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Editorial

The shape of things to come

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Is it progress if a cannibal eats with a fork?
—Stanislas J. Lac

In the current issue of *Neurology*, Anjan Chatterjee[1] makes a compelling argument that neurologists need to enter the debate about the proper uses of the fruits of the biomedical revolution. In so doing, he has performed an important service to the neurological community. Chatterjee reminds us that advances in neuroscience carry with them the likelihood, intended or otherwise, of medical applications that go well beyond the traditional goals to prevent, diagnose, and treat disease.

Chatterjee focuses our attention on biomedical advances that are likely to provide new ways to modify behavior, improve performance, extend lifespan, and generally give the user a competitive edge over his or her fellow humans.[2-5] It addition to the traditional concept of relieving suffering, these advances will also improve the perceived quality of life, a concept that will have different interpretations depending on one's point of view. One of my colleagues has noted, somewhat sarcastically, that in a free market economy the proximate goals of genetic engineering are as likely to focus on correcting male pattern baldness and increasing height as on curing disease. Individuals will go considerable distances to seek advantages, even trivial ones, both for themselves and their children. In the words of Bill McKibbon,[2] "people will do far-out things for less than pressing purposes." The rampant use of cosmetic surgery, use of growth hormone for children within the range of normal height for age, and the apparently widespread use of performance-enhancing drugs by professional (and in some circles amateur) athletes, are but a few examples of this behavior.

Several authors have commented on the slippery slope encountered along the path from treating diseases to eliminating predispositions to actively enhancing functions. Depending upon one's interpretation of our role as physicians and the goals of medical science, one could conceivably endorse all of these missions as appropriate. In the eloquent original charge by Congress to the newly formed NIH in 1952,[6] the purpose of biomedical research was defined as follows:

> To help provide the practicing physicians of this nation—and of the world—with better means for ameliorating physical suffering and emotional imbalance, for prolonging human life, and for making all the years of that span more useful both to the individual and to society.

This is a broad charge indeed that might be reasonably applied by proponents to support the widespread use of Prozac for malaise, Ritalin for rambunctious boys, performance-enhancing drugs for athletes, and also stem cell therapy for tissue replacement. Many of these interventions have strong arguments both for and against, arguments that will undoubtedly change over time, with shifting political winds, and with improved technologies. How does one define physical suffering? Does unhappiness due to lack of athletic prowess, unattractive features, or low-normal intelligence satisfy the criterion of "emotional imbalance" as defined by Congress? Should limits be placed on the goal of "prolonging human life" (assuming, of course, that we can even agree on the definition of human life)?

Emerging medical technologies. It is evident that a major expansion will soon occur in the repertoire of selective biologic manipulations available to physicians and that many of these new therapies will involve enhancements that fall within the purview of neurology. The changes that we can expect to happen over the short, medium, and long term are likely to be substantial, and it is as preposterous to think that these can be predicted accurately as it is to imagine that the knowledge base required to practice neurology today will be adequate 10 or 20 years from now. These uncertainties notwithstanding, it is likely that six major areas of science will profoundly impact neurology in the next generation.

1. Cosmetic pharmacology. The increasing use of designer drugs to improve such attributes as mood, focus, energy, as well as perhaps memory and motor performance is to be expected, fueled by the identification of "druggable targets" through human genetic

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studies. As with such currently available drugs as Prozac and Ritalin, behavior-altering drugs are likely to be approved for rather narrow medical indications. Who would reasonably deny use of a motor performance enhancement drug for stroke patients, or a memory enhancer for Alzheimer disease? However, there will certainly be considerable pressure to employ such drugs for additional, off-label, indications. Should we permit use of a safe memory enhancement drug for physicians who need to keep current with new developments in the field? What about a single-use indication for our kids as they cram for SAT exams? If yes, should our neighbors' kids have the same opportunity?

2. Human cloning. The capacity to clone whole organisms is obviously already with us, and the technical problems associated with current cloning methods—e.g., cloned animals tend to be unhealthy and less fit than their naturally born species mates—can undoubtedly be overcome in the near future. Although the widely publicized reports in 1999 that the Raelian cult had successfully cloned a baby named Eve (based upon a protocol obtained through UFO encounters) turned out to be a hoax, it is likely that successful human cloning will be carried out somewhere, notwithstanding proscriptive laws against such activity enacted by most nations.

3. Stem cell research. This technology promises the possibility of prolonging life and improving its quality through cell and tissue replacement (e.g., nigrostriatal neurons for Parkinson disease, oligodendrocytes for multiple sclerosis, etc.). Stem cell–based therapies will undoubtedly find their way into neurologic practice, perhaps not via cell-based therapies but with traditional drugs that stimulate differentiation of adult stem cells in the body.

4. Preimplantation genetic selection. With the availability of high throughput genetic sequencing and improved informatics, this technology will increasingly permit parents to select inherited attributes of their offspring without the need to do any genetic engineering whatsoever. As noted above, distinctions between disease, predispositions, and enhancements will differ among reasonable individuals. If one could predict that an embryo has a 30% chance of developing multiple sclerosis, is termination ethical? Even more difficult, what about embryos in which the inherited component of intelligence falls at the low end of the parents' gene pool?

5. Genetic engineering. Here the genetic material is directly manipulated in an embryo or adult, either through the direct modification of selected genes or by insertion of a gene or genes that will improve some desired attribute. If the inserted genes are not incorporated into chromosomes and thus are not transmitted to offspring, do arguments against genetic engineering weaken? Are there ethical differences between delivery of gene therapy to correct muscular dystrophy due to dystrophin deficiency or to correct an inherited disadvantage in athletic prowess due to myostatin overexpression?[7]

6. Artificial interfaces and nanotechnology. Although a major impact of this technology appears to be further away than the above approaches, its presence is already beginning to be felt in neurology. Cochlear implants are the sentinel example of mechanical interfaces providing sensory input to the human nervous system. Neural stimulators—for movement disorders and epilepsy—are other examples of technologies currently in (increasing) use. Some worry that these successes represent the beginnings of Cyborgs—individuals who are part human and part machine. For more than 50 years science fiction writers have imagined the potential of such human–robotic chimeras. Nanotechnology promises the potential of designing micromachines capable of dramatically advancing the potential of such interfaces.[2-4]

The unique role of neurologists, core competencies, and training. Neurologists, as principal physicians of the human nervous system, must assume a role in shaping the debate about what it means to be fully human, healthy and normal, and about how society might define the boundary between interventions used to promote or restore optimal health and those used for enhancement. Neurologists led the discussion of brain death in the last generation, and similarly we must now lead the discussion about how to define conscious life and how to arbitrate the very difficult questions of quality vs quantity of life.

The neurologist of the future will be competent only if fluent in the language of science. Compassionate care is a given, but it is merely the vehicle through which competence is expressed. The next 20 years is likely to witness changes in neurologic practice and new technologies that we cannot now imagine, and yet by many measures our profession (medicine in general and neurology in particular) appears to be poorly prepared.[8] By some estimates, the number of physician–scientists on faculty in American medical schools has declined by 25% in the past generation, and the proportion of medical students who express a deep interest in science has also declined. Medicine remains a highly attractive career option for young people, and it has been argued that the decline in a passion for science exhibited by medical students may be due to a conscious (or unconscious) attempt by admissions committees to seek out applicants who are "well-rounded" or show evidence of humanistic values rather than a passion for science. As Faith Fitzgerald has argued, the best medical students appear to be defined not by their undergraduate areas of concentration but whether as people they are inherently curious and pursue their passions—whatever they may be—in depth.[9]

To meet the challenges and opportunities ahead, neurology should:

1. Redesign our training programs to ensure that they are models for the incorporation of neuroscience into clinical medicine.
2. Emphasize the role of neurologists as teachers in all practice settings; our small numbers (approximately one-half of 1% of American physicians) requires that most neurologic care will be delivered by generalists, not neurologists. All medical students also need to receive adequate training in neurology, including a mandatory clerkship of at least 4 weeks.
3. Recognize that the margins between academia, industry, and practice are likely to blur further in the next generation. This reality is recognized by the federal government and is a component of the roadmap initiative elucidated by NIH Director Elias Zerhouni.[10] We should work through our national organizations to create multidisciplinary consortia of neurologists in different practice and research settings, as has been done in oncology.
4. Include psychiatric disorders—especially the highly prevalent psychoses, affective, somatiform, and addiction disorders—as a key component of our larger mission as neurologists. It is critically important that the disciplines of neurology, psychiatry, and neuroscience ally themselves in new and meaningful ways.[11]
5. Avoid conflicts of interest, both personally and in our national organizations. It has been estimated that 90% of medical experts have financial ties to the pharmaceutical industry. I am not suggesting that such ties should be avoided absolutely; in many cases they serve the interests of all. However, we must give the public no opportunity to question our independence. We must be absolutely honest brokers if we hope to be major players in the coming debates on the appropriate uses of bioscience.

Finally, we should convey a message of profound optimism to the young people who plan to enter our profession or are just beginning their careers:

You could not have chosen a profession that, during the course of your careers, will be more important to humanity, nor one that is more fundamentally ethical. In the future, neurology will grow dramatically in importance if you live up to your responsibility and enter the debates on the life-altering technological advances, and threats, that will appear. One could not imagine a better time to begin your lives as neurologists.

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