

## Commentary

# Wishful Thinking And The Fallacy Of Single-Subject Experimentation

By Michal Jasieński

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Few elements in the public view of science and medicine rival the romantic image of a scientist drinking a self-concocted potion and risking his or her life to benefit humanity. Recently, K.S. Brown ([\*The Scientist\*, Dec. 11, 1995, page 1](#)) outlined the history of self-experimentation in biomedical science. In but two paragraphs, however, was there any suggestion that, apart from being unconventional or potentially dangerous to researchers, self-experimentation as a methodological option might have weaknesses. Non-objective data analysis is the least of the problems, however.

Experimenting on oneself is subject to an extreme form of the observer's effect, when the observer becomes the observed. Self-observation is not only, as philosophers of science put it, "theory-laden," but also heavily influenced by the subject's mood and yesterday's diet.

One might assert that self-experimentation represents only a minor current in research and as such poses little threat to the overall quality of biomedical science. However, self-experimentation is a special case of much more widespread research involving single subjects.

Single-subject studies, such as a widely publicized attempt to use baboon bone marrow for AIDS treatment involving a single patient, named Jeff Getty (see story on page 3), represent a seriously flawed scientific methodology. Consequently, the results of all single-subject studies are bound to be erroneous.

Do the errors matter? After all, every result obtained during the process of a scientific inquiry has an error attached to it, because the scientific procedure that generated this result may be biased or inaccurate. The imprecision and bias of our results may be evaluated only by statistical analysis of repeated observations. Without statistics, there is no way of knowing if the errors matter, and there can be no statistical analysis on samples of one. Can we then base our biomedical policies on estimates with unascertainable errors?

The essence of empirical research is a constant tension between the Scylla of rejecting a correct explanation of a phenomenon and the Charybdis of accepting a false explanation. Science is about navigating between them and finding an explanation through separating unique from repeatable properties of subjects under study. Both types of properties are hopelessly confounded within any single individual, and no amount of technological progress will undo such confounding. The only way is through "averaging out" the superficial differences among individuals, to see what meaningful similarities remain (representing, for example, the effects of a medical treatment).

Averaging out with single-subject experiments does not work; at best, with a proper experimental design one can demonstrate on one subject the presence or absence of some treatment effects. The critical proviso is "with a proper experimental design": Lack of it is transparent in the Getty experiment. This

ambitious trial was crippled by the absence of control subjects and by the placebo effect of unknown magnitude. Contrary to the claims of success, this particular experiment must be considered a failure, becoming victim of its own novelty and the politics surrounding the issue. The shortsightedness of the Food and Drug Administration -- which permitted this single-subject trial, rather than promoting larger, controlled experiments -- is indeed baffling. The shortsightedness of some AIDS activists opposing fully controlled studies -- those in which some subjects do not receive treatment -- (L.K. Altman, *New York Times*, Feb. 6, 1996, page A1), on the grounds that they are unethical is indeed tragic.

Jeff Getty's uniqueness, resulting in part from the pre- and post-transplant treatment he received from his doctors (including radiation and a battery of antiviral, immunosuppressive, and other drugs) and the media spotlight, makes the failure of the transplant (L.K. Altman, *New York Times*, Feb. 9, 1996, page A14) uninterpretable. Even if the treatment did turn out to be harmless and efficacious, how far from optimal would it be for different people? What if Getty also had a rare, undetectable metabolic error that, unbeknownst to him, influenced his response to the new treatment? Would the whole line of research be modified, leading us astray? Can therefore a single person represent all potential target patients? Of course not!

Experimentation on single subjects (and self- experimentation in particular) violates basic assumptions of scientific inquiry and must be abandoned.

It precludes statistical analysis and lets the dark forces of wishful thinking and preconceived notions creep into objective experimental methodology. With clinical medicine becoming more scientific (through awareness of statistical methodology, inter-individual variability, and so forth), there should be no place for single-subject experimentation. Progress in medicine requires well-designed trials that yield recommendations of optimal procedures, optimal drug dosages, and optimal ways of administering them, leading to the maximization of the treatment efficacy. Although less romantic, Dr. Jekyll's self-imposed transformation or Jeff Getty's brave determination could have been much more informative had they involved appropriate experimental design.

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