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The promise and predicament of cosmetic neurology

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The promise and predicament of cosmetic neurology

Abstract
Advances in cognitive neuroscience make cosmetic neurology in some form inevitable and will give rise to extremely difficult ethical issues.

Keywords
cognitive neuroscience; neuropharmacology; brain disorders; cosmetic neurology

Comments
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NEUROETHICS

Cosmetic neurology

The promise and predicament of cosmetic neurology

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Consider the following hypothetical case study. A well heeled executive walks into my cognitive neurology clinic because he is concerned that he is becoming forgetful. It turns out that he is going through a difficult divorce and my clinical impression is that his memory problems stem from the stress he is experiencing. I place him on a selective seratonin reuptake inhibitor, sertraline, and in a few weeks he feels better. Around this time his 13 year old daughter has difficulty at school and is diagnosed by the school psychologist as having attention deficit disorder. I place her on adderall, a stimulant combination drug, which seems to help with her behaviour in school. My patient then comes to me because he is experiencing the "tip of the tongue" phenomena more frequently. He is concerned that his word finding difficulty interferes with his ability to function in high level meetings. I suggest we try a cholinesterase inhibitor to see if this helps. I am careful to explain that the Food and Drug Administration does not approve such a use for this medication. He wants to try it and is pleased with the results.

A few months later, this patient visits me with his 16 year old son, a talented middle distance runner. His father thinks if he were just a bit better, among the elite high school runners in the state, he would be far more competitive as an applicant for selective colleges. We discuss various options. Because of a recent report that sildenafil, which is used conventionally for male impotence, may improve oxygen carrying capacity, I prescribe this medication. The son does not object.

Encouraged by these pharmacologic successes, my patient approaches me with an interesting problem. He is planning a trip to Saudi Arabia in a couple of months to bid for a lucrative contract. He thinks that learning Arabic would give him a decided edge over his competitors and is enrolling in an intensive crash course to learn the language. He wants to know if I can help. Because of data suggesting that amphetamines promote neural plasticity and improve recovery in aphasic patients, I advise him to take a small dose of dextro-amphetamine half an hour before each of his classes.

When he is ready to fly to Saudi Arabia I give him my recently patented "travel pack"—a hypnotic, zolpidem, to be taken when he gets on the plane and a stimulant, modafanil, to be taken when he gets off the plane. He goes to Saudi Arabia, impresses the royal family with his Arabic, and wins the contract. Triumphant, he makes a large donation to my research programme. And we all live happily ever after.

Or do we? If such a scenario is plausible, is it desirable or is it dystopic? In what follows, I review what is plausible in the practice of pharmacological enhancements and the kinds of ethical issues that would surface from such a practice. While the hypothetical case described may seem extreme now, it might not in the future.

THE PROMISE

What can be done in cosmetic neurology and what is likely to be possible in the near future? This topic has received some attention in the lay press[1–6] and in the scientific literature,[7,8,9,10] but relatively little in clinical circles.[11] The possibilities for enhancement fall into three broad categories: motor abilities, cognition, and affective systems.

The targets for enhancement of motor abilities encompass cardiovascular, peripheral motor, and central nervous systems. For cardiovascular systems, human erythropoietin is used to increase oxygen carrying capacities for better endurance.[12] New transfusion methods are likely to be used in this way, and, as mentioned already, sildenafil may have similar effects.[13] To enhance motor systems, athletes use anabolic steroids commonly, an issue that has preoccupied even those at the highest level of American politics.[14] Insulin like growth factor may increase muscle mass and prevent muscular decline associated with ageing.[15,16] Musicians frequently use beta blockers to dampen physiological tremors in order to improve their performances.[17] Finally, targeting the central nervous system, dopamine agonists may improve the acquisition of motor skills. Such agonists are associated with greater neural plasticity, and the use of dextro-amphetamine, when paired with physical therapy, appears to hasten motor learning following stroke.[18,19]

Intense research efforts in the last few decades are yielding novel treatments for cognitive disorders such as Alzheimer's disease and attention deficit disorder. These medications are also likely to modulate attention, memory, and learning in healthy individuals. Cholinesterase inhibitors may improve normal performance under some circumstances.[20] Modafinil can be used to improve vigilance and reduce impulsive responding,[21] especially in sleep deprived states, and it is being studied extensively by the armed services.[22] New non-addictive stimulant medications, such as atomoxetine, are also likely to improve levels of arousal in normal subjects. Based on the belief that these drugs improve test performance, the use of stimulant medications among college students in the US is widespread.[23] Interestingly, the effects of these medications may be influenced by genetic endowments such as which catechol O-methyltransferase alleles are inherited.[24] This observation raises the possibility that enhancement cocktails might eventually be tailored to individual genetic profiles.

Particularly intriguing are the development of new classes of drugs, such as ampakines and cyclic AMP response element binding protein (CREB) modulators. They are striking, because they are not being developed with a disease in mind. These medications promote the intracellular cascade of events leading up to the structural neural changes associated with the acquisition of long term memories.[25–28] Most of the drugs discussed in this paper are developed to treat disorders. As an afterthought, they may also enhance normal abilities. By contrast, ampakines and CREB modulators are developed to augment normal encoding mechanisms. They might then also apply to disease states.

Finally, we continue to refine ways to modify affective systems. Such developments are desirable given that some estimate that up to one in five Americans are depressed,[29] and recent surveys suggest that close to half of adult Americans suffer from affective and substance abuse illnesses.[30] Given that affective illnesses often lie on continua, more people than those who meet checklist criteria might actually benefit from these medications. Beta blockers, sometimes used for anxiety, appear to help with post-traumatic symptoms in individuals who come to emergency departments after car crashes.[31] Serotonin reuptake inhibitors are used widely and seem to promote affiliative behaviour in healthy states.[32,33] Around the corner are a host of potentially new ways of controlling affective states with the modulation of neuropeptides[34] such as substance P, vasopressin, galanin, and neuropeptide Y. Corticotropin release factor (CRF) seems to mediate the long term effects of stress,[35,36] and blocking CRF may blunt these effects.[37] The subtlety with which affective states might be modulated in the future is hard to predict. However, heralding the way in which emotional states might be "fine tuned", a recent study found that inhaling oxytocin promotes feelings of trust, and that these feelings affect behaviour.[38]

The general point that I would like to highlight is the following. The armamentarium of drugs that could be used to enhance healthy individuals is growing. We can expect that this growth will continue for the indefinite future. Medications for impotence, hair loss, and obesity are sometimes referred to as "lifestyle" drugs.[39] The medications under consideration here seem to have more pervasive effects—where the altering of substance rather than style is what is at issue. We can expect that drugs will be targeted for specific effects and that they will be targeted for specific genetic profiles.

THE PREDICAMENT

Four reasons might give pause to the practice of cosmetic neurology. These concerns have to do with safety, character, justice, and autonomy.

Safety concerns are familiar. Most medications can have unpleasant side effects. Are the risks of these effects worth the expected benefits? The use of drugs in various combinations could complicate the safety concern in unpredictable ways. Physiological and psychological addictions might occur. Since most clinical trials are designed to test safety over relatively short periods, potential long term toxicities are not known when drugs are introduced into the market. In disease states, one weighs the potential benefits versus the potential risks in making decisions. Thus, one might tolerate significant risk

when the alternative is a relentlessly progressive disease like Jacob Creutzfeldt disease. Are any risks tolerable when the alternative is normality?

In my view, safety is more of a pragmatic than an ethical concern. The nature of drug development is that some problematic effects will occur that could not be predicted. However, all the parties involved—patient/consumers, physicians, and pharmaceutical companies—are interested in having drugs that are safe. Since there are no inherent conflicts of interest, and as long as information about side effects is not suppressed, the ethical issues do not cut deeply.

The character concern has to do with undermining our sense of identity and what gives meaning to our lives.[40] The concern is often placed in a "no pain, no gain" framework. Struggling in some situations and experiencing distress and failure are quintessential aspects of human experience. Enhancing cognition is somehow cheating. Side stepping distress is somehow cheapening. These experiences give rise to desirable personal attributes. Recent studies find that observing someone in pain activates the same neural circuits that are involved when one experiences pain.[41,42] One infers from such studies that some painful experiences are probably necessary in developing empathy.

The character concern is hard to dispense with. While this remains a deep concern, it is hard to see how this concern would precipitate into public policy or even into consistent social norms. Who decides which pains should be suffered to build character and which can be reasonably avoided? The meaning given to pain that women might experience in childbirth has varied in different settings, from atonement for original sin to promotion of mother infant bonds.[43] Pain and suffering more generally can take on spiritual significance.[44] Yet many would not accept mandates that prohibit the amelioration of specific pains. In cultures with strong libertarian tendencies it is hard to see how individuals will not insist on making decisions about what to do with their own bodies and brains, for better and for worse.

The justice concern is about equitable distribution of resources. Medications used for enhancements are unlikely to be paid for by insurance companies or by socialised healthcare systems. That means the wealthy will avail themselves of designer drugs, whereas the poor will be confined to coffee, booze, and cigarettes. On the assumption that the enhancement drugs work to improve abilities, unequal access to them will widen disparities at the ends of the economic spectrum.

Concerns about distributive justice are also difficult to dispense with. Again, it is hard to see how these concerns will prevent the use of pharmacological enhancements. In the US, wide disparities in access to and quality of health care and education are tolerated. Pharmacological enhancement may not be so different from these other "life enhancers".

The autonomy concern is directed at the possibility that what starts out as a matter of choice ends up as a coercive force. These coercive forces may be explicit or implicit. Explicit coercion might be seen with classes of individuals who might be expected to take certain medications for the greater good. Such precedents exist in the military,[45] and they

may seep into other specialised professions. One study found that commercial pilots taking a cholinesterase inhibitor performed better in emergency situations on simulation experiments than did pilots taking placebos.[20] If these results were robust and reliable could pilots be encouraged through financial incentives to take these? Could they be required to take such medications? Could individuals with medical contra-indications to these medications be banned from the profession?

The implicit coercive pressures are more complicated, and, in some sectors of society, they are likely to be quite forceful. In winner take all environments, slight incremental advantages have disproportionate consequences.[46] This point is made most clearly in sports. Thus, the difference between being first or fourth in the 100 meters at the Olympics is huge, even though objectively both athletes are indistinguishable when compared to the population at large. Similar pressures apply to athletes in other professional sports, such as baseball or football. The pressure to take advantage of slight improvements is sufficient to have athletes risk significant side effects of medications as well as public sanctions for their behaviour. Also, many athletes are willing to engage in pharmacological enhancements in an environment in which "fairness" is explicitly valued. Many business and professional environments are set up to make the most of competition. It is not unusual for professionals to work 80 or 90 hours a week, while their children enrol in several sports programmes and after school music programmes to ensure they can make competitive applications to colleges. The pressures for such children to take stimulant drugs to help with academic performance are already evident. The worry is that we may encounter the "Red Queen" principle.[47i]

When Alice in Wonderland finally catches up with the Red Queen she finds that they are both running hard, but not moving forward. The Red Queen points out to Alice that sometimes one needs to run as fast as possible, just to stay in place. In some sectors of our society one might need to make use of every possible advantage including enhancements, just to stay in place.

In my view, the practice of cosmetic neurology is inevitable. This claim is predictive, not prescriptive.[48] While the ethical concerns are real and run deep, the countervailing social pressures seem overwhelming. Pharmaceutical companies have significant economic incentives to expand their markets to healthy individuals. Since 1997, the Food and Drug Administration has allowed direct advertising to consumers. Television advertisements now give permission to indulge in a pepperoni pizza without the fear of heartburn because one could take an H2 blocker prophylactically. One would be surprised if similar advertisements did not recommend getting an edge with cognitive enhancers or a boost with mood manipulators.

While the coming of cosmetic neurology is in my view inevitable, the specific shape it will take may vary in different locations—for example, winner take all pressures vary in different cultures and within different sectors of society. The ways that these promises and predicaments will settle into practice is likely to be reflective of cultural norms. Education is an example of an enhancer that is potentially available to everybody and has a huge impact on social wellbeing. Perhaps current disparities in availability and quality

of education in different countries may predict future norms of access to pharmacological enhancements.

A (HYPOTHETICAL) CLINICAL SCENARIO

My clinical practice of neurology has changed. Having struggled through a classic winner take all environment, the world of National Institutes of Health (NIH) research funding, I have given up my career as a physician/scientist. In the last few years, NIH funding rates dropped by half of what they were in an already extremely competitive environment. Grant awards are based on increasingly slight and probably unreliable differences in judgments about the merits of an application. These small differences have disproportionate impacts on peoples' careers. Encouraged by my original patient, I open a cosmetic neurology clinic on elegant Rittenhouse Square in Philadelphia. My patient, who has invested in this clinic, is a great advocate. Largely fuelled by word of mouth, I soon have a busy and lucrative practice. The patients are wealthy and for the most part grateful. They sign all the necessary waivers, understand that no specific effects are guaranteed, and the medications are being used in ways not specifically approved by the Food and Drug Administration. I no longer bother with bureaucratic burdens imposed by insurance companies. Things go so well, that we open another clinic on Madison Avenue in New York. This clinic is also enormously successful. We are now negotiating to open a clinic in London, with a further eye to Paris and Milan. I am invited frequently to give talks at corporations. Motivational speakers routinely include a discussion of pharmacological enhancements in their exhortations. A few other brain spas are opening, but this simply increases the demand for services at my clinics. I work harder to keep ahead.

CONCLUSION

My intentions in this paper are threefold. Firstly, I have tried to make the case that advances in cognitive neuroscience and neuropharmacology make cosmetic neurology plausible and in some form inevitable. The issue is not isolated to doping athletes or pharmacologically insomniac students. These examples are simply the nose of a camel that is well on its way into the tent.

Secondly, I have tried to emphasise that the ethical issues that arise, particularly those centred on character, coercion, and justice are extremely difficult. My own views on these issues are not settled. I think it makes little sense to have a singular opinion about the prospect of cosmetic neurology. Each possibility would need to be considered on its own merits. Particularly tricky are situations in which individuals' desires to engage or not to engage in enhancements are at odds with societal desires.

Thirdly, I expect that the practice of cosmetic neurology will challenge conventional notions of the role of physicians. In the last century plastic surgery struggled with its identity as demand for services shifted from reconstructive to cosmetic procedures.[49] In the coming century, clinical neurosciences are likely to struggle similarly. The challenge for physicians will be sorting out their relationships with individuals as patients and consumers, especially when fiduciary and commercial interests collide.

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FOOTNOTES

[i] Evolutionary biologists use the Red Queen principle to describe pressures for survival among co-evolving species.

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