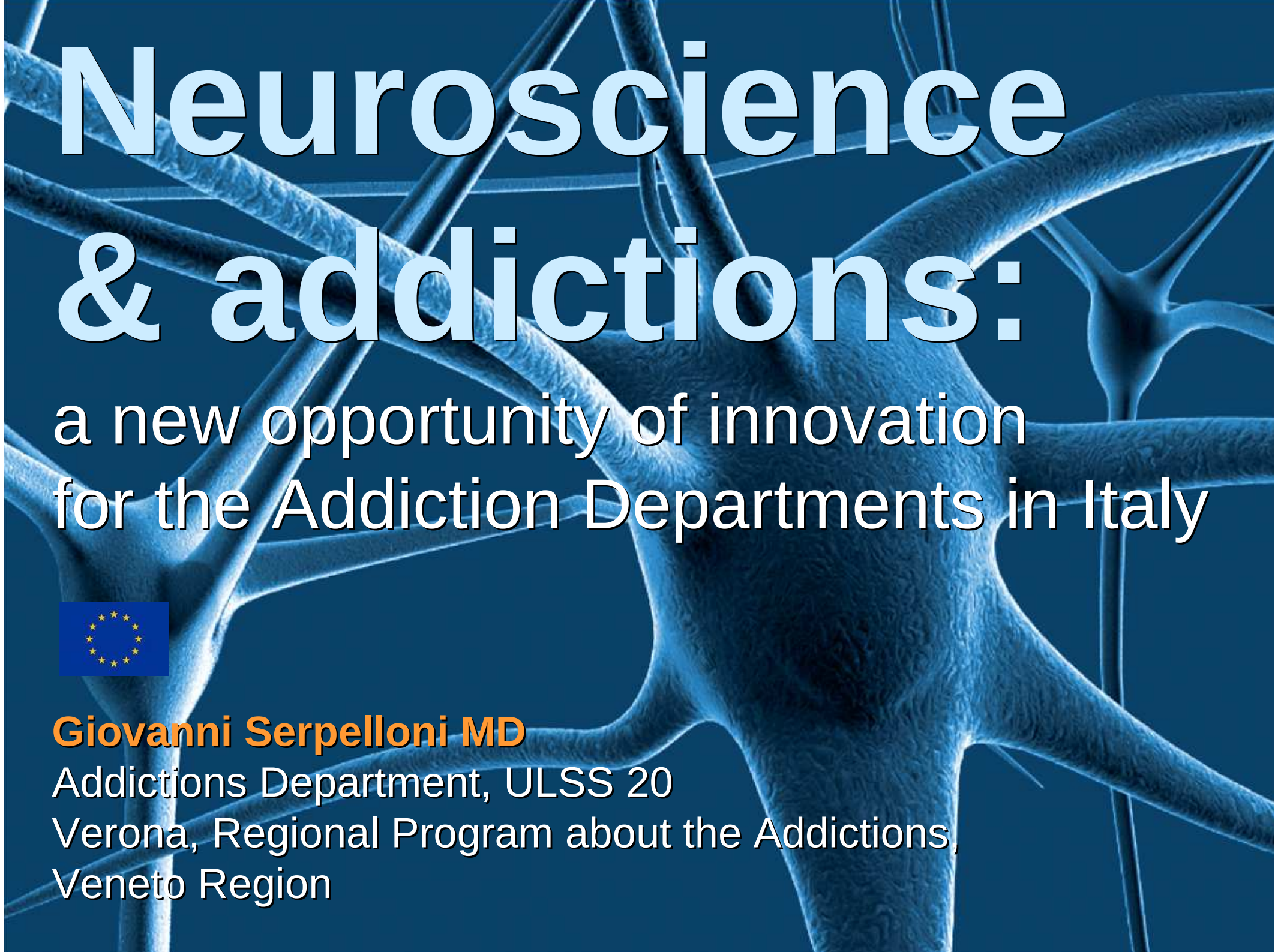

Neuroscience & addictions:

a new opportunity of innovation for the Addiction Departments in Italy

Giovanni Serpelloni MD
Addictions Department, ULSS 20
Verona, Regional Program about the Addictions,
Veneto Region

Organization

Veneto Region

Azienda ULSS 20 – Verona

Regional Program about Addiction

REGIONE DEL VENETO

Giunta Regionale

Direttore: Dott.ssa Maria Giuseppina Bonavina

DR. STEFANO VALDEGAMBERI
Assessore alle Politiche Sociali
Regione del Veneto

ON. DR.SSA FRANCESCA MARTINI
Assessore alle Politiche Sanitarie
Regione del Veneto

Patronage

UNITED NATIONS Office on Drugs and Crime
Ministero della Salute
SINS Società Italiana di Neuroscienze
Ministero della Solidarietà Sociale
FNOMCeO Federazione Nazionale Ordine Medici Chirurghi e Odontoiatri
Ordine Nazionale Psicologi e Ordine Regionale - Regione Veneto
IPASVI Federazione Nazionale Collegi Infermieri
Ordine Assistenti Sociali Nazionale e Regione del Veneto
ANEP Associazione Nazionale Educatori Professionali

http:// www.dronet.org
http:// ang.dronet.org
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Acknowledgements

AddictioNeuroscience group

UNITED NATIONS
Office on Drugs and Crime

MINISTERO DELLA SOLIDARIETA' SOCIALE

MINISTERO DELLA SALUTE

SINS
Società
Italiana di
Neuroscienze

Ernest Gallo Clinic and Research Center
AT THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

FNOMCeO

Ordine Nazionale Psicologi
Ordine Regionale Psicologi-Regione Veneto

IPASVI **Federazione Nazionale Collegi Infermieri**

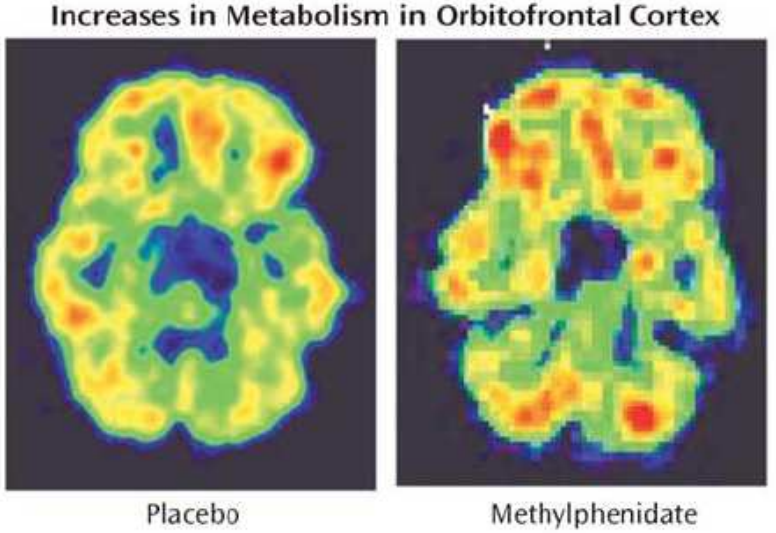
ORDINE ASSISTENTI SOCIALI Consiglio Nazionale
ORDINE ASSISTENTI SOCIALI del Veneto

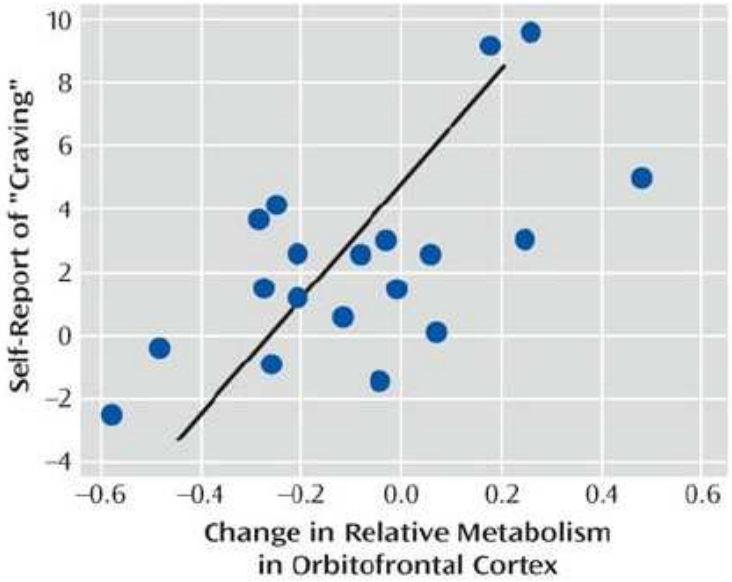
ANEP **Associazione Nazionale Educatori Professionali**

Comune di Verona

Knowing more for intervening better

The knowledge of different cerebral areas and cerebral structures, their normal functions and their variations under the influence of the drugs, will be the base to support the correct understanding of the phenomenon and to define the future way of intervention and treatment.





P.W. Kalivas [1]
N. D. Volkow [2]

[1] Department of Neurosciences, Medical University of South Carolina
[2] National Institute on Drug Abuse (NIDA)

Cerebral functions under drugs effects

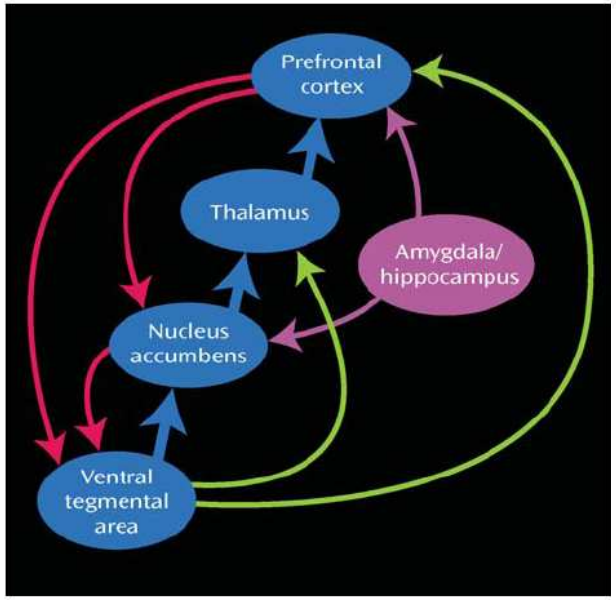


Figura 6. Interazioni dei circuiti mesocorticali e mesolimbici con la tossicodipendenza

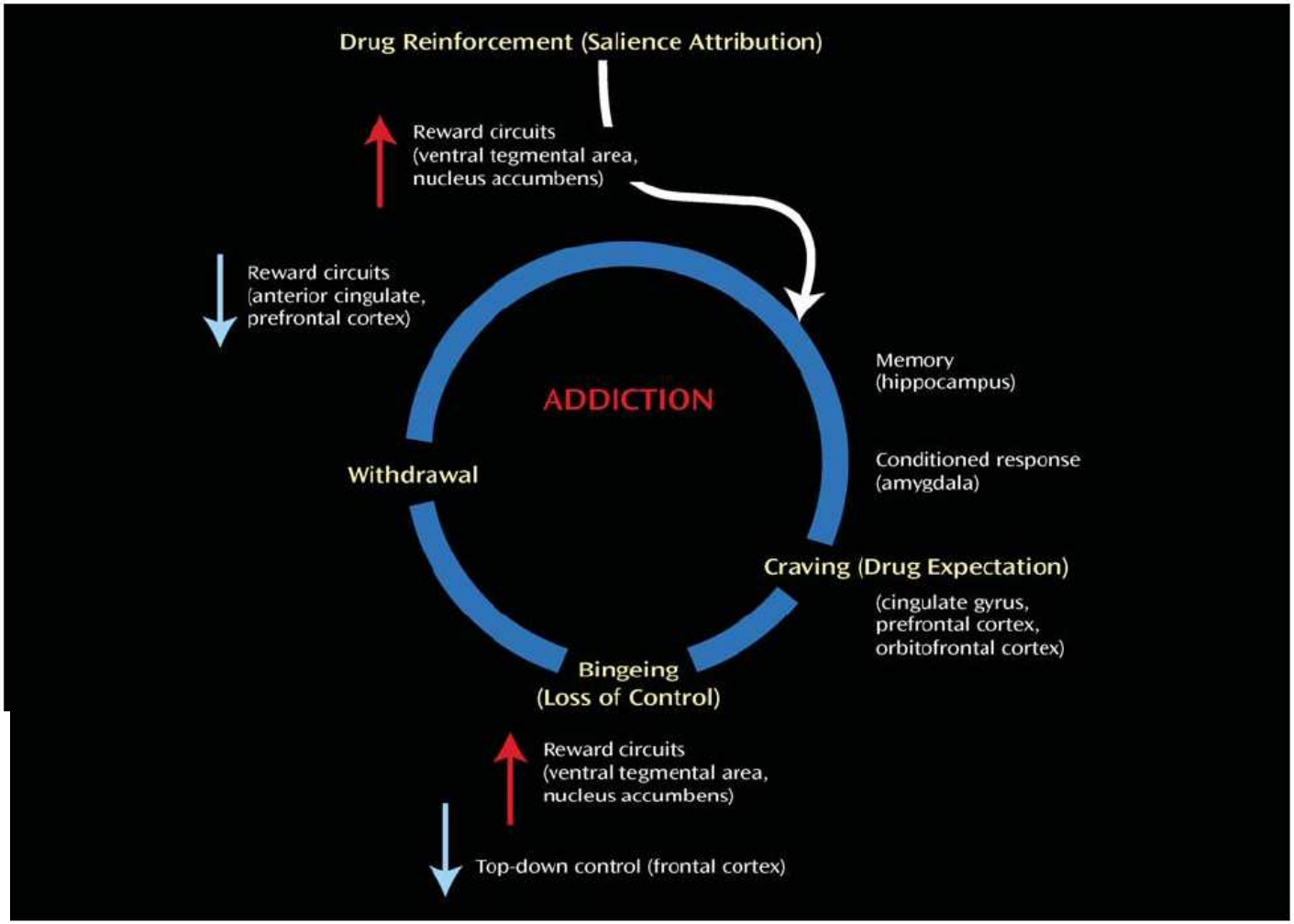


Figura 7: Modello integrativo di Cervello e Comportamento: la sindrome I-RISA (Impaired Response Inhibition and salience attribuition)

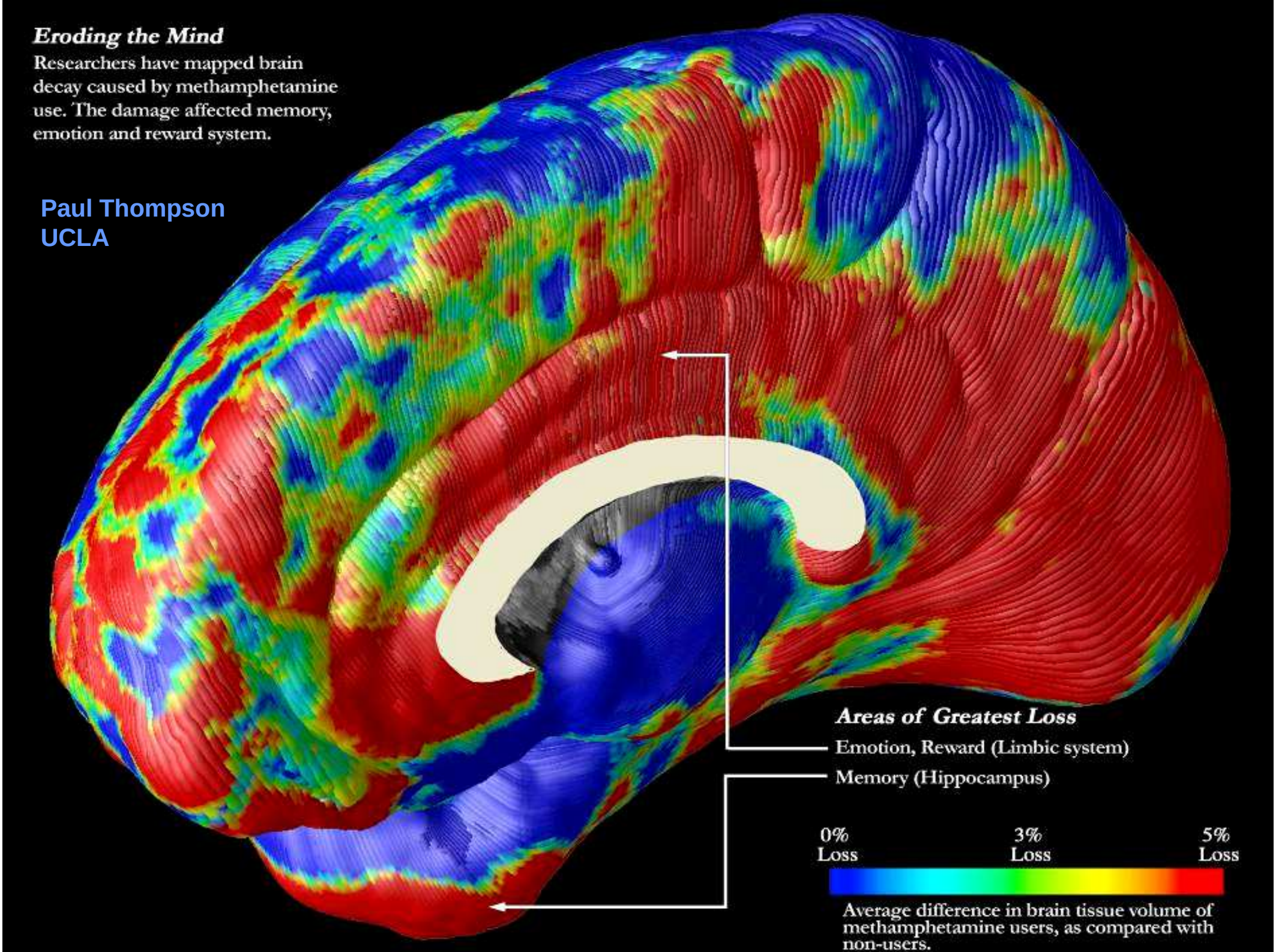
R. Z. Goldstein [1]
Nora D. Volkow [2]

[1] Brookhaven National Laboratori, Upton, NY
[2] National Institute on Drug Abuse (NIDA)

Some remarkable discoveries

- the substances abuse are able to alter deeply the cerebral structures with:
  - alteration of the motivation system
  - of the learning/memory
  - of the reward system
  - of the emotion system

Bechara, A., Nader, K. And Vander Kooy, D., 1998; Phillips, A. G., Ahn, S. and Howland, J. G., 2003; White, N.M., 1996; Tiffany, S.T., 1990; Grace, A.A.,1995


Eroding the Mind
Researchers have mapped brain decay caused by methamphetamine use. The damage affected memory, emotion and reward system.
Paul Thompson
UCLA
Areas of Greatest Loss
Emotion, Reward (Limbic system)
Memory (Hippocampus)
0% Loss
3% Loss
5% Loss
Average difference in brain tissue volume of methamphetamine users, as compared with non-users.

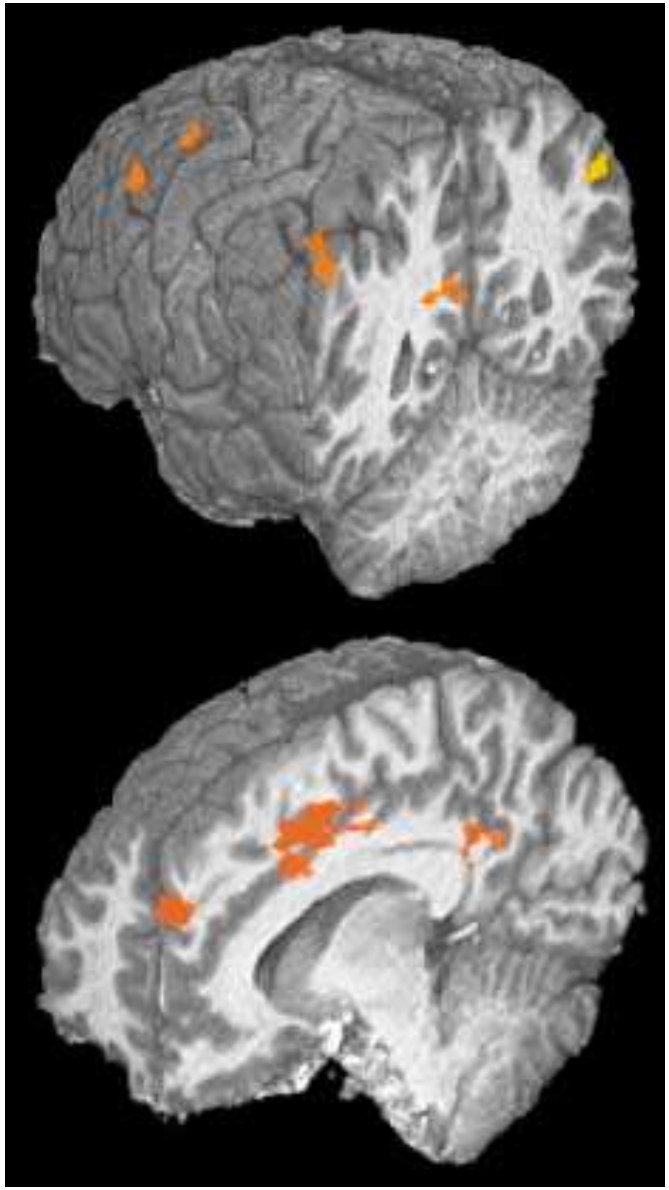
The damage of the decision making process

- At the same time we have been able to well define the damage:
  - of the social reasoning
  - of the decision making process

Adolphs,R., 2003; Stone, V.E., Cosmides, L., Tooby, J., Kroll, N. and Knight, R.T., 2002

Visible craving areas

- Today the craving can be made visible through a "topographical photo" of the cerebral areas that are activated in consequence to stimuli (inside and/or external) able to activate such condition



Cocaine craving

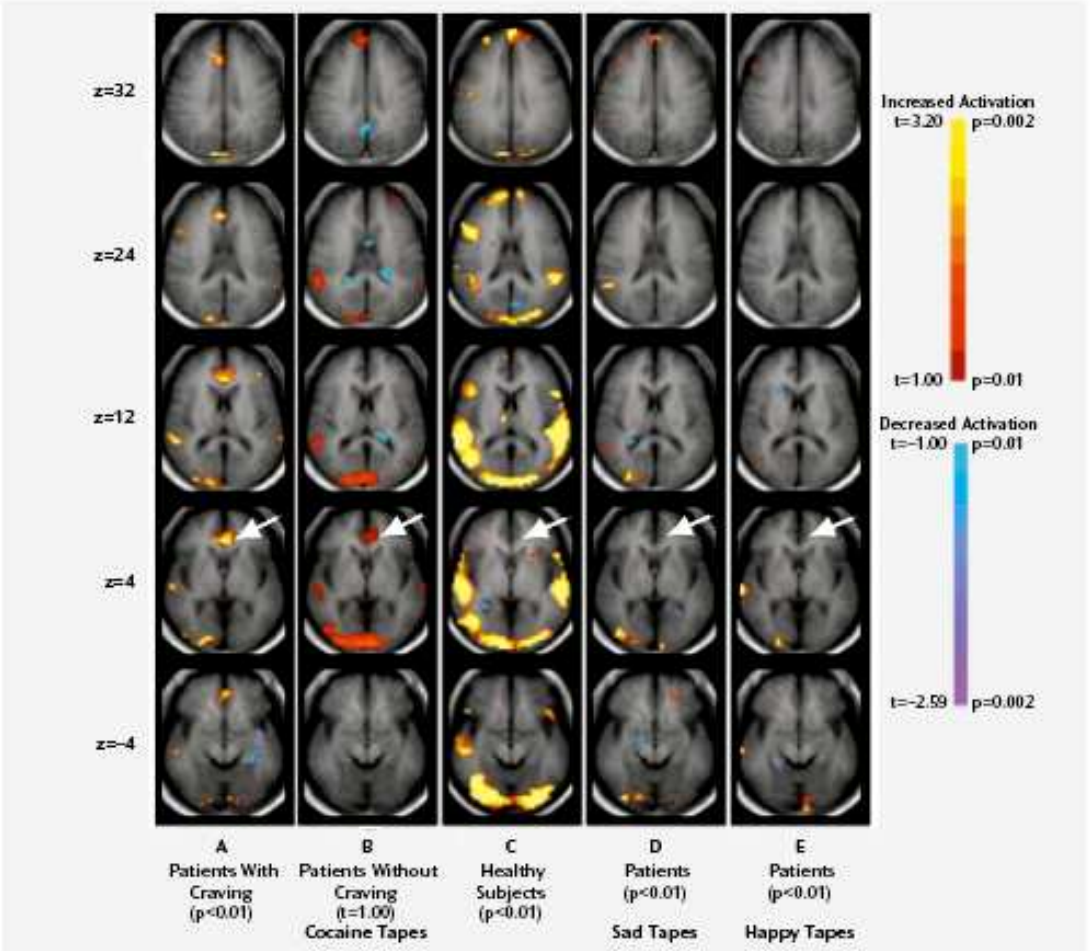
Article

Functional Magnetic Resonance Imaging of Cocaine Craving

Bruce E. Wexler, M.D.
Christopher H. Gottschalk, M.D.
Robert K. Fulbright, M.D.
Isak Prohovnik, Ph.D.
Cheryl M. Lacadie, M.A.
Bruce J. Rounsaville, M.D.
John C. Gore, Ph.D.

(Am J Psychiatry 2001; 158:86–95)

FIGURE 2. fMRI Images Comparing Regional Brain Activations During Initial Videotape Viewing and at Baseline in 11 Cocaine-Dependent Patients and 20 Healthy Comparison Subjects Who Watched Videotapes Designed to Evoke Cocaine Craving, Happiness, and Sadness[a]



[a] The epochs involved are defined in Figure 1; the images represent emotion 0 minus baseline 1. The numbers of patients and healthy subjects varied among tapes. The z values indicate the distance in millimeters below or above the plane of the anterior and posterior commissures. The arrows point to anterior cingulate activity in cocaine addicts watching cocaine-cue tapes and the absence of such activity in all other conditions. The left hemisphere is on the right side of each image. The p values on the color bars refer to columns A, C, D, and E; t values refer to column B. See text for details of the data analysis.

A strategic area : the prefrontal cortex

- Various studies of imaging have shown that these dysfunctions of the voluntary control following the use of drugs were in relationship with alterations of the prefrontal cortex

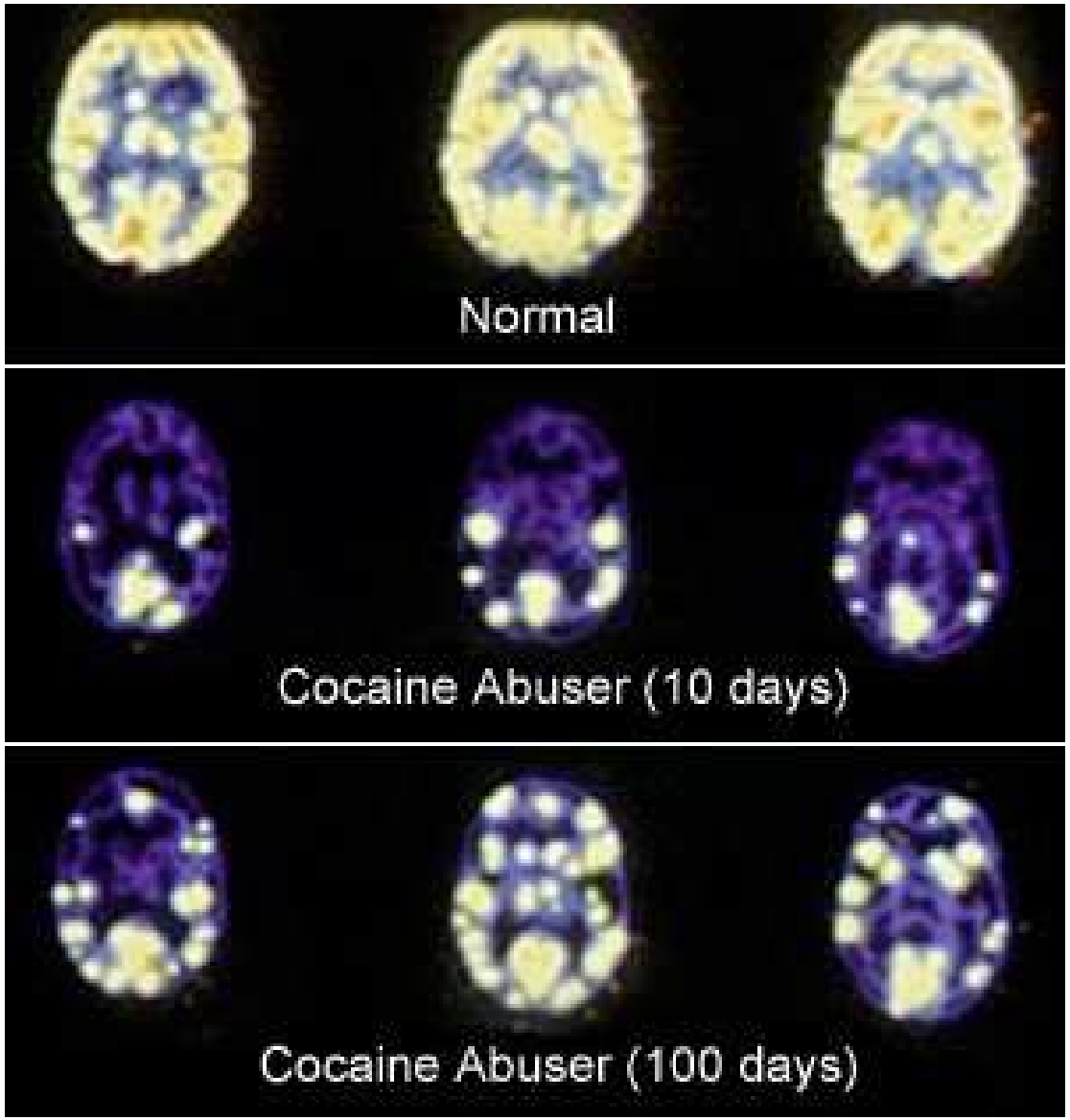
(Frith, C.D., Friston, K., Liddle, P.F. and Frackowiak, R.S., 1991; Zhu, J., 2004; Spence, S.A., Hirsch, S. R., Brooks, D.J. and Grasby, P.M., 1998)

- also showing implications with important pathologies as the schizophrenia

(Spence, S.A., Hirsch, S. R., Brooks, D.J. and Grasby, P.M., 1998; Marshall, J.C., Halligan, P.W., Fink, G.R., Wade, D.T. and Frackowiak, R.S., 1997)

- and opening so a new way of interpreting these pathologies, to diagnose them and probably to take care of them.

Cocaine use and prefrontal cortex



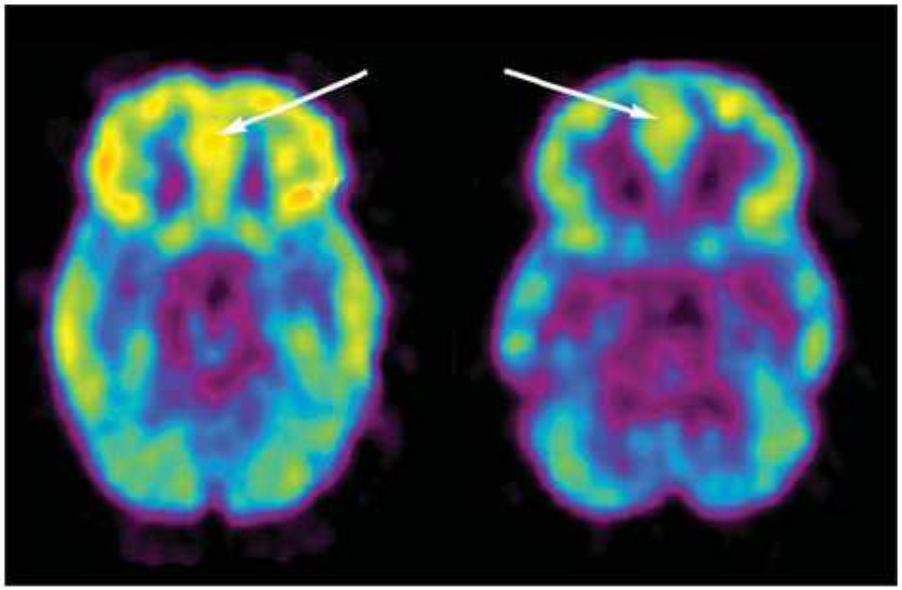
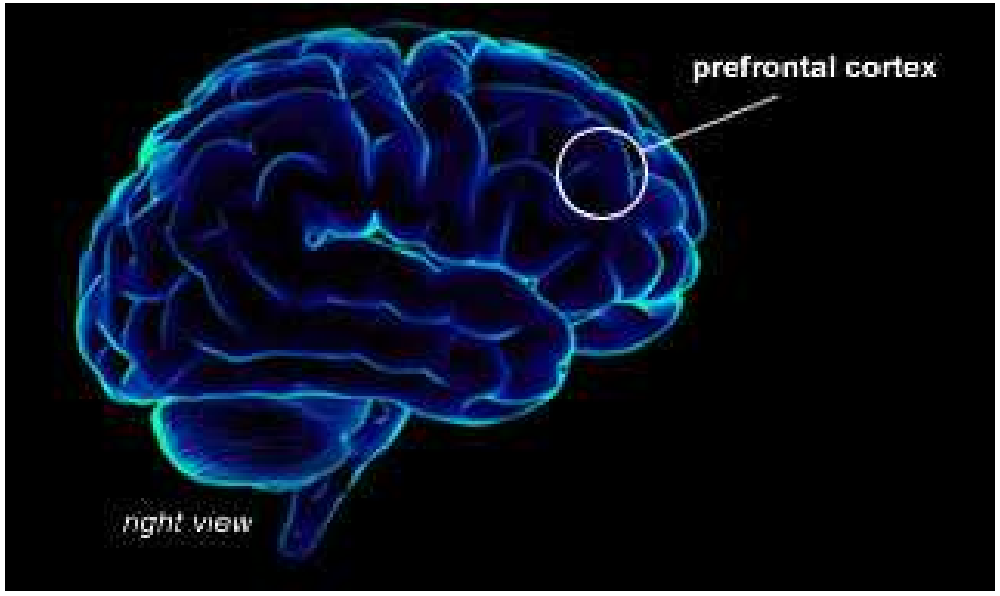


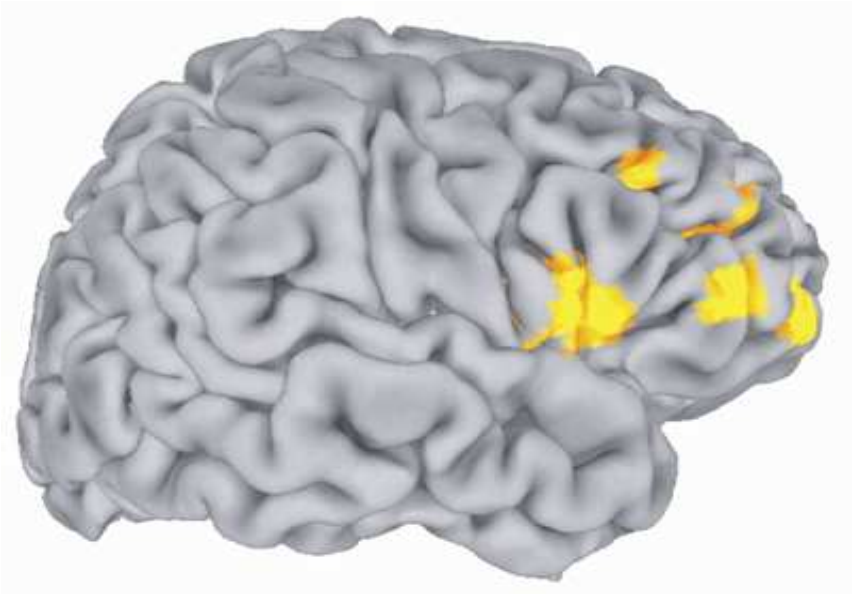
Figura 8. PET: i consumatori di cocaina presentano un metabolismo ridotto nella corteccia orbitofrontale

Prefrontal cortex and control

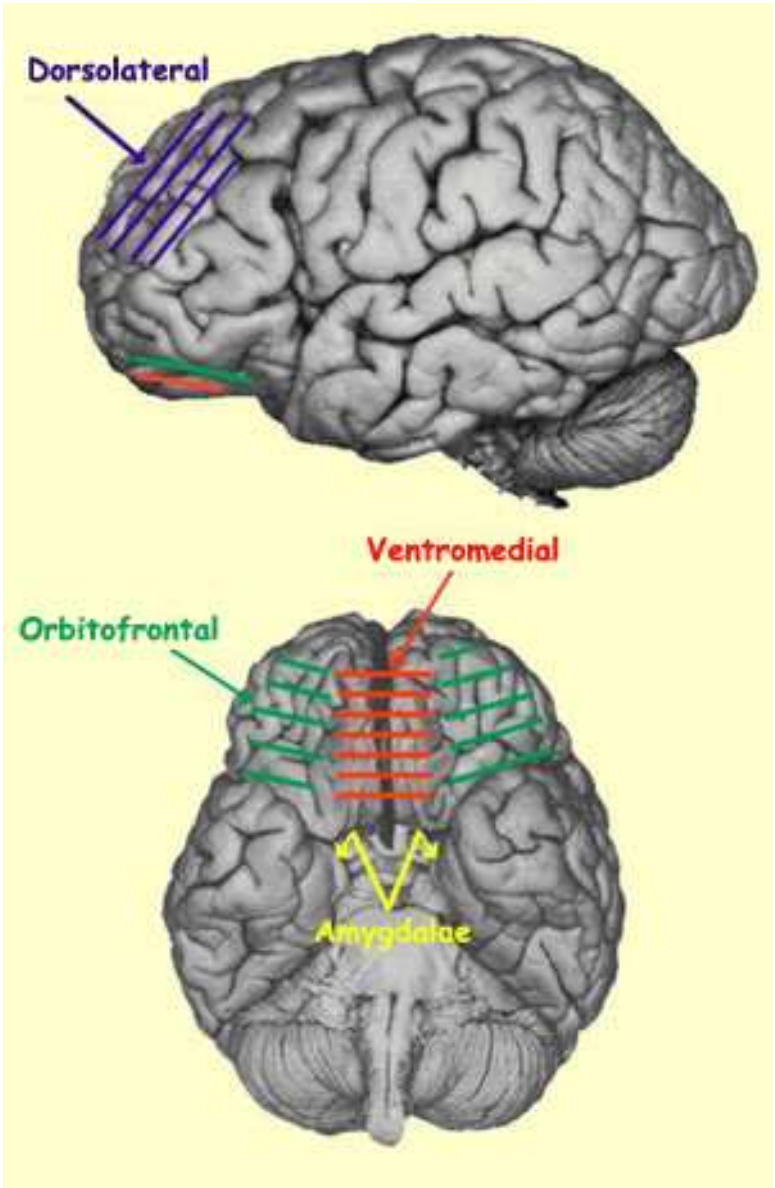
- The prefrontal cortex is the elective center of the cognitive functions and the behavioral control .
- It has a role of “controller” after the activation of the craving
- It intervenes in the decisional process for the cognitive and behavioral control .

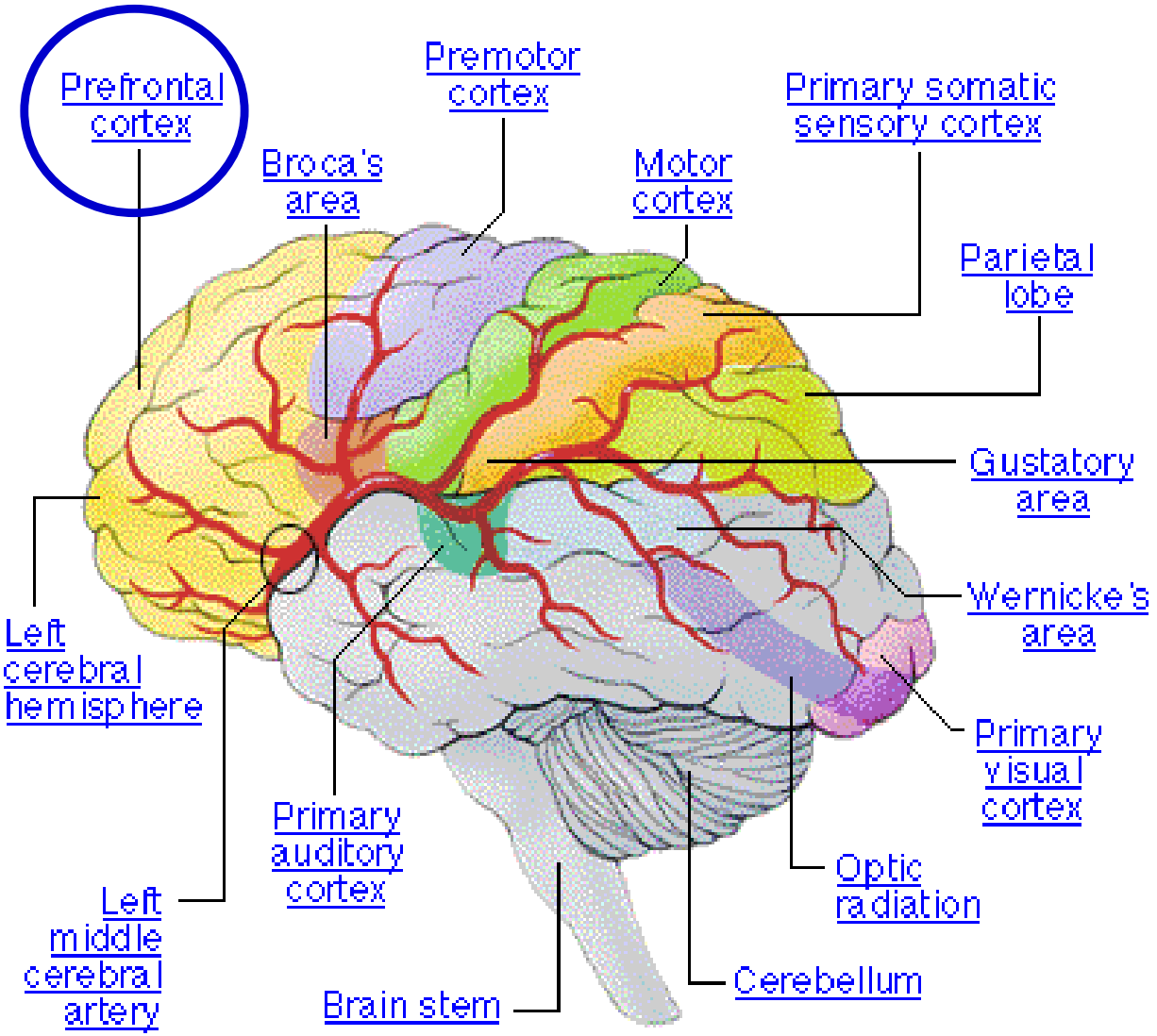
(Wexler 2001, Paulus 2002, Kauman 2003)





Prefrontal cortex (PFC)

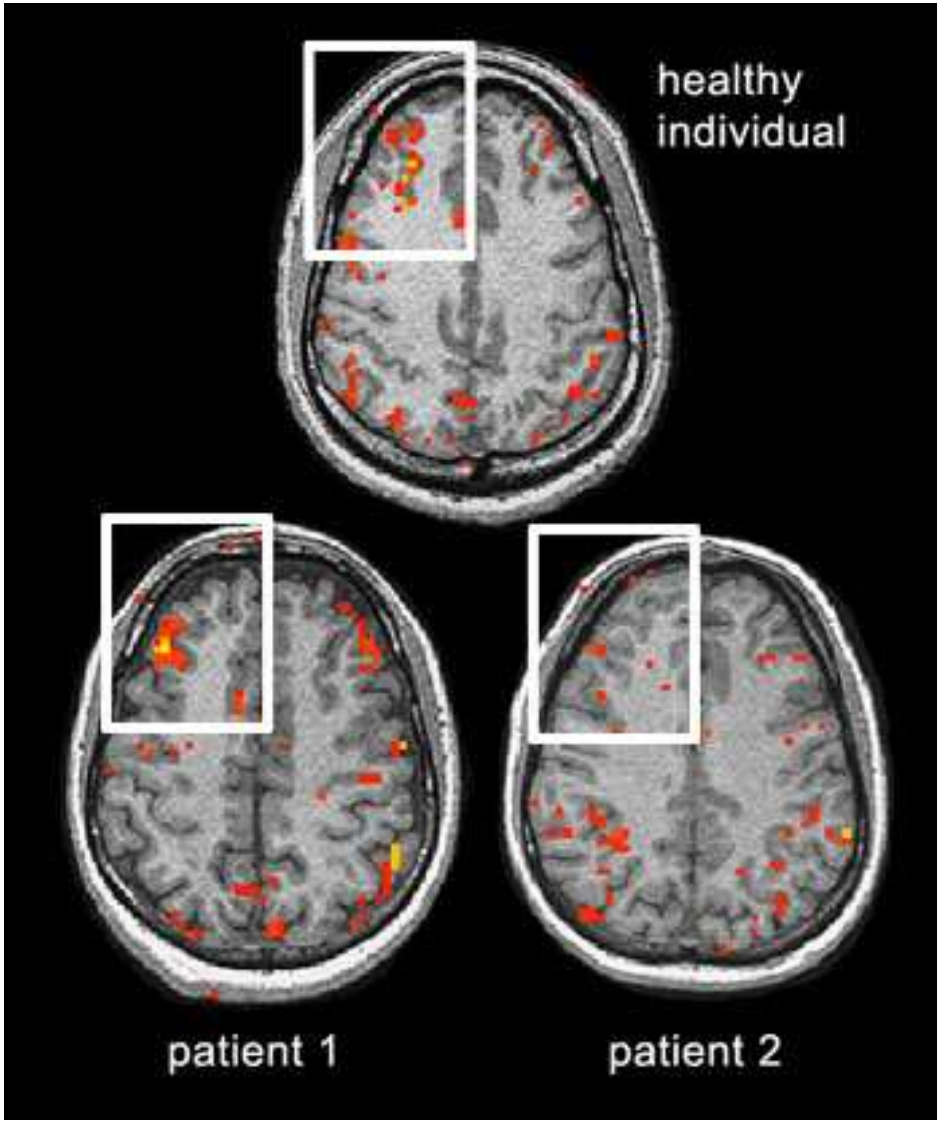




Disturbances in prefrontal cortex (PFC) in schizophrenia and affective disorders

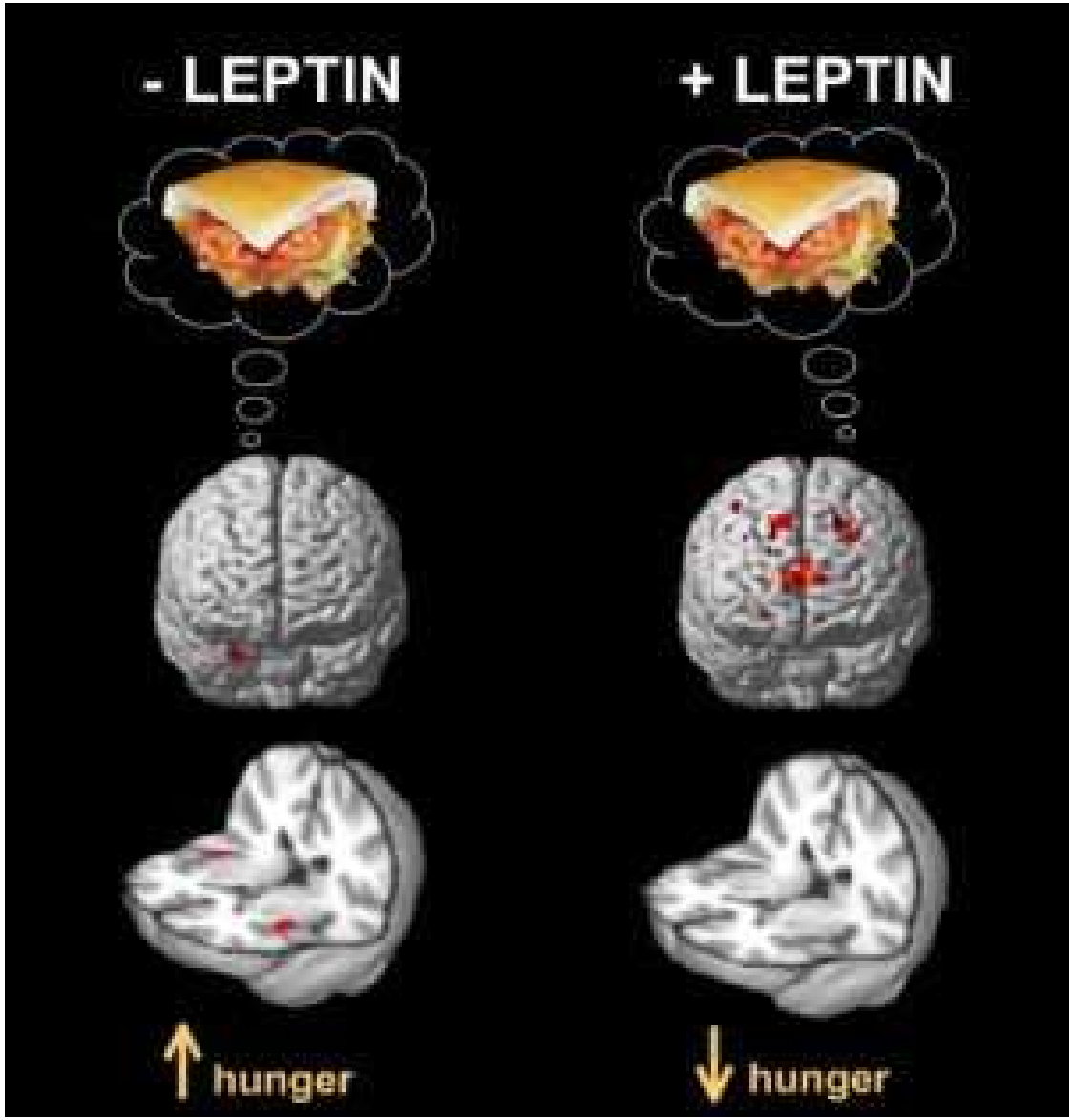
Several lines of evidence suggest that there are relevant disturbances in prefrontal cortex (PFC) in schizophrenia and affective disorders.

Brain images on the right show examples of patients who have (patient 2) and do not have (patient 1) this abnormality.



Dr. Sweeney's team

UCLA researchers identify the brain circuits controlling hunger



In adults who have a rare gene that confers leptin deficiency, food cues produce hunger and increases activity in the insula and other brain regions linked to hunger (left). Leptin supplementation reduces hunger while increasing activity in the prefrontal cortex, a brain region linked to inhibitory control and satiety (right).

A new reading of mental disorders

- Mental disorders should be analyzed also in relation to neural, functional and structural correlates, detectable with neuroradiology techniques TAC, MRI but also PET, fMRI, VBM-MRI.

A new perspective: **neuropsychology**

- In order to better understand and interpret drug abuse and possible clinical, educational, social interventions, it is necessary to refer also to a new perspective, **neuropsychology.**

(Yücel M. et al. 2007)

"Change your mind and you will change your brain"

- Behavioural-cognitive therapy has proved its ability to create modifications of neuronal activity and structure, and to induce physical alterations of the central nervous system with important psychic changes.

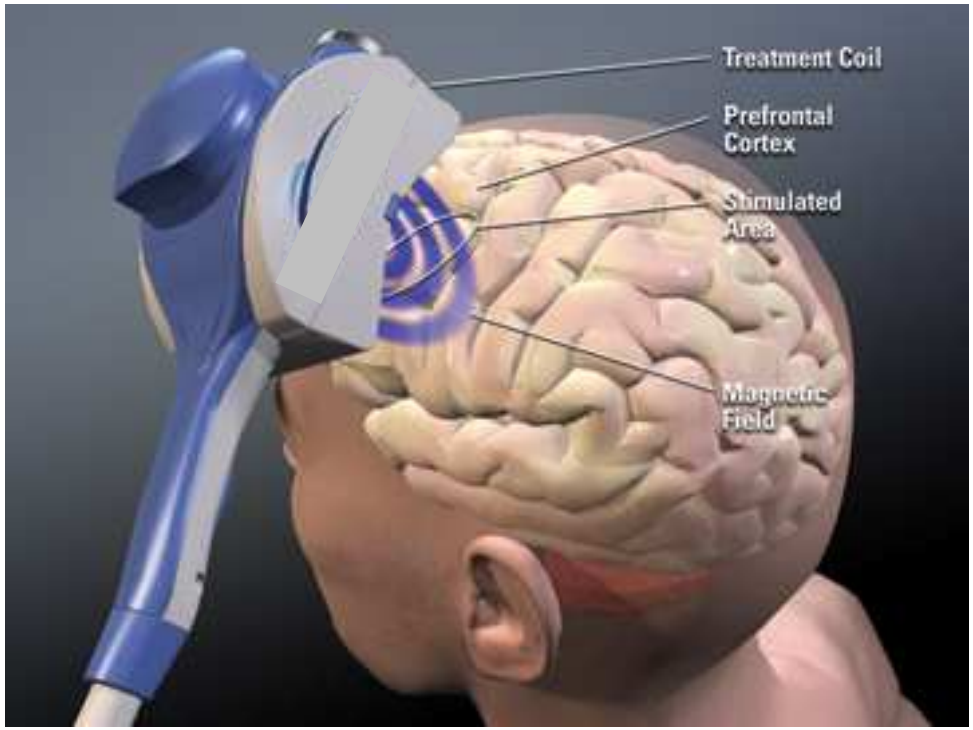
Paquette V. (2003): psicoterapia cognitivocomportamentale per il trattamento della fobia specifica per i ragni

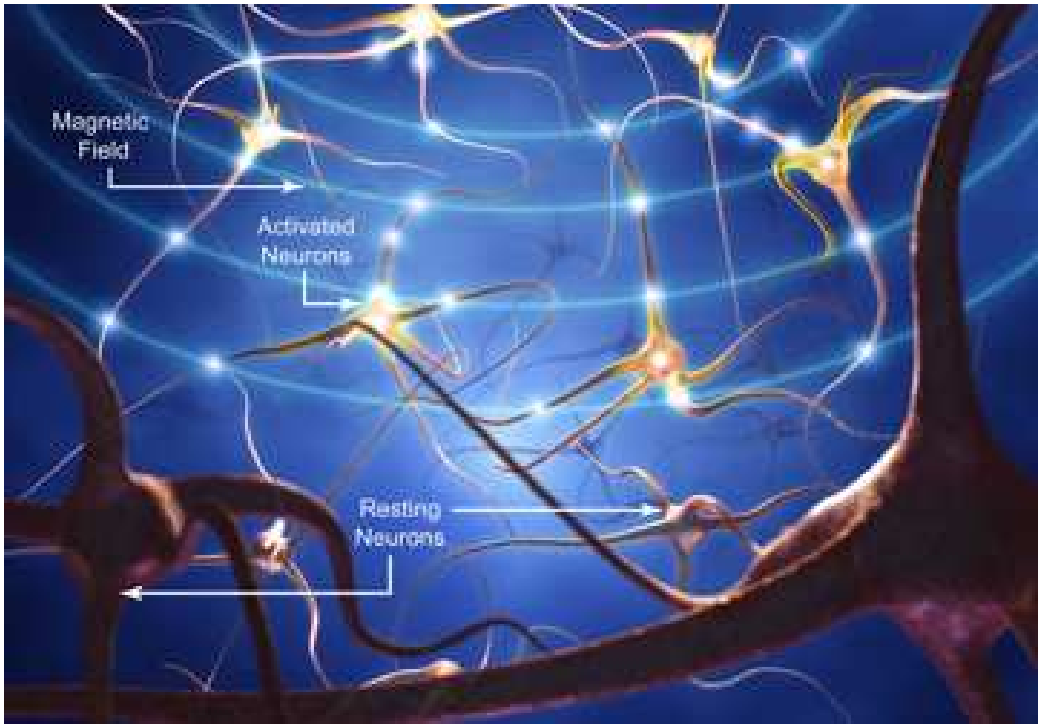
Neuroplasticity and addiction

- This remodelling process of brain structures could play a crucial role in overcoming substance abuse.

- **Can we stimulate the areas supporting this process in order to anticipate recovery?**

The left prefrontal cortex and TMS therapy as a treatment for major depression.





The **left prefrontal cortex** is used to access these structures non-invasively from outside the brain with TMS Therapy.

Neuroimaging

Neuroimaging techniques (FRMI, MRI, PET, SPECT, etc.) have given a great contribution to better define these mechanisms. (Fowler, 2007).

Nowadays, these techniques allow to both underline and represent the structures, the operations and the activities of the cerebral areas. They also show the cerebral connections differently involved in the dysfunctional processes causing addiction

Neuroimaging technologies

- FRMI, MRI, PET, SPECT, etc.:

- In the next future, thanks to technological progress and to an increasing diffusion of these tools, we cannot exclude that neuroimaging technologies will become easily and wildly available

Neuroimaging is useful in the study of the metabolism and of the dopaminergic system as well

Other techniques coming from the nuclear medicine (PET and SPECT) have allowed to acquire further evidences (**Fowler 2003, Kung 2003)** on the **recettorial cellular systems and on the metabolism of the neurotransmitters**. Thanks to the use of radiotracing, allowing the measurement of the cerebral metabolism of the glucose, these techniques provide researchers with a precise cerebral map.

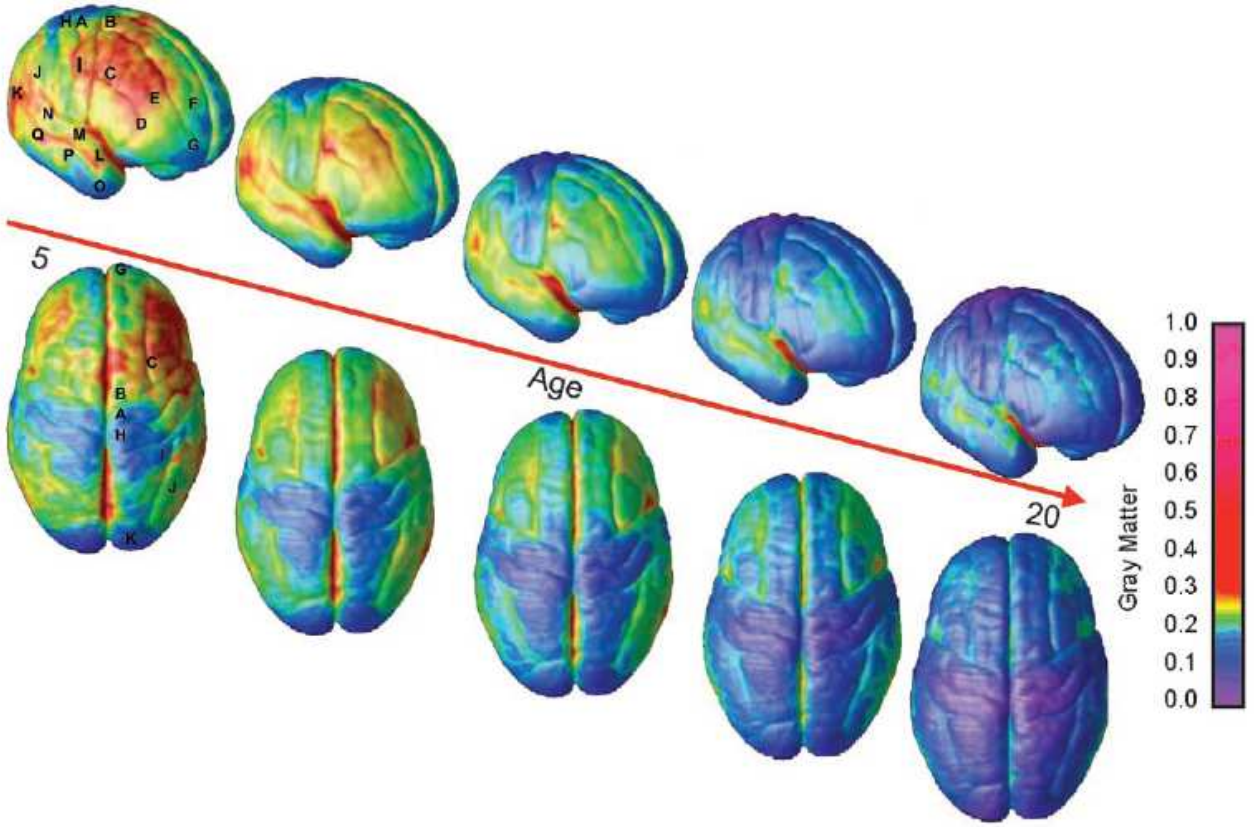
In this way we are been able to understand better also the **role of the dopamin** in the consequent euphoria to the use of substances **(Volkow 2003)** and, contemporarily, as and how much some stimulating ones, for example the metamfetamines, reduce the cellular activity in the areas of the brain appointed to **the ability of judgment (Bolla 2003),** what the orbitofrontal, cortex important in thestrategic decisional process.

That's not new

- For a long time, structural studies have pointed out differences in prefrontal lobes of polyaddicted subjects (Liu X. 1998, Stapleton 1993, Volkow, 1991) compared to control groups (no drug users), pointing out and documenting brain lesions related to drug use.

Brain growth and the need for a new prevention strategy

- The brain maturation is completed after the 20 years
- “keep your brain healthy ”



In prevention strategies, as soon as possible we must activate specific programs of early diagnosis to identify the use of substances, especially among the youth (12-18 years).

New scenerios and new patterns of drugs abuse

- "More and more young people"
  - More socially integrated
  - With a variety of contemporaneous addictions (polidrugs abusers)
  - Very conscious of their pathology and of the need for care
  - With prevailing use of stimulating and hallucinogenic drugs
  - With greater prevalence of psychiatric pathologies

A necessary reorganization of the addiction departments

- Old systems of diagnosis and care do not allow a precise definition of the problems and a good differentiation of the various types of addictions
- Difficulty to assess the results and the effectiveness of the various therapies through the observation of variations of structures and cerebral functions
- Since a long time, the regional systems and the addiction departments need a deep innovation and an update of their diagnostic, clinical and rehabilitation models.

What's the direction?

- What kind of approach?
- What kind of vision?
- How to read the phenomenon?
- How to intervene?
- How to redirect the health organization according to health economic issues and to decision making processes?

Addiction and neuroscience

- The scientific research and the neurosciences of the addictions are:
  - an important incentive of thinking
  - a new key for reading the phenomenon
  - the base to updating and planning our interpretative models and treatments for this complex pathology.

The neuroscience

The starting point

for a reading based on the correct interpretation of the mechanisms correlated to the addiction.

Utility and applicability

- Getting information about physiopathological mechanisms of addiction involves a deep change in current conceptual model of reference underlying the diagnostic and therapeutical processes of the addiction departments.

A daily improvement

- Neurosciences can improve our daily work and our relationship with our patients in the addiction field as well.

Neuroimaging and evaluation of treatments effectiveness

- Another great advantage of this innovative approach is the possibility of better monitoring treatments evolution and results at different levels:
  - Behavioural
  - Brain structural
  - Brain functional

Which possible practical consequences?

- In a near future, new methods and activities could be studied and evaluated. They will aim at:
  - reducing the activation of the areas involved in the craving and/or
  - stimulating, through highly integrated interventions (i.e behavioural cognitive, educational, pharmacological, magnetic stimulation etc.), the activation of the frontal control areas
  - improving the relapse control

The national net of services for the addicts' care (2007)

544 Public Addiction Services ("Sert")

5000 health workers providing care to:

176.000 Outpatients

24.640 new clients/year entering treatment
151.360 already known patients

1197 Therapeutic Community
(financed with public money) providing care to:

11.760 Inpatients inside 730 residential services

2.346 Outpatients in 204 day hospitals,

4.430 Outpatients in 183 outpatient clinics

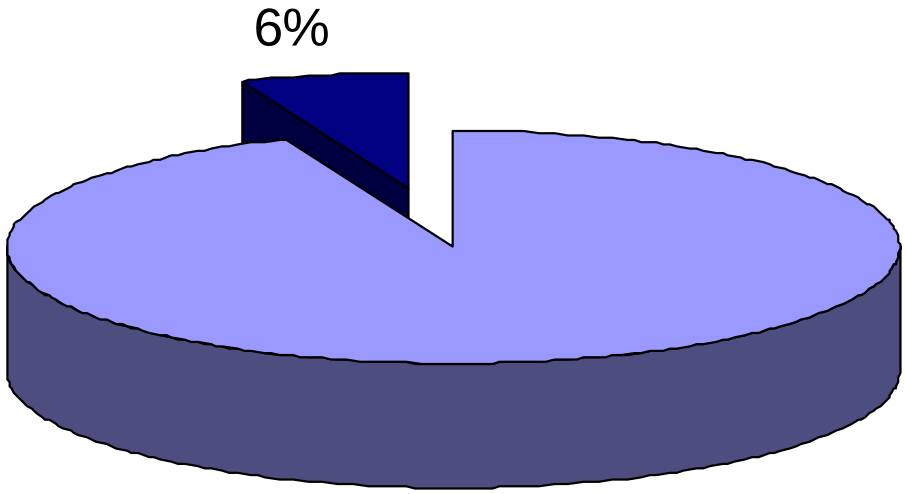
SOURCE: RELAZ. PARLAM. 2007

The national net of services for the addicts' care (2007)

182.776 Outpatients

11.760 Inpatients

194.536 TOTAL



SOURCE: RELAZ. PARLAM. 2007

BUT.....→

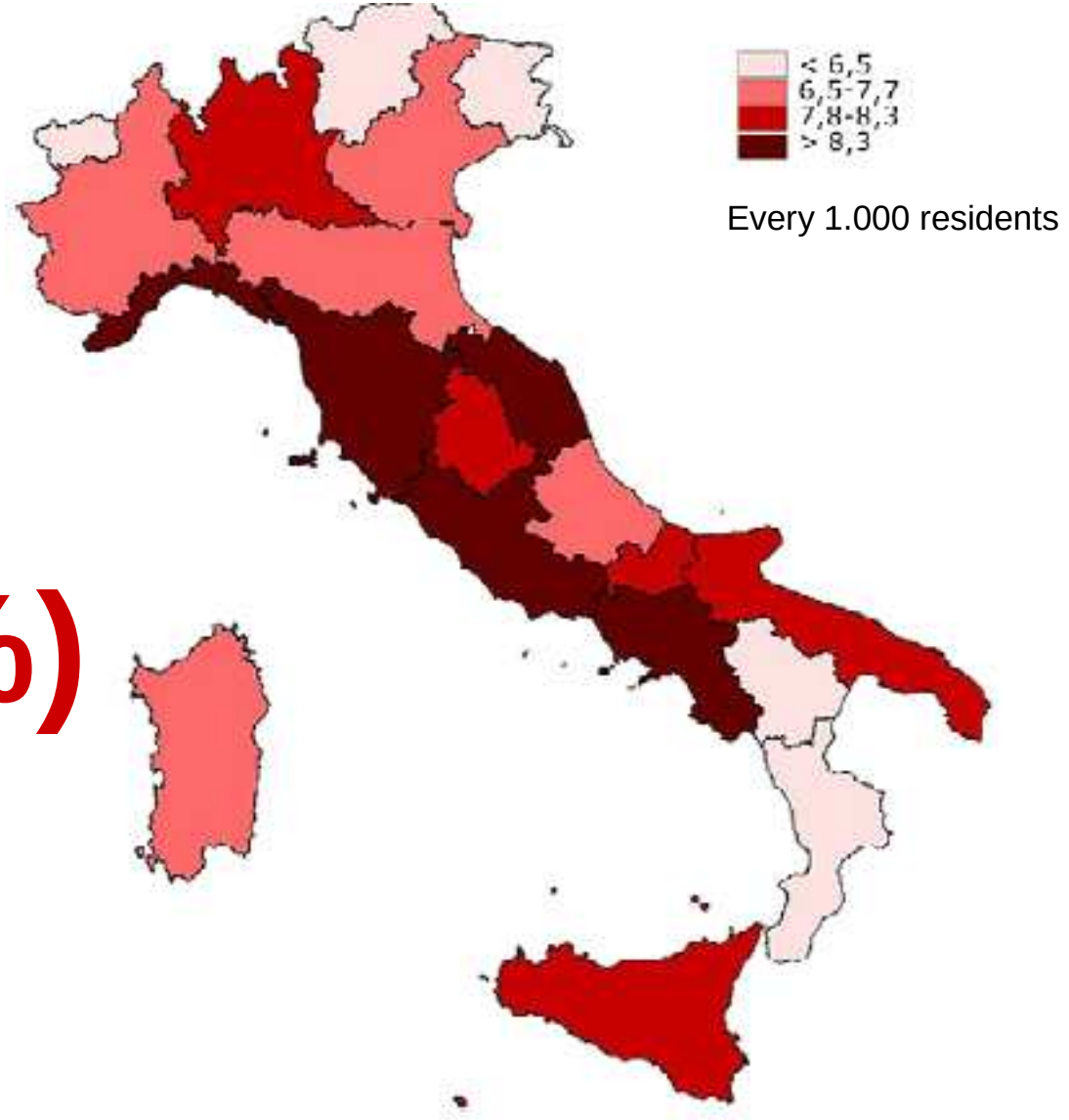
ADDICTS in need for therapy

312.000

estimated number
of addicts in Italy

117464 (38%)

addicts not yet in care
in the services



SOURCE: RELAZ. PARLAM. 2007

Just a dream?

Maybe for someone….. but we prefer to live it as a hope for improving treatments for our patients.

New “offers”

- Necessity for changing the current offer’s organization that appears fossilized on old assistance models, no more accepted by the “new” drug users, especially by those affected by cocaine, metamphetamines and cannabis addiction.

Supporting collaborations

- Neuroradiologies
- Neurosciences Institutes
- Genetic research centers
- Neurophysiologies
- Neuropsychology and social neuroscience centers

It is not just a matter of resources!

- The Addiction Departments must get out of their cultural/ professional and technical/ scientific isolation they have often experienced in these years.

TODAY A NEW ROUTE BEGINS FOR US.

Keep always in mind that …..

In order to treat a brain, first of all the brain must exist.