohol-specific cues. Changes in subscale of alcohol craving between nonalcoholic and alcohol pictures were correlated with changes in D_2 values in the left frontal (F_3) region in alcoholic subjects.

Conclusions: These findings suggest that, when subjects are exposed to alcohol cues, changes in the EEG complexity are induced in frontal, right posterior temporal, and occipital areas, which may be key brain structures for alcohol craving. In addition, nonlinear measures like the D_2 are useful in evaluating alcohol cue-induced brain activity from the EEG.

Key Words: Alcohol Craving, Complexity, EEG, Alcohol Cue Exposure.

- 니코틴은 acetylcholine 수용체의 nicotine아형(nACh receptor)에 대한 효현제로 작용한다.
- 흡인된 니코틴의 약 25%가량이 혈액 내에 흡수되고 15초 이내에 뇌에 도달한다. 반감기는 약 2시간이다.
- 니코틴은 dopamine 경로를 활성화 시켜 긍정적 재강화와 중독성을 갖는다.

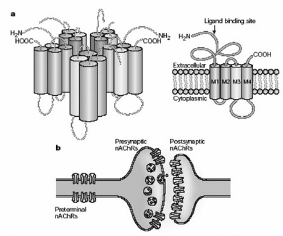


Figure 1 | The structure of neuronal nicotinic acetylcholine receptors (nAChRs). **a** | Although the precise molecular structure of nAChRs is not known, they are believed to be pentameric ion channels. Each nAChR is composed of five subunits arranged in either homomeric or heteromeric complexes of α- or β-subunit arrangements (left). Different subunit combinations confer unique functional properties to the ubiquitously distributed nAChRs throughout the brain. The schematic on the right shows the transmembrane topology of a single nAChR subunit. The transmembrane domains are labelled M1–M4. The larger amino-terminal domain contains the acetylcholine-binding site, whereas the M2 domain determines the ionic selectivity of the receptor and faces the inside of the channel pore. **b** | nAChRs are located at the soma, on presynaptic terminals and on postsynaptic boutons. This widespread localization confers the receptor with a wide range of functions, influencing neuronal signaling at the pre- and postsynaptic levels.

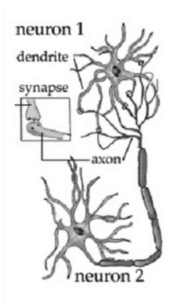
Nicotinic Partial Agonist for Smoking Cessation

Nicotinic Receptor Family

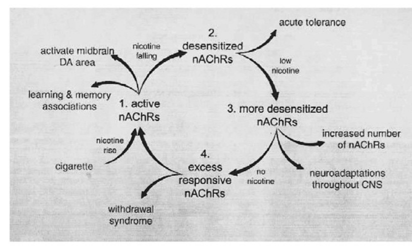
10 α subunits   4 β subunits   δ,γ/ε subunits

Functional receptors composed of 5 subunits, and may be:

Heteromeric: e.g.	muscle nic Rs	$= (\alpha_1)_2\beta\gamma\delta$
	neuronal	$= (\alpha_4)_3(\beta_2)_2$
Homomeric:	neuronal	$= (\alpha_7)_5$



A Simplified Cycle for Continued Tobacco Use, Based on Nicotine's Cellular Actions



The nAChRs are initially and transiently activated when nicotine first arrives. The desensitization of the receptors follows as the concentration of nicotine slowly decreases. The increased number of nAChRs and the neuroadaptations are hypothesized to develop after chronic use of nicotine.