Editorial

The Curiously Misunderstood Role of Evidence in Designing New Technology

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“Flying safely has not developed using experimental and control groups of air passengers and counting victims.”

—Ülo Kristjuhan

RECENTLY, I TOOK PART in a radio interview together with the demographer Jay Olshansky. Jay and I have been friends for over a decade, and we have done this before: indeed, he and I have for most of that period been among the most frequently appearing academic gerontologists in mainstream media. The interview was trailed as being about the desirability of combating aging,1–3 a topic on which Jay and I wholeheartedly agree. In practice, however, the interviewers chose to focus heavily on the feasibility of doing so. On this point, Jay and I are sharply at loggerheads. While he believes that there may be some modest progress in slowing “the basic process of aging” in the coming few decades, he is adamant that there is no chance of success in using regenerative medicine to comprehensively reverse aging. I take the opposite view on both counts: I consider that appreciably slowing the accumulation of molecular and cellular damage that underlies aging is an extremely daunting challenge, since that damage is created as intrinsic side effects of metabolism, whereas repairing pre-existing damage is far more realistic.

So far, so tedious. Scientists often disagree about the interpretation of data, and in this particular case the views that Jay and I expressed were not even novel.4,5 But the situation becomes more worthy of analysis when one delves into the reasoning we used in justifying our predictions. Both of us appeal, in support of our conclusions, to the existence or absence of evidence. Specifically, Jay avers that there can be no evidence to support the efficacy of regenerative medicine against aging other than the successful extension of a mammal’s healthy life using such techniques, and he views my claims to the contrary (specifically, claims that we already have evidence that such an approach will probably work) as unscientific.

It is tempting to dismiss Jay’s views here on the basis that he is “only a demographer,” not versed in the evaluation of experimental data, but that would be wide of the mark: not only because it is ad hominem, but also because highly distinguished experimentalists share his view. For example, the respected gerontologist Robin Holliday published an article recently with the uncompromising title “The extreme arrogance of anti-aging medicine,” and in correspondence arising from it, he described the application of regenerative medicine to aging as pseudoscience, and made clear that he shared Jay’s view as to what data would count as evidence to the contrary.

So, what is the issue here? It is, in fact, very simple: it concerns the distinction between science and technology.

First let’s be clear about what that distinction is. In science, the objective is to discover the way the world works, whereas in technology, the objective is to exploit science to change how things work. Science is ultimately about predicting nature, while technology is about manipulating nature.

But science and technology have a great deal in common — or at least, that’s how it seems at first sight. In both, there is a process of alternation between action and interpretation: we try something, we observe the result, we consider what the result means for what might achieve further progress, we try that, and so on. Thus, one might suppose that people who are good at science would also be good at technology and vice versa. But they’re very often not, and in my view the main reason why they’re not resides in step three above, the interpretation of data.

The results of scientific experiments are very often open to multiple interpretations. An ideal experiment minimizes this problem: it is typically designed to have two possible outcomes, clearly distinguishable from each other, each of which falsifies (or at least challenges) some hypothesis that is consistent with the results of all previous experiments. But it is often remarkably difficult to attain this ideal in the real scientific world. One thing that makes it so hard is that cutting-edge experiments typically involve the use of sophisticated specialist equipment and techniques, such that the actual outcome can be explained in a manner consistent with either of the hypotheses between which one hoped to distinguish, based on errors in execution of the experiment. Another problem, arguably most acute in fields such as biology where the object of study is a hugely complex system, is that there are typically a plethora of hypotheses only marginally ranked by parsimony, such that a given result’s challenge to a given hypothesis tends to be quite weak.
What this leads to is a dictum, applicable across the whole of science, that the most direct evidence relating to a given hypothesis is the most reliable. Indirect evidence ostensibly challenging a hypothesis tends to be easy to reconcile with that hypothesis by use of only slight creativity and elaboration of the hypothesis. Direct evidence is a more reliable way to avoid doing experiments that in fact teach one nothing.

Contrast this with technology. In designing a new way to manipulate nature, one often has no direct evidence from which to start. What’s more, when one does have direct evidence, it’s very often not the most useful: on the contrary, it may lead one into a cul-de-sac. The most obvious example is the idea that one might achieve powered flight by emulating birds: it took quite a while for aspiring aviators to look beyond flying by flapping and think more laterally.\textsuperscript{6}

But does this mean that technologists do not rely on evidence? Certainly it does not. What it means is that technologists use evidence differently. They dissect their problem into sub-problems, each of which has already been solved (or for which there is direct evidence that a particular solution will work), and then they construct the overall solution and try it. Until that final moment, the evidence that the technologist has used is only part of the story—a vital part, but only a part. The dissection into sub-problems is no more nor less than a leap of faith, for whose validity the technologist has no prior direct evidence whatsoever. And yet, technology works.

Medicine—especially modern medicine, with all its complexity—is technology, and the defeat of aging is most assuredly the domain of medicine. In the case of medicine, the first use of a given therapy in humans typically follows extensive testing in non-human animal models, which indeed provides pretty direct evidence for efficacy and safety; but that doesn’t invalidate the generalization I outline herein about how technology is developed, because the leap of faith is simply taken at that earlier stage, the first test in an animal model.\textsuperscript{7} The first human test is then equivalent to the first jetliner.

You may wonder why I have expended so many words laying out such an obvious fact. It indeed seems astonishing that anyone would need it laid out. But, as the remarks of Olshansky, Holliday, and a depressingly large number of other respected basic scientists reveal, it is not obvious to everyone. These individuals know how to use evidence in their own work, and they refuse to contemplate that it might be appropriate to use evidence differently in a wholly different sphere of human endeavor. And unfortunately, they are misleading funding sources and thereby costing lives by such myopia, because they are honored with the title of “biogerontologist” and thus presumed, by opinion formers and the public alike, to be the only people who know what they are talking about when they pronounce on the question of intervening in aging.\textsuperscript{8–10}

What is needed is a cadre of respected biomedical gerontologists—experts who understand what we know and do not know about aging and who also understand how to rationally design interventions based on that partial knowledge. That cadre already exists if one omits the word “respected”: experts in all the biomedical fields relevant to regenerative medicine for aging are increasingly aware of the applicability of their technologies to mankind’s greatest medical problem—but unfortunately they are all too rarely called upon to offer their views, because their expertise generally does not span the whole of aging and they understandably do not advertise themselves as gerontologists. But this must change, and fast, if we are to develop “real anti-aging medicine” as quickly as technologically possible. Asking a biogerontologist how to combat aging is like asking a seismologist how to prevent earthquakes: it’s a question that they have most of the knowledge to address, and the means to obtain the knowledge they do not have, but they will nonetheless be unlikely to give useful answers, because it is not what they think about, and it is not the way they think. But at least the seismologist will generally have the good sense to admit this. Unfortunately, many of the world’s most vocal biogerontologists do not.

References

5. de Grey ADNJ. Curiosity is addictive, and this is not an entirely good thing. Rejuvenation Res 2008;11:1–3.

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