

Considering research on neuro- enhancement in the next revision of the Declaration of Helsinki

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Overview

- Trend: Neuro-enhancement
 - What is it?
 - Prevalence
 - Ethical discussion
 - Effectiveness and safety
- Relevance for the Declaration of Helsinki
 - General concern
 - Challenge to weigh risks and benefits
- Discussion

Neuro-enhancement

Improvement of cognitive or emotional capacities in *healthy* people *without therapeutic or preventive intention* with pharmacological or neurotechnological means

Neuro-enhancement

What and how?

Goals:

physical capacities

cognitive capacities

affective functions

social and moral capacities

longevity and symptoms of aging

spiritual capacities

Means:

deep brain stimulation

ultrasound

neuro-protheses

magnetic stimulation

Brain-machine Interfaces

psychopharmacology

Just a small selection

To offer:

- Vinpocetine - a cerebral enhancer;
- Get Smart™- brain formula: Increase your IQ
- Idebenone - the ultimate anti-aging drug?
- SAME - the nutrient for mood, liver, heart, joint and brain protection
- Piracetam - the original nootropic
- NADH - the supervitamin body and mind energizer
- Growth Hormone - the real "fountain of youth!"
- 5-HTP - Prozac's true alternative
- The energy program at a glance - tired of being tired?
- Life Extension Mix - just 14 capsules a day!
- Centrophenoxyne - the anti-aging brain
- Galantamines - opens your memory, rescues brain cells: old becomes young
- Pregnenolone - reducing stress and increasing productivity

- Prescription not required ... (<http://smart-drugs.com>)

Prevalence

- Little accurate data available
 - Up to 25% of American students use psychostimulants (range 3-25% in colleges) (McCabe et al. 2004, 2005)
 - 46% increase in ADHD prescriptions from 2002-2010 (Chai et al. 2012)
 - Estimates:
 - 5% of the working population in Germany use pharmaceutical drugs to enhance their cognitive functions
 - 2% of surveyed German students use drugs to compensate for stress and increase performance (Franke et al. 2011)
- Non-therapeutic use and prescription of drugs happens mainly off-label
- Availability of these prescription medications rises -> rates of medication diversion and misuse rise as well
- Note: Assuming and communicating high prevalence numbers might lead to a **self-fulfilling prophecy**

Ethical debate

- Neuro-enhancement is growing trend that is vividly debated regarding ethical and social questions
 - Justice & fairness
 - Coercion & pressure for conformity
 - Open and subtle pressures in working and personal life
 - Value of the normal
 - Personality changes
 - Naturalness
 - Authenticity
- Rarely considered:
 - Effectiveness, safety, side-effects...

Effectiveness

- Expectations regarding the effectiveness exceed actual effects
- Stimulants (methylphenidate; modafinil)
 - Mainly effects on memory, some effects on executive functions in sleep deprived subjects (Repantis et al. 2010)
- Antidepressants (mainly SSRIs)
 - Uncertainty regarding size and robustness of effects
 - Dependence on dosage, individual differences, specifics of the task
- The claimed and assumed benefits are often exaggerated

Side-effects

- US FDA warning on the packets of methylphenidate:
 - *"amphetamines have a high potential for abuse. Administration of amphetamines for prolonged periods of time may lead to drug dependence ...Misuse of amphetamine may cause sudden death and serious cardiovascular adverse effects."*
- **Risk of addiction**
 - Highly selective, direct effects on dopamine release (e.g. by psychostimulants methylphenidate and modafinil)
 - Habitized drug intake (counter-regulatory neuroadaptive processes are induced and strengthened)
- „The immediate and long-term risks to individuals seeking cognitive enhancement remain unknown.“ (Smith and Farah 2011)

Empirical studies are needed – **if wanted**

- Public interest contrasts with paucity of data on specific enhancement effects of available agents
- Decision of healthy individuals on the usage of enhancement should be based on exhaustive information provided by scientifically valid studies
- Investigating enhancement usage
 - Dosages, length of intake, and risks might differ
 - Definition of efficacy of enhancement intervention must be clarified
 - Large longitudinal studies
 - Large samples
 - Comparative designs

Why considering this?

- Challenge to the purpose and scope of biomedical research and medical practice
- §7 of the current DoH version:
 - *„The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best current interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.“*
- Reconsider the basic assumptions of justifying medical research

Risk-benefit balancing anew

- *“In medical practice and in medical research, most interventions involve risks and burdens.” (§8)*
- *“Medical research involving human subjects may only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects.” (§ 21)*
 - *What are acceptable risks?*
 - *When is it justified to expose human beings to potential harm?*
- Risk-benefit balance for research on enhancement
 - Which ratio would be acceptable?
 - How to weigh societal benefits against individual risks?
 - Potentially unfavorable ratio given side-effects BUT high demand given social trend
 - Research on enhancement in the healthy not as essential as research on disease
 - Consider prioritization of healthcare; responsible use of finite resources
 - Legitimacy of this research needs scrutiny and “regulation”

Vulnerable populations

- Children and adolescents show particularly high increase in usage and acceptance
- Studies on enhancement are lacking
- Off-label use, diversion, and social pressure raise
- Specific regulations for enhancement in pediatric populations necessary (e.g. for practitioners; Graf et al. in progress)

Conclusion

- Enhancement is prevalent despite paucity of data on effectiveness and safety
- Empirical studies on enhancement are not covered by current version of Declaration of Helsinki
- Deliberation of general stance and adequate risk-benefit balancing is needed in the context of regulating biomedical research
 - Decisions will strongly influence ethical debate
- Suggestion: No ban, but cautious positioning

Thank you for your attention!

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