

BOTTOM-UP: GENES

# “the special status of the brain”

Roskies 2002

TOP-DOWN: LIVED EXPERIENCE

## 2007 addiction & neuroethics highlights

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**San Matteo e l'angelo,**  
Oil on canvas, 223x183, 1602,  
Kaiser Friedrich Museum, Berlin,  
Germany

**TODAY**

**TO  
MEASURE**



**TO BE ABLE**



**If I can...**

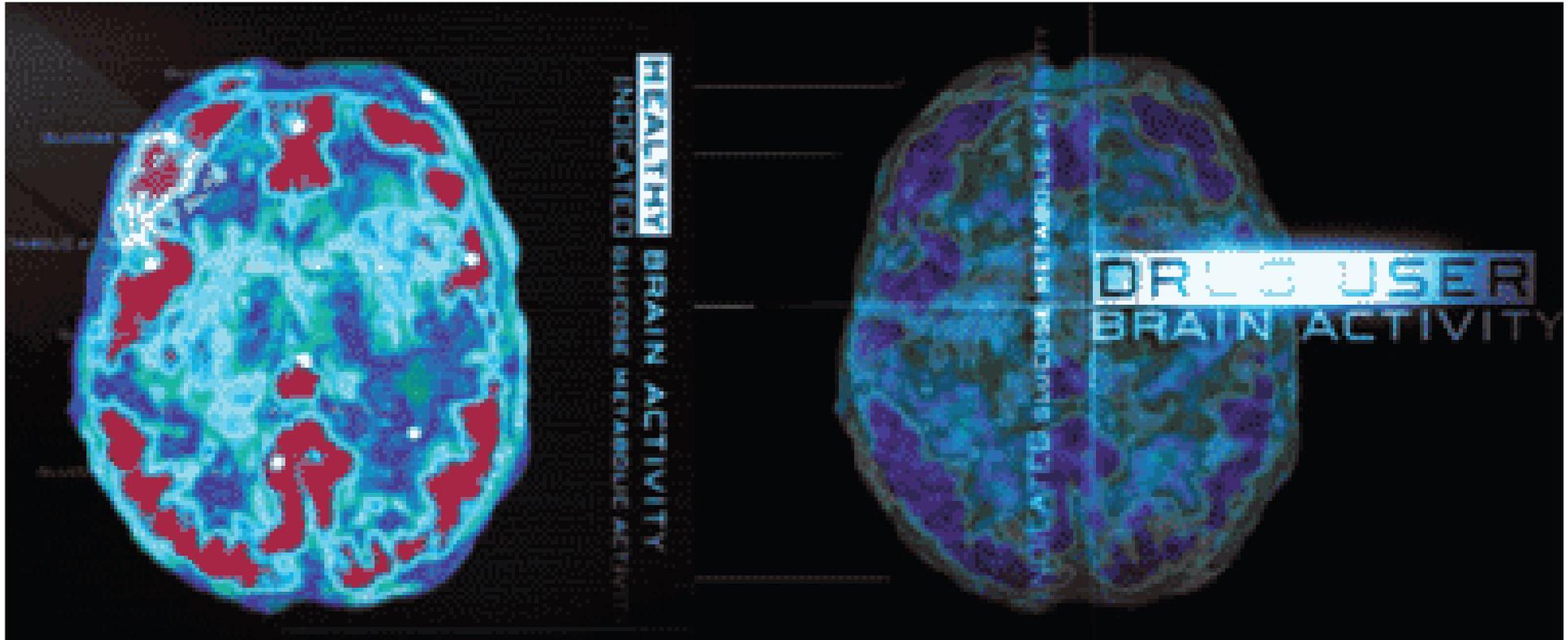
The major justification for demarcating neuroethics from the broader field of bioethics derives from **the special status of the brain** (Roskies 2002), which is the causal underpinning of our conscious mental lives and of our behavior.

This is not a reductionist claim. The structure and function of the brain is influenced not only by “**bottom-up**” factors such as genes, but also by **top-down** factors such “lived experience” and context.

Steven E. Hyman, The Neurobiology of Addiction: Implications for Voluntary Control of Behavior. *The American Journal of Bioethics*, 7(1): 8–11, 2007

Roskies, A. 2002. Neuroethics for the new millennium. *Neuron* 35(1):21–23.

# FRAMEWORK



***"Drug addiction is a brain disease  
that can be treated."***

Nora D. Volkow, M.D.  
Director  
National Institute on Drug Abuse

## FRAMEWORK

### TO PREVENT

National drug use surveys indicate some children are already abusing drugs by age 12 or 13

### TO DIAGNOSE

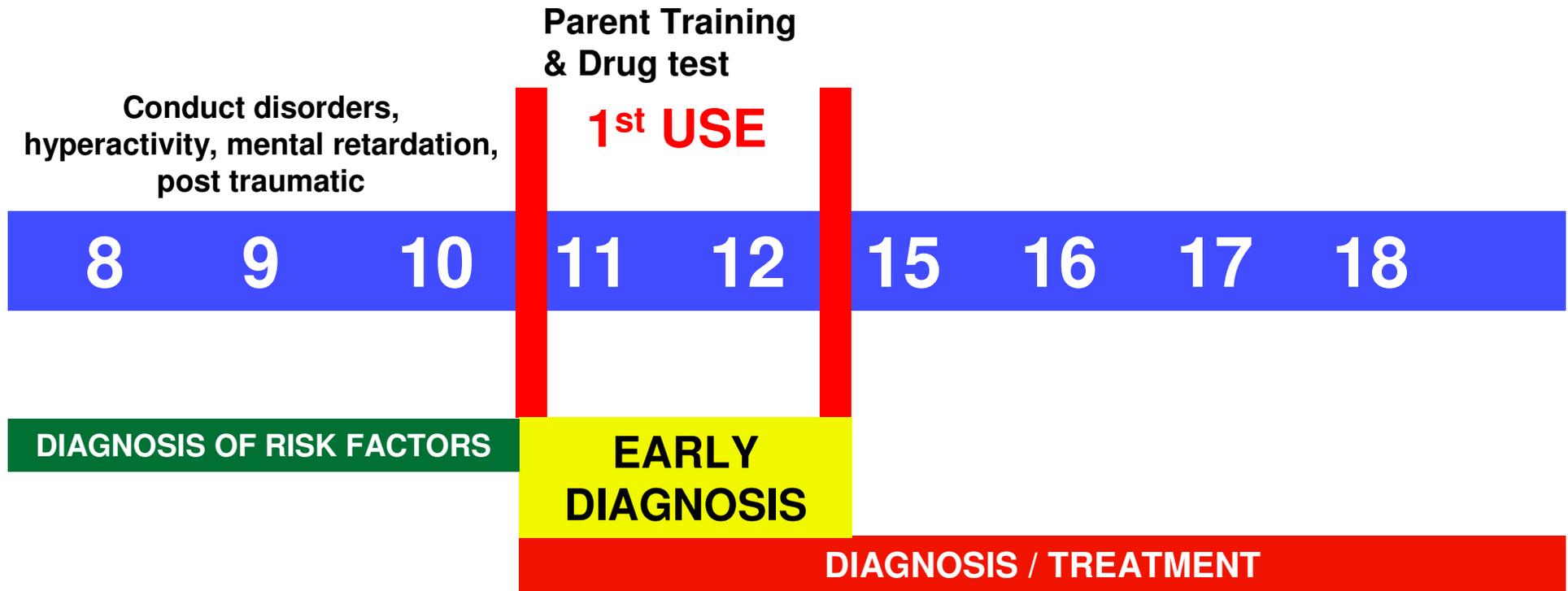
**10 substances:** opiates, alcohol, nicotine, sedatives, hallucinogens, caffeine, cocaine, cannabis, inhalants

### TO TREAT

**Agonist / Antagonist (4/10):** opiate, alcohol, nicotine, sedative

**NO TREATMENT:** cocaine, cannabis, metamphetamine

# FRAMEWORK



**1** INFANCY: IS THE TIME TO DIAGNOSE RISK FACTORS

**2** PREADOLENCE: IS THE TIME FOR EARLY DIAGNOSIS OF DRUG USE

**3** ADOLESCENT: IS THE TIME OF DRUG ABUSE DIAGNOSIS / TREATMENT

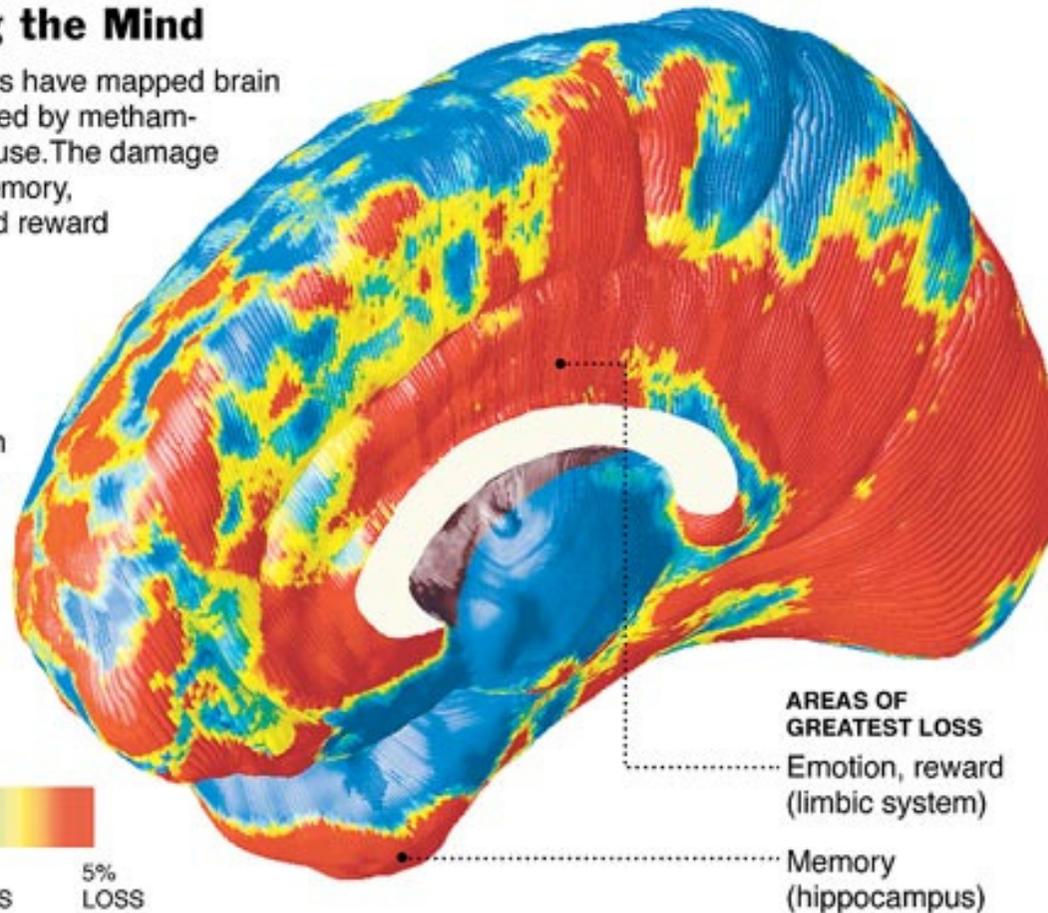
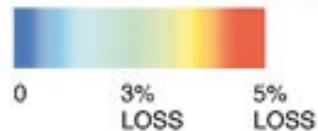
# BRAIN DAMAGE

## DRUGS DAMAGE IN ADULTS

### Eroding the Mind

Researchers have mapped brain decay caused by methamphetamine use. The damage affected memory, emotion and reward systems.

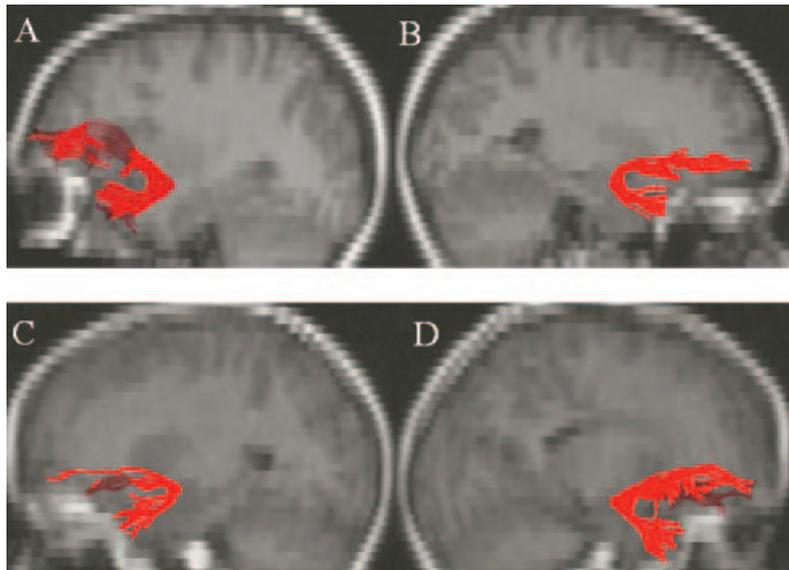
Average difference in brain tissue volume of methamphetamine users, as compared with non-users:



Source: Dr. Paul Thompson, U.C.L.A.

# BRAIN DAMAGE

## SOCIAL DEPRIVED BRAIN



The uncinate fasciculus overlaid on T1-weighted MRI scans co-registered to the DTI images.

A, Left uncinate fasciculus in a normal child.

B, Right uncinate fasciculus of the same normal child.

C, Left uncinate fasciculus in a socially deprived child (note the thinner and poorly organized tract).

D, Right uncinate fasciculus of the same socially deprived child.

## MATERNAL CIGARETTE SMOKING

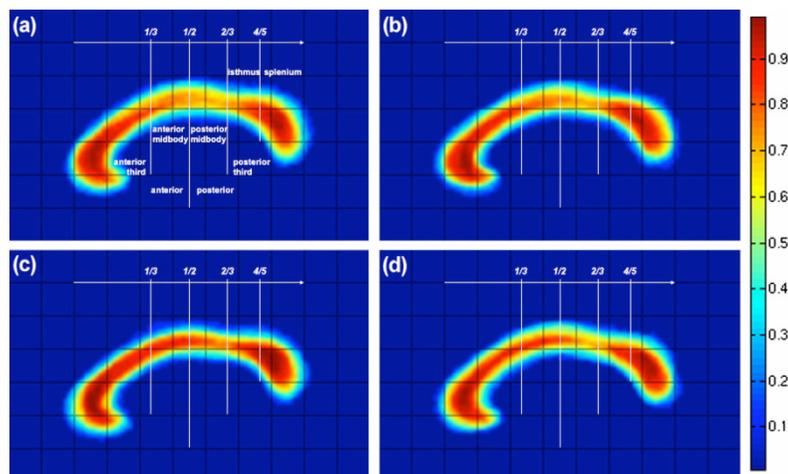
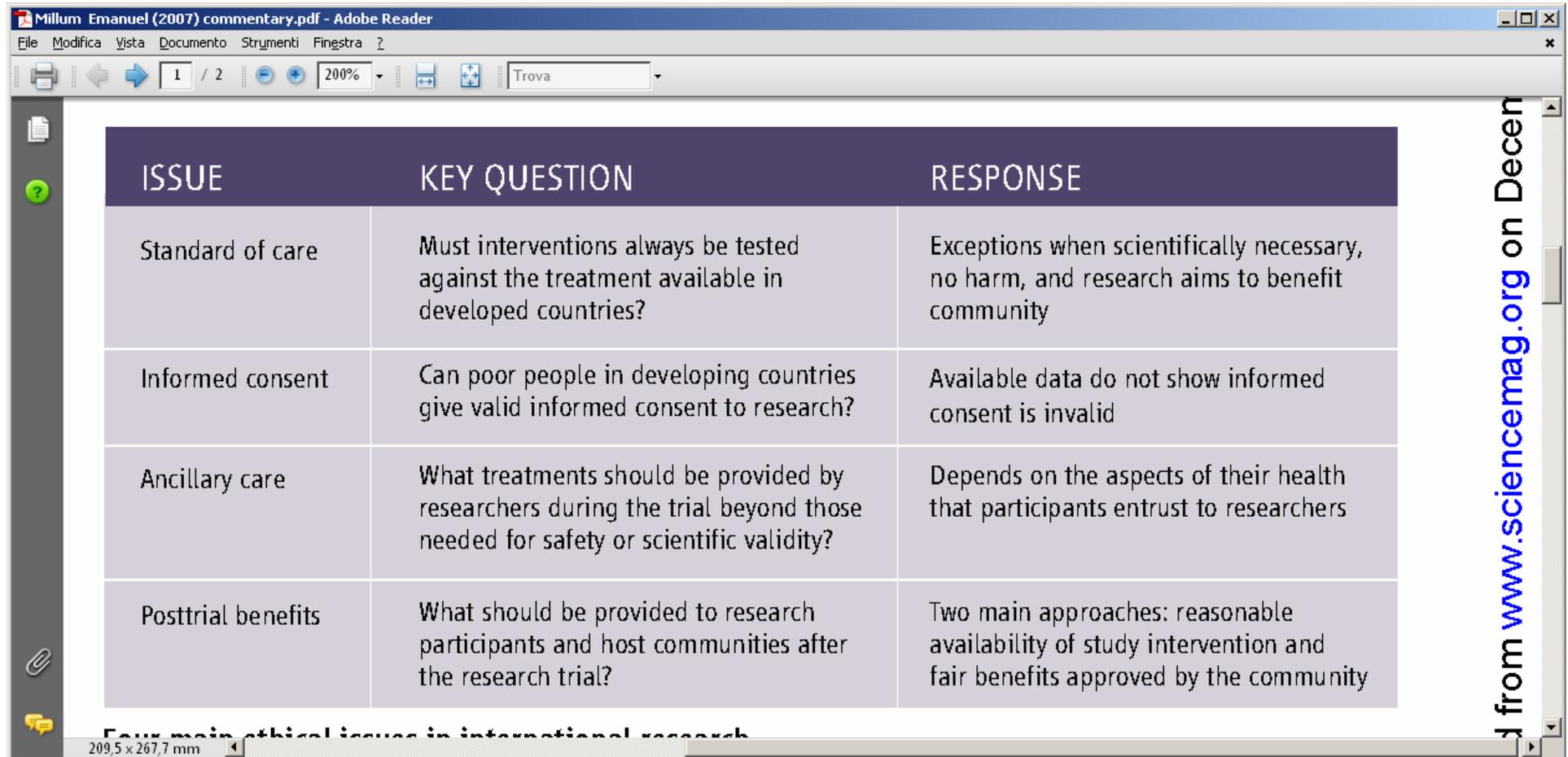


Fig. 1. Probabilistic maps of the corpus callosum: (a) female adolescents, non-exposed to maternal smoking during pregnancy; (b) male adolescents, nonexposed;

(c) female adolescents, exposed; (d) male adolescents, exposed. The scale indicates the probability, at each voxel, of finding white-matter tissue belonging to the corpus callosum in a given group of subjects. Subdivisions of the corpus callosum illustrated in (a) are based on previous works (Witelson 1989; Bermudez and Zatorre 2001).

# BRAIN DAMAGE

## NEUROETHICS CRITERIA



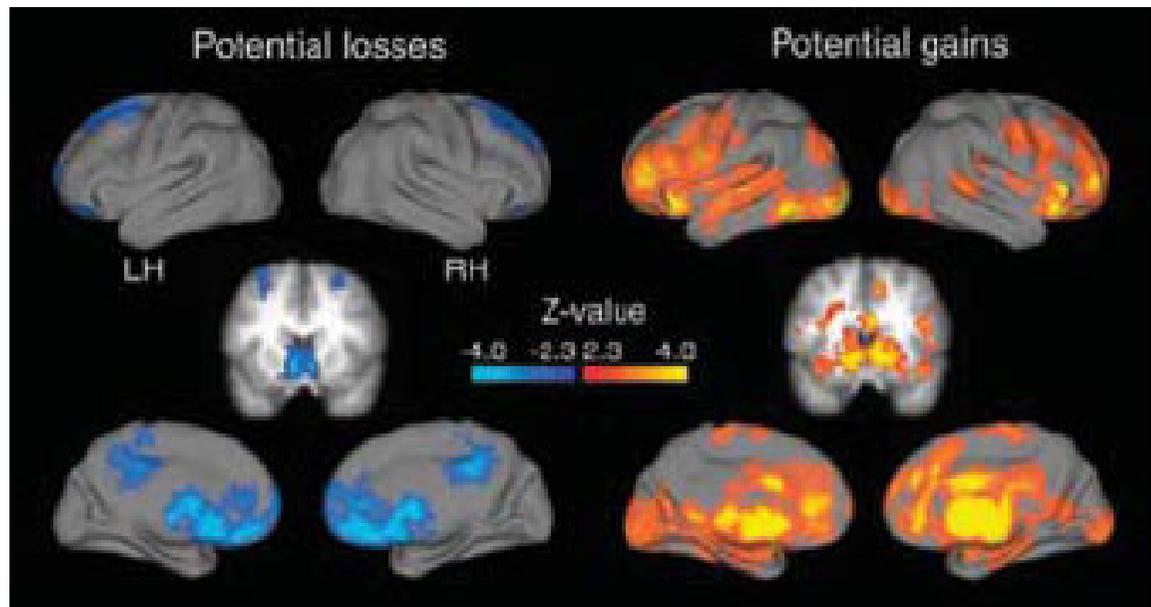
The image shows a screenshot of a PDF document titled "Millum Emanuel (2007) commentary.pdf" viewed in Adobe Reader. The document contains a table with four rows, each detailing an ethical issue, a key question, and a response. The table is titled "Four main ethical issues in international research" at the bottom. The table has three columns: ISSUE, KEY QUESTION, and RESPONSE. The rows are: 1. Standard of care: Must interventions always be tested against the treatment available in developed countries? Exceptions when scientifically necessary, no harm, and research aims to benefit community. 2. Informed consent: Can poor people in developing countries give valid informed consent to research? Available data do not show informed consent is invalid. 3. Ancillary care: What treatments should be provided by researchers during the trial beyond those needed for safety or scientific validity? Depends on the aspects of their health that participants entrust to researchers. 4. Posttrial benefits: What should be provided to research participants and host communities after the research trial? Two main approaches: reasonable availability of study intervention and fair benefits approved by the community. The table is presented in a dark purple header and light purple body. The Adobe Reader interface includes a menu bar (File, Modifica, Vista, Documento, Strumenti, Finestra), a toolbar with navigation and search icons, and a search box containing "Trova". The status bar at the bottom shows the page number "1 / 2", a zoom level of "200%", and the dimensions "209,5 x 267,7 mm". A vertical watermark "d from www.sciencemag.org on Decen" is visible on the right side of the page.

ISSUE	KEY QUESTION	RESPONSE
Standard of care	Must interventions always be tested against the treatment available in developed countries?	Exceptions when scientifically necessary, no harm, and research aims to benefit community
Informed consent	Can poor people in developing countries give valid informed consent to research?	Available data do not show informed consent is invalid
Ancillary care	What treatments should be provided by researchers during the trial beyond those needed for safety or scientific validity?	Depends on the aspects of their health that participants entrust to researchers
Posttrial benefits	What should be provided to research participants and host communities after the research trial?	Two main approaches: reasonable availability of study intervention and fair benefits approved by the community

Four main ethical issues in international research

Millum J, Emanuel EJ. The Ethics of International Research with Abandoned Children. Science. 2007 Dec 21;318(5858):1874-5.

# RESPONSABILITY

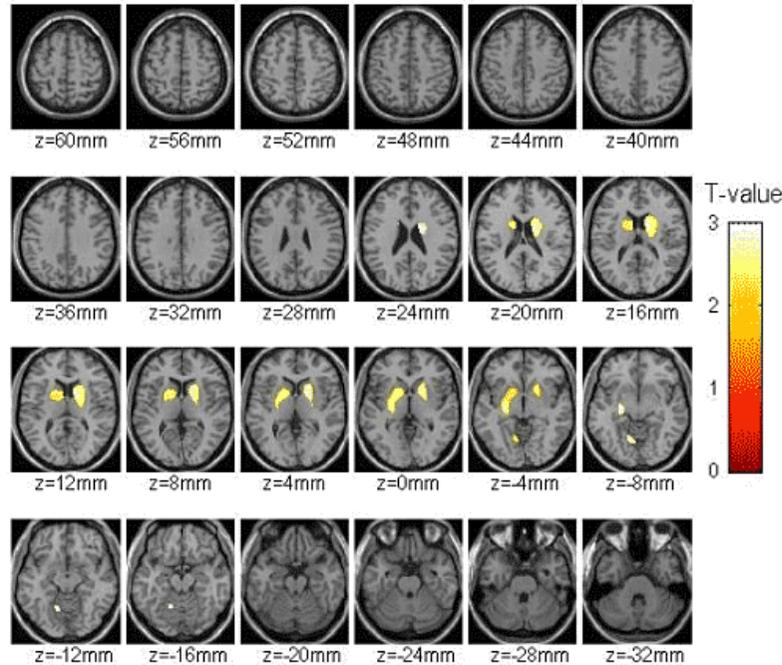


The **blue areas** at left are those that become deactivated as we make decisions that will likely cause us to **lose money**. The **orange** and red areas at right show the activation that occurs in the brain when we believe the odds are in our favor and we'll **win money**.

Those who abused these substances were viewed as exercising their free will and choosing not to limit or control this behavior. Society therefore tended to blame and punish offending individuals rather than to understand the processes that contribute to addiction or strategies for rehabilitation.

RESPONSIBILITY

**CRAVING & BINGING**



**AGONIST THERAPY**

## RESPONSABILITY

**“a sober heroin addict must be considered competent, autonomous and capable of giving consent. “**

Bennett Foddy & Julian Savulescu. Addiction and Autonomy: Can Addicted People Consent to the Prescription of Their Drug of Addiction? *Bioethics* 2006; 20(1): 1–15.

**“Only when they have been subjected to prolonged cravings their self-control resources are depleted, and their autonomy correspondingly weakened. Most of the rest of the time – for the great majority of the time, in fact – addicts are as autonomous as you and me.”**

Levy N. Addiction, Autonomy and ego-depletion: a response to Bennett Foddy and Julian Savulescu. *Bioethics Volume 20 Number 1 2006*

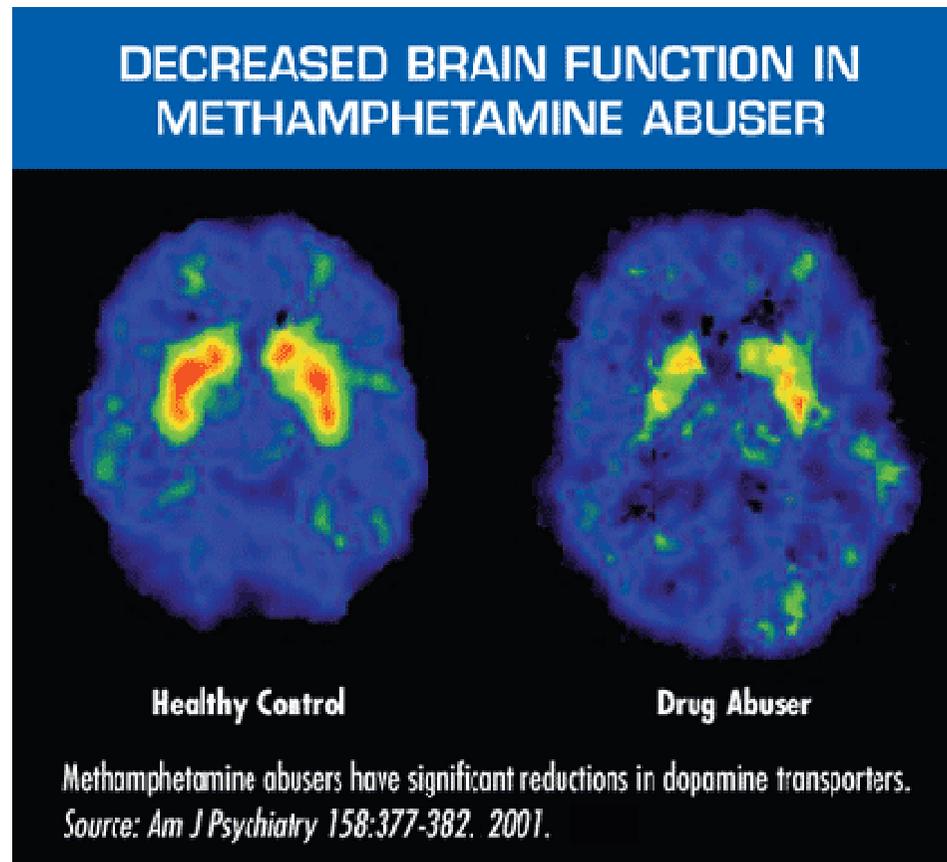
# GENETIC

**“My genes made  
me do it.”**

Levitt M, Manson N. My genes made me do it? The implications of behavioural genetics for responsibility and blame. *Health Care Anal.* 2007 Mar;15(1):33-40. Review.

Peele S, DeGrandpre R. My genes made me do it. *Psychol Today.* 1995 Jul-Aug;28(4):50-53, 62, 64, 67-68.

# GENETIC



**First, at the scientific level, the sheer complexity of neuroscience research poses challenges for integration of knowledge and meaningful interpretation of data.**

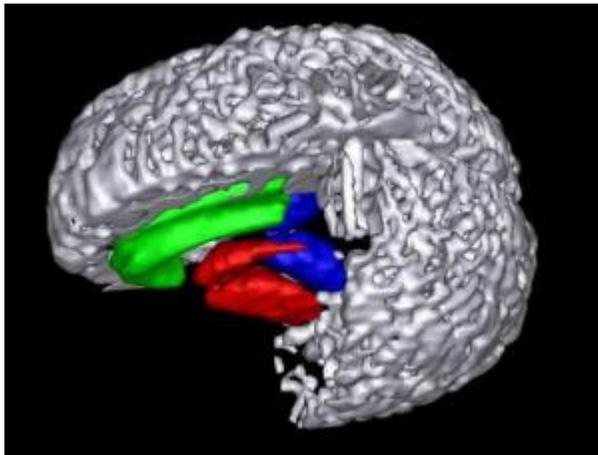
**Second, at the social and cultural level, we find that interpretations of imaging studies are bound by cultural and anthropological frameworks.**

Illes J, Racine E. Imaging or imagining? A neuroethics challenge informed by genetics. *Am J Bioeth.* 2005 Spring;5(2):5-18.

## GENETIC

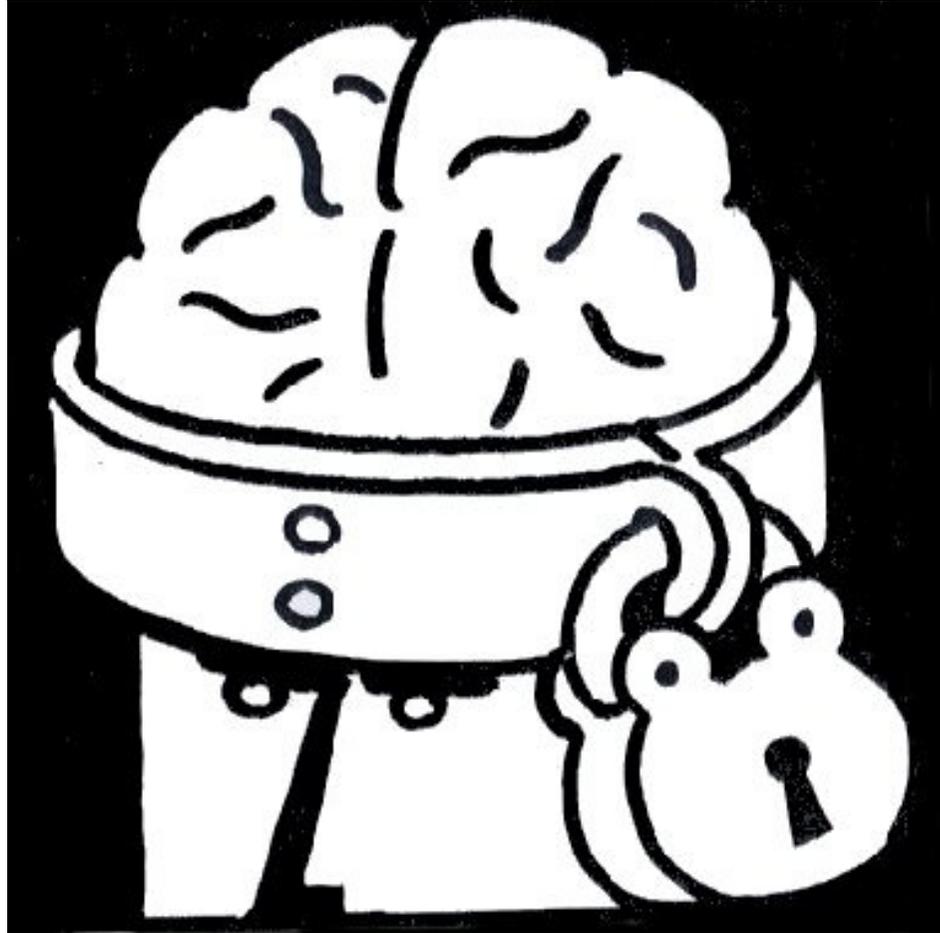
In particular, the introduction of concepts of self and personhood in neuroimaging illustrates the interaction of interpretation levels and is a major reason why ethical reflection on genetics will only partially help settle neuroethical issues.

Indeed, ethical interpretation of such findings will necessitate not only traditional bioethical input but also a wider perspective on the construction of scientific knowledge.



*Brain scans of smokers studied by Duke researchers revealed three specific regions deep within the brain that appear to control dependence on nicotine and craving for cigarettes. Shown in blue in this illustration is the thalamus, an region of the brain critical to one's ability to calm down when stressed. In red is the striatum, a region implicated in the pleasure system of the brain. In green is the anterior cingulate cortex, a region vital to self-control and concentration. (Credit: Image courtesy of Duke University Medical Center)*

# BRAIN PRIVACY



Brain Data

# BRAIN PRIVACY

Neuroimaging Compute Facility - Windows Internet Explorer

http://cbs.lsddiv.harvard.edu/ncf/ComputingFacility.htm

File Modifica Visualizza Preferiti Strumenti ?

acer Y! Cerca Traduci la pagina Entra Mail Answers Mio Il Mio Yahoo! Notizie Sport Finanza Giochi

Google oimaging memory storage Cerca Segnalibri 149 bloccati Controllo Traduci Invia a neuroimaging memory storage Impostazioni

Neuroimaging Compute Facility

## COMPUTING RESOURCES

### Hardware

**120 CPU high performance compute cluster**  
The main computational server includes 30 Dell 1955 Blade Servers that each house two dual-core 2.66GHz processors. Twenty-six of these nodes have 8G of RAM, while the remaining four have 16G of RAM for high memory jobs. They are configured to run Linux and Solaris operating systems.



**High volume, high performance disk space**  
An EMC Clariion CX3-40 currently provides over 54TB of usable, RAID-protected disk space for the user community, expandable to 150+ TB. The Clariion is fronted by an EMC NSX gateway that allows file level access via NFS.



**Secure data backup and archive**  
Tape backup (regular running snapshot of data) and archive (permanent storage) is provided by a ADIC Scalar I2000 tape Backup System. The current capacity of 80TB of backup space is easily expandable to over 600TB.



**Secure, fast network access**  
Connectivity to the cluster and storage is provided via 10G links on an enterprise class Cisco 6509 switch. Backup data is routed separately over Cisco MDS 9120 SAN switches. The network is secure and protected by firewall.



Fine Internet | Modalità protetta: disattivata 100%

## BRAIN PRIVACY

**“fraught with uncertainty” (Glannon, W. 2007)**

So, what makes functional neuroimages so “exceptional” as to deserve protections beyond those established by the HIPAA privacy rule?

**We currently do not understand well enough the meaning of the neuroimages to include them in the same part of the record that may be seen by at least several thousand individuals.**

# BRAIN PRIVACY

## Health Insurance Portability and Accountability Act (HIPAA)

The following are among the uses of PHI permitted by HIPAA without patient authorization:

- 1) Quality assessment and improvement, outcomes evaluations, protocol development, case management;
- 2) Reviewing the competence or qualifications of health care professionals, conducting training programs for non healthcare and health care professionals, accreditation, certification;
- 3) Health insurance underwriting premium rating;
- 4) Conducting medical review, legal services, auditing functions, and fraud and compliance programs;
- 5) Business planning and development; and business management and general administrative activities of the entity (U.S. Department of Health and Human Services [HHS] 2002, Part 164.501) whatever information they can access, even if that information is not completely appropriate to the decision being made.

Genetic information, although often unreliably predictive may still be the "best" information these companies... have upon which to base economic decisions... (Alpert 2003, 316).

# PEDIATRIC NEUROETHICS

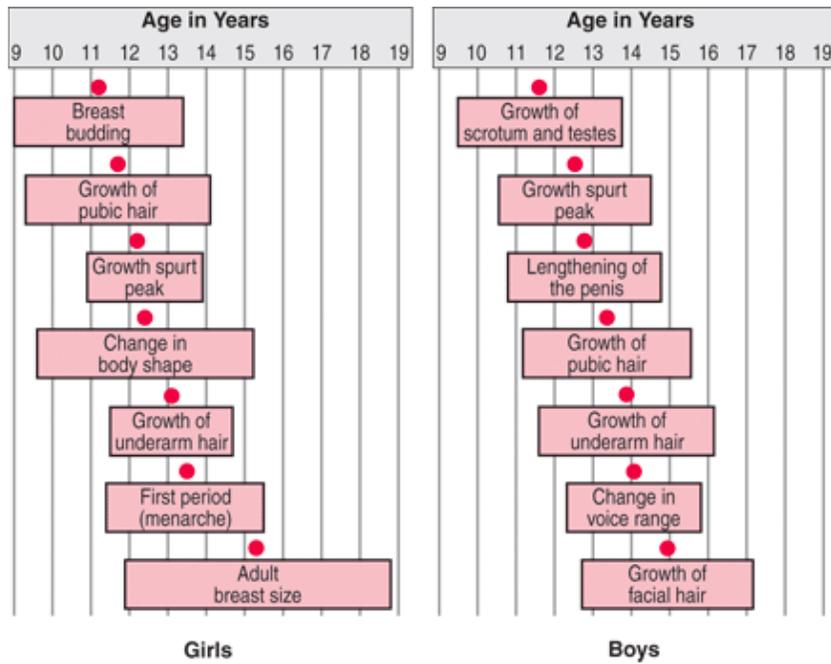
HOW DEVELOPMENT CAN GO OFF TRACK?



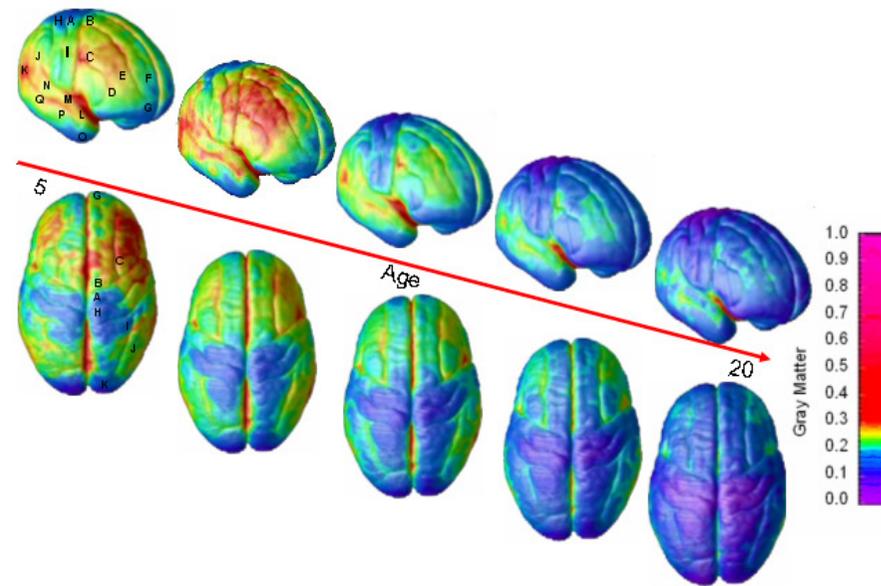
Illes J, Raffin TA. No child left without a brain scan? Toward a pediatric neuroethics. *Cerebrum*. 2005 Summer;7(3):33-46

# PEDIATRIC

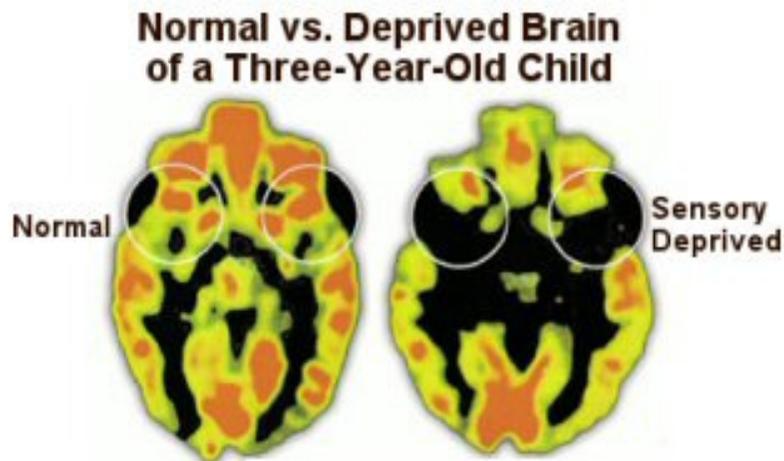
## EXTERNAL VIEW



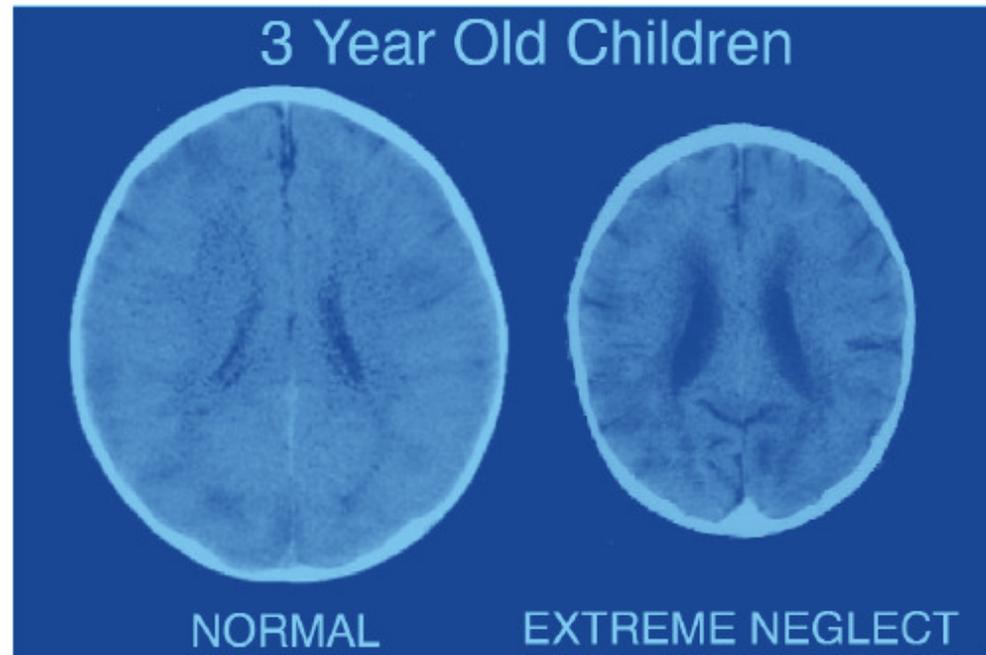
## INTERNAL VIEW



## PEDIATRIC



Source: Newsweek, Spring/Summer 1997 Special Edition:  
"Your Child: From Birth to Three", pp. 20-31



*These images illustrate the negative impact of neglect on the developing brain. The CT scan on the left is from a healthy three-year-old with an average head size. The image on the right is from a three year old child suffering from severe sensory-deprivation neglect. This child's brain is significantly smaller and has abnormal development of cortex.*

# NEUROENHANCEMENT

2004

Chatterjee A. Cosmetic neurology

2007

Hall W. “Feeling ‘better than well’”

2008

Volkow N. The action of enhancers can lead to addiction.

## NEUROENHANCEMENT

“Neurologists and other clinicians are likely to encounter **patient-consumers** who view physicians as gatekeepers in their **own pursuit of happiness.**”



## NEUROENHANCEMENT

Among high-school students, abuse of prescription medications is second only to cannabis use.

**As we increase our knowledge of how the brain works, we may one day have safe interventions to improve cognition. In the meantime, we need to learn from history and avoid using them unnecessarily**

**Nora Volkow, 2008**

# SURGERY TREATMENTS

Gao G, 2003; Medvedev 2003



Wang TY. 1997; Li B. 2000



## SURGERY TREATMENTS

### 1997 & 2000 GAMMA KNIFE?

### 2003 STEREOTACTIS

28 heroine dependence  
Blocking mesocorticolimbic  
circuit

15 month follow up  
11 no relapse

**Gao G, 2003**

348 heroine dependence  
Blocking mesocorticolimbic  
circuit

187 subjects follow up  
with 45% abstinence

Rarely complication

**Medvedev, 2003**

### 2007 “MISTAKE”

1. anxiety disorder and secondary depressive disorder
2. bilateral deep brain stimulation (DBS) of the nucleus accumbens was carried out.
3. Despite the absence of desired improvement in his primary disorder, we observed a **remarkable although not primarily intended alleviation of the patient's comorbid alcohol dependency.**

## SURGERY TREATMENTS

### LIMITATIONS

The choice of opiate addiction.  
Certified/referred agonist/antagonist treatment  
When does it fail?  
Condition of informed consent?  
Local Laws?

### BENEFITS

The studies have been published in English language.  
Local Governments interrupted experimentation  
Severe criticisms have been done by Hall W.

# SUMMARY

**If I can, I do it**

“non-clinical use in healthy individuals”

I use fMRI to check my son/daughter off track...

I use cognitive enhancers to have better performance...

**NO MORE YES NO**

**Are enhancers safe?**

**When enhancers are necessary?**

**NEUROETHICS CRITERIA**

## SUMMARY

# A NEW COMPLEXITY

### THE FAST RABBIT

technology grows up

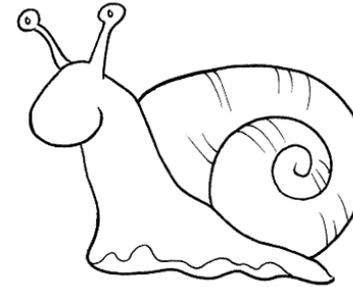


If I can, I just do it

“non-clinical use in healthy individuals”

### THE SLOW SNAIL

the power of good questions  
the power of the minority?



“efficacy  
security  
ethic”

neuroeducators training

## WHICH NEW FRAMEWORK?

## WHICH NEW GOALS?

It's not possible to see it, it has been destroyed in the 2<sup>nd</sup> World War in Berlin



Refused by committer because too much human

1. [Cruickshank WM](#). A new perspective in teacher education: the neuroeducator. [J Learn Disabil](#). 1981 Jun-Jul;14(6):337-41, 36
2. Steven E. Hyman, The Neurobiology of Addiction: Implications for voluntary Control of Behavior. *The American Journal of Bioethics*, 7(1): 8–11, 2007
3. Roskies, A. 2002. Neuroethics for the new millennium. *Neuron* 5(1):21–23.
4. Richard J. Bonnie, Responsibility for Addiction. *J Am Acad Psychiatry Law* 30:405–13, 2002
5. Chugani HT, Behen ME, Muzik O, Juhász C, Nagy F, Chugani DC. Local brain functional activity following early deprivation: a study of postinstitutionalized Romanian orphans. *Neuroimage*. 2001 Dec;14(6):1290-301
6. Eluvathingal TJ, Chugani HT, Behen ME, Juhász C, Muzik O, Maqbool M, Chugani DC, Makki M. Abnormal brain connectivity in children after early severe socioemotional deprivation: a diffusion tensor imaging study. *Pediatrics*. 2006 Jun;117(6):2093-100
7. Stereotactic neurosurgical treatment of addiction: minimizing the chances of another 'great and desperate cure'. *Addiction*. 2006 Jan;101(1):1-3.
8. [Gao G, Wang X, He S, Li W, Wang Q, Liang Q, Zhao Y, Hou F, Chen L, Li A](#). Clinical study for alleviating opiate drug psychological dependence by a method of ablating the nucleus accumbens with stereotactic surgery. *Stereotact Funct Neurosurg*. 2003;81(1-4):96-104.
9. [Kuhn J, Lenartz D, Huff W, Lee S, Koulousakis A, Klosterkoetter J, Sturm V](#). Remission of alcohol dependency following deep brain stimulation of the nucleus accumbens: valuable therapeutic implications? *J Neurol Neurosurg Psychiatry*. 2007 Oct;78(10):1152-3.
10. Tovino SA. Currents in contemporary ethics. The confidentiality and privacy implications of functional magnetic resonance imaging. *J Law Med Ethics*. 2005 Winter;33(4):844-50
11. Glannon, W. 2007. *Bioethics and the brain*. Oxford, UK: Oxford University Press
12. Chugani H. What can we learn from functional neuroimaging in children? *Indian Pediatr*. 2006 Mar;43(3):203-6
13. Millum J, Emanuel EJ. The Ethics of International Research with Abandoned Children. *Science*. 2007 Dec 21;318(5858):1874-5.



# **NEUROSCIENCE & MEDIA**

# **TRATTAMENTI FARMACOLOGICI**

# TRATTAMENTI FARMACOLOGICI

Fan, L.-S.; Huang, W.-S.; Cheng, C.-L.; Chu, P.-J.; Hao, H.-C.; Hsieh, C.Y.; Hsu, S.H.; Chin, A.; Hsueh, K.; Lee, C.-C.; Chang, J.; Liu, E.; Huang, A.; Chien, C.; Yeh, A.; Chen, J.-H.; Wu, W.; Lai, C. Magnetic resonance microsystems for life science applications Solid-State Sensors, Actuators and Microsystems, 2005. Digest of Technical Papers. TRANSDUCERS apos;05. The 13th International Conference on Volume 2, Issue , 5-9 June 2005 Page(s): 1998 - 2001 Vol. 2