6

"Positive Biology" and Well-Ordered Science

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Abstract

Going back to the Ancient Greeks (e.g., Plato and Aristotle), philosophers have long asked profound questions such as "What is knowledge?" and "What is the good life?" Such questions compel us to engage in a deeper level of introspection and examination than most of us are typically accustomed to in our daily lives. The philosophical question contemplated in this chapter is "What constitutes 'well-ordered science'?" Invoking a virtue epistemological construal of knowledge as "success from ability," I argue that the study of pathology must be supplemented by the study of the determinates of exemplary positive phenotypes (e.g., healthy aging and happiness). This requires transcending the limitations of what I call "negative biology," and treating "positive biology" as an integral element of well-ordered science in the twenty-first century. Positive biology can help bring to the fore the importance of understanding the evolutionary and life history of our species, thus helping to provide the intellectual frameworks needed to inspire the development of novel and feasible interventions to improve human health and happiness.

Going back to the Ancient Greeks (e.g., Plato and Aristotle), philosophers have long asked profound questions such as "What is knowledge?" and "What is the good life?" Such questions compel us to engage in a deeper level of introspection and examination than most of us are typically accustomed to in our daily lives. Intellectual curiosity and the challenging of our established beliefs are important because we are prone to cognitive biases and superstitious beliefs which exemplify epistemic *vice* (e.g., simplicity of casual

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explanation, confirmation bias, etc.) rather than epistemic *virtue* (Zagzebski, 1996), which includes attention to the relevant facts, intellectual humility, adaptability of intellect, etc.

The introspection that philosophy encourages us to engage in can often be a catalyst to new insights because philosophy requires one to make *explicit* the hidden assumptions behind our beliefs and cultural practices. And then, once these assumptions are explicit, the philosopher will critically assess the soundness of these hidden assumptions.

The philosophical question I would like to contemplate in this chapter is "What constitutes 'well-ordered science'?" In the next section I lay some preliminary foundations for addressing this question by elaborating briefly on the virtue epistemological construal of knowledge as "success from ability" (Greco, 2010). This is achieved by drawing a contrast between superstitious beliefs and scientific knowledge. I then invoke James Flory and Philip Kitcher's (2004) definition of well-ordered science (an account that prioritizes asking the most significant questions) and link this to the medical sciences and the fixation on the question "what causes disease?" Drawing a contrast (detailed in a later section) between what I have described elsewhere (Farrelly, 2012a) as "negative biology" and "positive biology," I urge that the study of pathology be supplemented by the study of the determinates of exemplary positive phenotypes (e.g., healthy aging and happiness). Two subsequent sections then detail how this has already been be applied, respectively, to the fields of geroscience and positive psychology. I conclude that positive biology can help bring to the fore the importance of understanding the evolutionary and life history of our species, thus helping to provide the intellectual frameworks needed to inspire the development of novel and feasible interventions to improve human health and happiness that go beyond what is likely to be achieved by functioning solely within the intellectual assumptions of "negative biology."

"Scientia Potentia Est"

> "Knock on wood!"
> "Find a penny, pick it up; and all day long you'll have good luck!"

These two popular sayings express superstitious beliefs. Beliefs which, if taken seriously as actually possessing *prescriptive* action-guiding advice,

would be folly to adhere to. The person who, after knocking on wood or finding a penny, undertakes a risky course of action thinking they will be protected from any potential hazards puts themselves in peril. What is it that separates credulous beliefs from *knowledge*?

Virtue epistemologists define knowledge as "success from ability" (Greco, 2010) or "a state of cognitive contact with reality arising out of acts of intellectual virtue" (Zagzebski, 1996, p. 270). Unlike superstitious beliefs, the insights of epidemiology, agricultural science, physics, and chemistry all have *predictive* power that can be tested and verified in the empirical world. These disciplines constitute "knowledge," even if only provisional and far from complete, because they permit us to enjoy different types of success in navigating through our precarious world. The success science has achieved ranges from protecting populations against infectious disease and providing sufficient water for agriculture, to applying the laws of motion to inform vehicle safety regulations (e.g., speed limits, seat belt requirements) and chemistry to develop safe pharmaceuticals to treat or manage disease.

The word "science" is derived from the Latin *scientia*, which means "knowledge." "*Scientia potentia est*" (or "knowledge is power") is a slogan often attributed to Francis Bacon (1561–1626), and it appears in Thomas Hobbes's *Leviathan*. This motto coheres with the virtue epistemological understanding that knowledge is "success from ability." Acting from a position of knowledge—versus ignorance—permits us to more successfully navigate the perils of the external world so that we may flourish as individual persons and collectively as societies.

The world is a complex and constantly changing environment, and thus knowledge itself will not be fixed or static. The normative value of different types of knowledge will be *context-specific*. In one context certain empirical insights about the world might prove to be vital in helping us protect a population from disease and premature death. But those same empirical insights might be, in a different context, of much more limited use and significance because the most pressing external threats to human populations are different.

This point can be illustrated with the following example. Consider the historical context of fifteenth-century England, where life expectancy at birth would have been less than 40 years of age. If we could travel back in time to the fifteenth century and offer the people living then one—and only one—of the following public health insights to improve population health, which one would we choose to share with them?

1. Edward Jenner's research into cowpox and immunology that helped, eventually, to eradicate smallpox from the world by 1980.

or

2. The knowledge that tobacco is a carcinogen, and that smoking cessation can help prevent lung cancer.

In a world dominated by high rates of early and mid-life mortality and a projected increased risk of infectious diseases like smallpox (as the size of urban populations in cities like London would grow through the seventeenth and eighteenth centuries), Jenner's discovery of the vaccine against small pox would be *significantly* more valuable than a public campaign of smoking cessation in fifteenth-century England. The latter would not offer a significant benefit to population health because other threats, such as infectious disease and poverty, killed most humans before reaching the advanced age when lung cancer would likely develop (which is typically older than 65).

However, today, in the twenty-first century, with smallpox eradicated and life expectancy at birth at age 72 (World Health Organization, n.d.), smoking cessation is a very significant public health priority to help reduce global cancer mortality. The health vulnerabilities facing today's aging populations are different from those that human populations faced in centuries past. And this means that the scientific insights most conducive to health promotion will be constantly evolving as the empirical realities (e.g., risk of disease) facing the world's populations change.

I posit this hypothetical thought experiment of fifteenth-century England to illustrate the point that an empirical insight (or general theoretical framework) can be valuable life-saving knowledge in one context but something that simply satisfies our intellectual curiosity (without being translatable into practical action that could substantively improve population health, happiness, or prosperity) in a different type of context.

Since the rise of epidemiology in the nineteenth century, the central question which has been the primary focus of both clinical medicine and public health is: *What causes disease*? In this chapter I argue that this fixation on *disease-research* (evident in oncology, cardiology, psychiatry, etc.) must now (i.e., in the twenty-first century) be supplemented by a zeal to also invest in and support basic scientific research into the causation of exemplar *positive* phenotypes. These phenotypes range from exceptional healthy aging and HIV resistance to emotional resilience and human happiness. In this chapter I defend and expand upon the intellectual paradigm which unifies these

disparate areas of enquiry, what I call "positive biology." I make the case for considering positive biology as an integral part of "well-ordered" science in the twenty-first century.

In the following section, I define what constitutes well-ordered science. I then expand on the contrast between negative and positive biology and the importance the latter places on understanding both the proximate and evolutionary causation of positive phenotypes. The subsequent two sections illustrate the prescriptive potential of positive biology by drawing attention to, respectively, insights from "geroscience" and "positive psychology."

What Constitutes Well-Ordered Science?

I believe a virtue epistemological understanding of knowledge as "success from ability" is helpful because the account of knowledge it champions is one which prescribes that we aspire to achieve a state of cognitive contact with reality that arises from the exercise of *epistemic virtue*. It is only through this cognitive contact with reality that we can hope to flourish in a precarious and uncertain world. For example, with the knowledge of medicine, foreign affairs, and economics we can better secure the desired aims of health, peace, and economic prosperity. Such aims are unlikely to be realized if our actions are guided by mere guesses, flipping a coin, or interpretations of a divine entity's plan for us derived from the celestial movements of the planets (e.g., astrology). Impulsivity or placing faith in chance or dogmatism does not exemplify intellectual virtue. On the contrary, they exemplify epistemic *vice* by ignoring evidence, failing to display an appropriate amount of humility, etc. Belief, for virtue epistemologists, is a kind of performance with a goal (Kelp, 2017, p. 224). *And the ultimate goal or standard for assessing our collective beliefs is their ability to enable us to flourish*.

Conceptualizing knowledge as "success from ability" reminds us that knowledge is not static. Knowledge involves having cognitive contact with an external reality that is constantly changing, sometimes changing in predictable and often unpredictable ways over time. Knowledge that once permitted us to have success against certain extrinsic risks might prove less helpful when new extrinsic risks (e.g., climate change) emerge to pose significant threats to our health and prosperity. And this then compels us to adapt and develop new conceptual tools and innovations if we hope to continue to flourish against new threats.

James Flory and Phillip Kitcher define the idea of well-ordered science as follows: "The pursuit of science in a society is *well-ordered* when the research effort is efficiently directed toward the questions that are most significant" (Flory & Kitcher, 2004, p. 59). Science would fail to be well-ordered, for example, if most of our time, energy and resources were invested in trying to answer trivial or trite questions while ignoring the really significant and pressing questions. In such a scenario our collective intellectual efforts would not yield much in terms of a tangible societal benefit that could improve human health and happiness.

If well-ordered science is defined as the research effort being efficiently directed toward those questions that are most significant, then the obvious place for us to begin our inquiry into the specifics of well-ordered science today is by grappling with the issue of "what makes a question *significant*?" There is a nearly infinite list of questions we could spend our limited time, energy, and resources trying to answer, so what makes some questions more significant than others?

Definitively answering this question goes beyond what I aspire (or could hope) to establish in this chapter. The issue of what constitutes the *most significant* questions in science is of course likely to be contentious, and robust disagreement is no doubt healthy because it helps guard against a society developing persistent epistemic blind spots. At least since the rise of epidemiology in the nineteenth century, one question has clearly dominated most research within the medical sciences—namely, "what causes pathology?" Elsewhere (Farrelly, 2012a, 2012b), I have called the research paradigm that presumes this question is the most significant question to answer the project of "negative biology." This research paradigm explains why the lion's share of money allocated by the National Institutes of Health (NIH; the medical research agency of the United States) goes to disease instead of health research.

With a current annual budget of approximately $39.2 billion (National Institutes of Health, n.d.) the vast majority of this funding is spent on research on disease and disorders. For example, in 2018, $6.6 billion was invested in cancer research, $5.8 billion on brain disorders, $4.9 billion on rare diseases, $3 billion on HIV/AIDS, and $1.7 billion on substance abuse (National Institutes of Health, 2019). Such significant investments are clear evidence of the dominance of the paradigm of negative biology.

The rise of the intellectual framework of negative biology has been one of the most significant achievements of our species. "In 1800, with nearly one billion people alive, life expectancy at birth did not surpass thirty years. By

2000, with more than six billion people alive, life expectancy reached nearly sixty-seven years amidst a continuing rise" (Riley, 2001, p. 1). Many factors account for this dramatic increase in life expectancy over only two centuries, including improved material prosperity, democratization, and birth control. The accomplishments of negative biology (the prevention of disease via public health measures like the sanitation revolution, immunizations, smoking cessation, etc.) coupled with advances in clinical medicine (e.g., treatments for specific disease like HIV, cancer, etc.), are an integral element of the story of this transformation from the "young" world where life was, as Thomas Hobbes described it, "nasty, brutish and short" to the world of today, where a baby born anywhere on the planet can expect to live long enough to become a senior citizen.

In *The Growth of Biological Thought*, Ernst Mayr claims that no biological problem is fully solved until both the proximate and evolutionary causation has been elucidated (Mayr, 1982, p. 73). Scott-Phillips, Dickins, and West (2011) provide the helpful example of a crying baby to explain these two levels of casual explanation. Proximate level explanations of phenotypes "are concerned with the mechanisms that underpin the trait or behavior—that is, how it works" (Scott-Phillips et al., 2011, p. 38). When explaining why an infant cries, for example, a proximate level explanation will invoke the immediate causal triggers that cause infants to cry, such as separation from a caregiver or being hungry or cold. The evolutionary explanation for why infants cry "appeals to the fitness benefits of the trait" (Scott-Phillips et al., 2011, p. 38). Crying behavior is adaptive, it helps improve the probability that vulnerable infants can survive the precarious stages of infancy. Infants who did not cry when in need of assistance were less likely to survive and pass on their genes. Hence the abundance of infants who display this behavior. Darwinian selection favors babies who are able to get their needs met over those that are less capable of doing so.

By emphasizing the importance of the two levels (proximate and evolutionary) of the causal explanation of biological problems, Mayr wanted to ensure that biologists transcended the myopic lens of fixating only on the proximate causation of problems. This myopic lens is something that can limit our study of health and disease. Consider, for instance, cancer. In 2018, approximately 9.6 million people (including my own father) died of cancer worldwide (World Health Organization, 2018). When we ask the question, "What causes cancer?" there are, as there is with infant crying behavior, two levels of explanation on which we might focus our answer. The proximate

level of explanation will focus on the factors that immediately contribute to cancer mortality, such as particular genetic mutations and exposure risks to carcinogens like tobacco or UV radiation, etc. And the evolutionary explanation will explain why aging occurs and why senescence makes our mind and body more susceptible to chronic diseases (like cancer) in late life.

Unlike infant crying behavior, cancer is not an adaptive trait. In *Good Reasons for Bad Feelings*, Randolph Nesse describes how when he and George Williams began working on evolutionary medicine they tried to find an evolutionary explanation for disease. Nesse refers to this serious error (which is common in evolutionary medicine) as *viewing diseases as adaptations* (VDAA). But diseases are not adaptations. Late-life diseases like most cancers are not selected for by evolution but are rather "aspects of the body that makes us *vulnerable* to diseases that do have evolutionary explanations" (Nesse, 2019, p. 14). Aging has an evolutionary explanation, known as the *disposable soma theory* (Kirkwood, 1977; Kirkwood & Holliday, 1979), which maintains that biological aging occurs because natural selection favors a strategy in which reproduction is made a higher biological priority (in terms of the utilization of resources) than the somatic maintenance needed for indefinite survival.

Michael Rose explains how the diseases of late life are the product of the "evolutionary neglect" that occurs when reproductive fitness is prioritized by evolution by natural selection.

> Natural selection discards bad genes, genes like those that cause fatal childhood progeria. Bad genes cause these effects by producing inborn errors of metabolism: letting toxins accumulate, impairing brain function, and so on. Many of the diseases that kill infants are the products of such bad genes. . . . Natural selection keeps genes with such devastating early effects rare, because the afflicted individuals die before reproducing. Bad genes destroy themselves when they kill the young. . . . But at later ages, the force of natural selection becomes weak. It leaves genes with late bad effects alone, because natural selection has stopped working. Its force has fallen toward zero. Bad genes that only have late effects will not be removed by natural selection. They can accumulate. There is no more automatic Darwinian screening. (Rose, 2005, p. 42)

This two-level casual explanatory lens could also be applied to human emotions like hedonic well-being (pleasure), anxiety, and romantic love.

One could elucidate the proximate causation of such emotions—the neurochemical reactions we experience when eating sugary foods or are exposed to external stressors like job loss or sharing emotional and physical intimacy with another. When we seek the evolutionary explanation for these same emotions we see that reproductive fitness looms large in explaining the potential adaptive benefits of our emotions, positive and negative. Pleasurable feelings can help motivate us to engage in behavior conducive to our individual and collective survival (e.g., gathering and consuming food, procreation, etc.). Anxiety can help prepare us to deal with threats to our survival and offspring. And love aids in the production and care of offspring.

Proximate-level explanations that focus on the role environment and heredity play in our susceptibility to disease and behavior are thus only one level of explanation. At best they provide a partial explanation of important phenotypes. A more complete understanding of our susceptibility to cancer, depression, and stroke must also delve into the ultimate, or evolutionary, explanation of these phenomenon.

Negative and Positive Biology

Our ability to prevent and treat disease is largely determined by how sound are our intellectual suppositions of well-ordered science. Just as the fixation on the proximate causation of disease can make us susceptible to myopia (by ignoring the evolutionary causation of disease), focusing exclusively on the question "what causes disease?" can also have myopic consequences. Prioritizing only disease-oriented research threatens to marginalize the study of exemplary positive phenotypes (exceptional healthy aging, resilience, and happiness, etc.). Knowledge from these areas of scientific inquiry might prove to be significantly valuable to human health and happiness, offering benefits that could not be achieved if we limited ourselves only to the study of pathology.

Elsewhere I draw the contrast between the intellectual suppositions of "negative" and "positive biology" as follows.

Starting Intellectual Assumptions

Negative biology: Health, longevity, and happiness are assumed to be a "given" or part of "normal species functioning" for humans.

> *Positive biology*: There is diverse variation in the genotypes which influence desired phenotypes, such as health. The evolutionary and life histories of different species help explain this variation and the different biological tradeoffs that determine age of reproduction, body size, senescence, complexity of the brain, etc.
>
> ***What Needs to be Explained?***
>
> *Negative biology*: The proximate causes of disease, frailty, and disability
>
> *Positive biology*: The proximate and ultimate causes of exceptional health, positive emotions and happiness, high cognitive ability, etc.
>
> ***Which Kinds of Interventions Ought to be Pursued?***
>
> *Negative biology*: Interventions that help prevent, treat, and cure specific diseases
>
> *Positive biology*: Interventions that increase the opportunities for health, happiness, and well-being (Farrelly, 2012a, p. 414)

One challenge facing the paradigm of positive biology is that research funding and support within the medical sciences typically flows to the basic research expected to have significant clinical relevance in terms of treating or preventing disease. A cure for one type of cancer or an intervention that reduces the risk of heart disease, for example, has a clear impact that we can measure in terms of mortality reduction. The paradigm of negative biology has helped individuals and populations live longer lives by reducing our susceptibility to early and mid-life mortality (e.g., infectious disease) and manage multimorbidity in late life. What potential benefits can positive biology potentially yield? Are there benefits to be had by studying the *absence* of pathology, something that might escape our attention if we only focus on the development of negative outcomes? And are these potential benefits significant enough to justify buttressing the amount of support invested in positive biology? In other words, is positive biology an integral component of well-ordered science in the twenty-first century?

I believe the answer to this question is a clear "affirmative!" And to make more concrete the specifics of the potential benefits positive biology can yield, I focus on two areas of research that can yield significant benefits in terms of preventative medicine: (1) geroscience and (2) positive psychology. The former studies the determinants of exceptional healthy aging, the latter the determinates of happiness and well-being. Taken together, I believe these two distinct areas of scientific research are essential components of

well-ordered science today that could improve the health and happiness of today's aging populations.

Geroscience and the Future of Preventative Medicine

Positive biology prescribes that we seek to understand exceptional positive phenotypes, and healthy aging is perhaps one of the most significant and fascinating examples of positive biology to study. Aging is a major risk factor for chronic disease. And chronic diseases like cancer, heart disease, and stroke are the leading causes of death in the world today. But how persons age can vary significantly. Most people experience at least one (if not several) major chronic disease by their seventh decade of life (Vogeli et al., 2007, 392), and the average life span is estimated to be approximately 85 years (Fries, 2005). Jeffrey Fries explains how estimates of the human life span are arrived at.

> There are several methods of estimating the human life span. One may use the anthropological formulas, reconstruct an ideal survival curve from the tail of the present curve using the assumption that these individuals have been essentially free of disease, make extrapolations from the rectangularizing survival curve, or use estimates based on observed decline in organ reserve. All suggest an average life span of approximately 85 years, with a distribution which includes 99 percent of individuals between the ages of 70 and 100. (Fries, 2005, p. 808)

The maximum human life span is estimated to be around 125 years (Weon & Je, 2009). And there are (rare) individuals who can live a century of disease-free life. Positive biology prescribes that we prioritize the study of the biology of such exemplary healthy aging. Rather than fixating on just the causation of one specific disease of aging, like cancer, heart disease, or stroke, understanding the disease resistance displayed by the longest lived humans (and other species) could offer vital insights into a novel strategy of promoting preventative medicine via an aging intervention.

Not all species biologically age at the same rate. Indeed, even within a species there can be quite a wide variation in the rate of biological aging (e.g., dogs). In *The Long Tomorrow*, Michael Rose notes that many factors can influence the longevity of a species because they impact the force of evolution by natural selection. Size, for example, really does matter in nature.

> If a species lives longer in nature, the force of natural selection will be increased at later years. Larger organisms can reproduce at later ages because they are more likely to be alive then, so the force will remain high at later ages. This fosters selection of genes that will tend to keep the larger alive still longer. (Rose, 2005, pp. 64–65)

The bowhead whale can grow to 20 meters in length and has a maximum life span exceeding 200 years. The bowhead whale is an important species to study for positive biology, and its genome has been sequenced. These whales do not become sexually mature until after age 20, and gestation takes more than a year. This can be contrasted with the biology of the tiny field mouse. In the wild, this mouse is vulnerable to many predators, and the winning strategy for the mouse is to reproduce early in life, with a short gestation period and a large litter.

The rate at which a species ages reflects the extrinsic risks it has faced in its evolutionary history. The disposable soma theory predicts that a greater investment in longevity should come at a cost to reproductive fitness. And a variety of studies support that conjecture. In a study (Tabatabaie et al., 2011) comparing the fertility rates of men and women who were young adults in the 1920s, before reliable methods of birth control were widely available, the exceptionally long-lived (both males and females) had an average of 2.01 children versus 2.53 children for the control group. These differences in fertility were not related to gender or education level. But there were developmental differences among the women with exceptional longevity. They tended to reach menarche a year later than average, have their first child 3 years later, and their last child 2.5 years later than average.

Studies examining the impact that castration has on the longevity of men are also evidence of this longevity/reproduction tradeoff. Castrated men residing in a mental hospital lived 14 years longer than intact men in the same hospital (Hamilton & Mestler, 1969). And historical Korean eunuchs had an incidence rate of centenarians at least 130 times higher than that of present-day developed countries (Min, Lee, & Park, 2012). Such findings support what the disposable theory predicts: that longevity comes at a cost to reproductive fitness.

In addition to castration, caloric restriction (CR) has been studied for decades in a variety of species (like mice) and extends life span by altering the rate of biological aging. CR induces stress response pathways in organisms, which results in more than simply longer lives. A longer life is not necessarily

desirable, especially if it is achieved by simply keeping an organism alive in a frail and incapacitated state. But CR does the opposite of this. It extends life by keeping an organism *healthy* for a longer period of time (extending the *health span*). Since research in the 1930s, scientists have known "that rats and mice that are given about 40 percent less food than they would eat on their own live about 40 percent longer than do fully fed controls" (Miller, 2002, p. 160).

Castration and CR (which is very burdensome and can be dangerous if a person does not receive enough essential nutrients) are not viable measures for humans to pursue to retard aging, but the genomic era has revealed particular genes that slow down biological aging as well as particular molecules that active those genes (Harrison et al., 2009).

Because positive biology prioritizes the study of exemplar positive phenotypes, well-ordered science ought to entail extensive study of the longest lived humans. This means extensive study of centenarians ought to loom large in the twenty-first century. The longest lived humans are an important biological puzzle to examine not simply because they live so long, but because they typically experience a delay and compression of morbidity. Centenarians are comprised of three different categories: "delayers," "survivors," and "escapers" (Evert, Lawler, Bogan, & Perls, 2007). The "delayers" are people who make it to 100 years with a delay of the onset of common age-associated illness. For "survivors," these are people who were diagnosed with an illness prior to age 80 but survived for at least two more decades. And the third category of centenarians are "escapers," people who escaped the most lethal diseases, such as heart disease, non-skin cancer, and stroke.

The suggestion that we pursue a novel strategy of preventative medicine via an applied gerontological intervention is not science fiction. It may quickly become a reality this century. The launch of targeting aging with meformin (TAME; Barzilai, Crandall, Kritchevsky, & Espeland, 2016), a clinical trial to test the drug metformin as a safe and effective intervention against several age-related diseases, is clear evidence of this. Metformin has been safely utilized as a pharmacological intervention to help control type 2 diabetes for decades. "Metformin exerts its therapeutic effects, through a number of mechanisms and physiological pathways that resemble those generated by caloric restriction (CR), an experimental model known to extend life span and health span in various organisms" (Novelle, Ali, Dieguez, Bernier, & de Cabo, 2016, p. 2).

In experiments on animals, metformin has been shown to slow aging. And now researchers are hoping a similar effect can be shown in humans. "If TAME demonstrates that metformin modulates aging and its diseases, beyond an isolated impact on diabetes, it would pave the way for development of next-generation drugs that directly target the biology of aging" (Barzilai et al., 2016, p. 1060). The researchers undertaking TAME describe the significance of the study as follows:

> In the TAME study, we plan to enroll 3,000 subjects, ages 65–79, in ~14 centers across the US. Rather than study the effects of metformin on each separate condition, we will measure time to a new occurrence of a composite outcome that includes cardiovascular events, cancer, dementia, and mortality. TAME will also assess important functional and geriatric end points.
>
> If successful, TAME will mark a paradigm shift, moving from treating each medical condition to targeting aging per se. We expect this to facilitate the development of even better pharmacologic approaches that will ultimately reduce healthcare costs related to aging. (Barzilai et al., 2016, p. 1063)

By studying exemplar examples of healthy aging in other species and in humans, geroscience could lead to one of the most significant advances in public health this century. Robert Butler (1927–2010), the first Director of the National Institute of Aging in the United States, has urged policy-makers to aspire to slow human aging and to consider this a major priority for public health (Butler et al., 2008). Aspiring to slow the aging process is distinct from the aspiration to treat or cure a specific disease of aging, like cancer, heart disease, or stroke. Supplementing our conception of well-ordered science to include a commitment to positive as well as negative biology might help usher into existence an aging intervention that could promote the health of the 2 billion persons who will be older than 60 by the middle of this century.

Happiness and Psychological Well-Being

Like geroscience's examination of exceptional healthy aging, positive psychology's examination of happiness is another paradigmatic example of positive biology. Rather than making depression and pathology the exclusive

focus of psychology, positive psychologists urge that the study of human happiness ought to also be a central focus of research and that the field should aspire to develop empirically valid prescriptions that could improve the well-being of the average person.

In "Positive Psychology: An Introduction," Martin Seligman and Mihaly Csikszentmihalyi make an appeal that the study of the worthwhile life ought to be an integral (instead of neglected) part of well-ordered science when they claim

> Psychology has, since World War II, become a science largely about healing. It concentrates on repairing damage within a disease model of human functioning.
>
> This almost exclusive attention to pathology neglects the fulfilled individual and the thriving community. The aim of positive psychology is to begin to catalyze a change in the focus of psychology from preoccupation only with repairing the worst things in life to also building positive qualities. (Seligman & Csikszentmihalyi, 2000, p. 5)

Positive psychology is perhaps the most prominent research area of positive biology. What Seligman and Csikszentmihalyi are calling for is a shift away from the exclusive focus on negative biology (i.e., pathology) to one that is also committed to positive biology (exemplar phenotypes).

What is happiness? And what are the determinates of happiness? These are deep philosophical and empirical questions, ones not easily answered. I will not attempt to answer them here (for more from philosophy, see Chapter 8 by William A. Lauinger and Chapter 9, by Anne Baril; for social science, see Chapter 13 by Margolis et al. and Chapter 15 by Xi and Lee; for theology, see Chapter 10 by Messer, Chapter 11 by Wynn, and Chapter 16 by VanderWeele, Long, & Balboni, all in this volume). Instead, I seek to make the case that positive psychology is an exemplar example of what positive biology can offer. Quality, and not simply quantity, of life is an integral concern of positive biology.

Happiness has been defined by philosophers, psychologists, and economists, often in different ways. Hedonistic accounts of human happiness, like that of the utilitarian Jeremy Bentham (1784–1832), equate happiness with subjective well-being (or the experience of pleasure). On this account of happiness, a person's "experiencing self" is the authority of a person's well-being. For example, researchers can ask people how happy they

feel while performing different types of activities: working, spending time with family, cleaning, exercising, while incarcerated, unemployed, married, divorced, living with a disability, etc. Once researchers accumulate enough responses from different people, particular patterns emerge about the activities associated with high and low levels of well-being.

One surprising and significant finding concerning people's ability to predict their future hedonic responses to events is that we are not very competent at doing this. We are not good at predicting how certain events (e.g., becoming paraplegic, winning the lottery, or moving to California) will impact our well-being. For example, if people are asked to predict how their happiness would be impacted if they became paraplegic, they are likely to answer that it would have a serious, adverse impact on their well-being. Conversely, if asked to predict how happy they would be if they won the lottery, most people would assume this event would have a dramatic impact and substantially increase their happiness. And yet, "in a famous study, the happiness of people 1 year after developing paraplegia was almost indistinguishable from the happiness of people 1 year after winning the lottery" (Ubel et al., 2001, p. 190). When it comes to predicting how happy you would be living in California (Schkade & Kahneman, 1998) or if you were richer (Kahneman, Krueger, Schkade, Schwarz, & Stone, 2006), the actual reports of life satisfaction from people in those circumstances are very different from what people predict the life satisfaction of people in those circumstances must be. When fixating on how the weather or money will impact our well-being we tend to overexaggerate the importance of these factors and ignore other important factors (e.g., the commute to work, relationships, fulfillment with work, etc.).

And this fact reinforces the urgency to derive and promulgate sage prescriptions from positive psychology versus just trusting our individual judgments about what will make us happy in the future as authoritative (especially when the average person is bombarded by consumerist messages daily). We are not reliable predictors of our hedonic states because we suffer from a variety of what Gilbert and Wilson (2007) call "prospection errors." *Prospection* refers to our ability to "pre-experience" the future by simulating it in our minds (Gilbert & Wilson, 2007, p. 1352). Prospection is a unique feature of the cognitive lives of humans. For example, such simulations can be *unrepresentative*. Simulations of the future are constructed from our memories. We retain a memory of extraordinary events (e.g., that time our plane was delayed on the tarmac for 2 hours!) rather than the representative memory (e.g., successfully taking off [approximately] on time). Simulations

of the future can also be *abbreviated*. This means that our simulations of the future typically focus on a few, select moments of a future event. For example, when we simulate a potential future where we have won millions in the lottery, we think of all the joy we can get purchasing new homes and automobiles for our family members. But what we do not simulate in our minds is the reality that we can still have interpersonal challenges in our relationships (indeed, winning the lottery might exacerbate those challenges). We fail to internalize how we will, in time, adapt to being much wealthier. Abbreviated simulations are unreliable predictors of our emotional well-being.

Knowledge about our susceptibility to prospection errors and how to minimize making such errors could improve our subjective well-being. But the potential for positive psychology goes much further than simply improving our subjective well-being. Like geroscience, positive psychology extends its scope to the ultimate causation of positive phenotypes like joy, interest, and love. This requires us to consider the type of species *Homo sapiens* actually is, a concern that goes back to at least Aristotle. The function (*ergon*) of a human being, according to Aristotle, consists in activity of the rational part of the soul in accordance with virtue (Aristotle, 1985; NE 1097b22–1098a20). *Eudaimonia* (or happiness) is the highest end, and all other goals—wealth, friendship, health, etc.—are secondary goals that are pursued because they promote eudaimonia.

Positive biology is not simply interested in the proximate causation of happiness; it also adopts an evolutionary lens. The process of evolution by natural selection yielded mental faculties that are much more complex than the picture presumed by Bentham, giving us reason to be skeptical that sage normative prescriptions can be gleamed from the conjecture that it is our nature to be "hedonic maximizers." In *An Introduction to the Principles of Morals and Legislation*, Bentham famously remarked

> Nature has placed mankind under the governance of two sovereign masters, pain and pleasure. It is for them alone to point out what we ought to do, as well as to determine what we shall do. (Bentham, 2008, p. 585)

Evolutionary biologists provide a much more expansive and complex account of our mental life.

> Our evolved natures should be treated with respect, but not with deference. We did not evolve to be happy: rather we evolved to be happy, sad,

> miserable, angry, anxious, and depressed, as the mood takes us. We evolved to love and to hate, and to care and be callous. Our emotions are the carrots and sticks that our genes use to persuade us to achieve their ends. But their ends need not be our ends. Goodness and happiness may be goals attainable only by hoodwinking our genes. (Stearns, Nesse, & Haig, 2008, p. 13)

Natural selection did not design us to be "hedonic maximizers." If our species only experienced positive emotions like those of the sensory pleasures (e.g., satiation), we would not have survived for long in the kind of environment that humans have historically faced. Martin Seligman (2002) distinguishes different kinds and levels of happiness. Hedonists who pursue the immediate positive feelings—like the pleasure of a food they enjoy or a compliment—seek the *momentary* happiness of what Seligman calls "the pleasant life." But these pleasures fade quickly and thus do not have a lasting impact on the subjective well-being of actors. Enduring happiness, the kind one enjoys when one lives the truly "excellent life," is realized when one leads a *meaningful life*. Such a life requires we become psychologically connected and continuous with others rather than just our self. After spending years of studying what makes people happy, Seligman remarks

> What does Positive Psychology tell us about finding purpose in life, about leading a meaningful life beyond the good life? I am not sophomoric enough to put forward a complete theory of meaning, but I do know that it consists in attachment to something larger, and the larger the entity to which you attach yourself, the more meaning in your life. (Seligman, 2002, p. 14)

A growing body of empirical studies appear to substantiate Seligman's contention. For example, in a study of the daily social behavior of happy people (Mehl, Vazire, Holleran, & Clark, 2010), researchers used an electronically activated recorder (EAR) to record and then later classify participants' daily conversations with others as either "small talk" (e.g., banal conversation) or "substantive talk" (e.g., conversations where meaningful information was exchanged). The study found that higher well-being was associated with having less small talk and having more substantive conversations. While such a study does not establish the factual truth of Socrate's famous claim that the "unexamined life is not worth living," it does suggest that our need to feel attached to something bigger than ourselves plays an important role in our happiness and well-being. And this hypothesis also coheres with

the findings of recent studies on spending money and happiness. Elizabeth Dunn et al. (2008) found that when individuals spend more money on *prosocial* goals, like charity, they actually experience greater happiness than when they spend money on themselves.

Taking evolution seriously means we must recognize that positive emotions—like joy, love, and interest—are, like the negative emotions, the result of our evolutionary history. "Negative emotions such as fear, sadness, and anger are our first line of defence against external threats, calling us to battle stations" (Seligman, 2002, p. 31). And the same is true of our positive emotions in that "they help illicit urges to act, though they are usually less specific than the actions urged by negative emotions" (Fredrickson, 1998, p. 303). Furthermore, as Barbara Fredrickson has argued, the positive emotions urge not simply physical action, but rather they also broaden what she describes as our "momentary thought-action repertoire" (Fredrickson, 1998, p. 303). And different positive emotions serve different purposes in broadening this repertoire. Love can foster many different positive emotions—like joy and interest—and permit a person to experience the new stimuli that comes from internalizing the beliefs, information, values, and aspirations of others. Love promotes social connectedness and expands our circle of concern and attention beyond just ourselves. And this connectedness can help provide meaning and purpose in our lives, thus enhancing our well-being.

Like love, play also promotes social connectedness as well as skill acquisition. Play can enrich human capacities in different and diverse ways (Brown, 2009). Physical play (like sports) can raise our awareness of the importance of endurance and strength as well as our physical limitations and vulnerability to injury. Playing sports can help develop balance, speed, and agility. These types of play, which we find intrinsically valuable, also promote other capacities, like bodily health, thought, and the senses.

Most physical play is also a form of *social* play. Playing helps socialize us by helping us internalize the negotiated rules of games, compelling us to control our emotions and providing concrete examples to us of the benefits of social cooperation. Social play helps build trust, communication, empathy, etc. Once a person participates as a member of a team they become psychologically connected and continuous with the team. The player's own cognitive states track the trials and tribulations of the team. A team win can bring the individual player elation, while a loss brings disappointment and a determination to try even harder next time. Indeed, this phenomenon is not limited

to just the direct participants in a sport. Even spectators who care passionately about a sport and team often experience similar levels and degrees of "connectedness" to a team.

Play shapes our brain and stimulates many positive emotions. Indeed, some believe that the human capacity to play separates humans from all other animal species. Stuart Brown, for example, argues

> Of all animal species, humans are the biggest players of all. We are built to play and built through play. When we play, we are engaged in the purest expression of our humanity, the truest expression of our individuality. Is it any wonder that often the times we feel most alive, those that make up our best memories, are moments of play? (Brown, 2009, p. 5)

Love and play thus serve to broaden one's "momentary thought-action repertoire," which in turn builds the enduring personal resources necessary for eudaimonia. Understanding the proximate and evolutionary causes of subjective well-being and eudaimonia are an integral element of positive biology.

Like an applied gerontological intervention, the prescriptions generated from positive psychology offer significant potential to function as a form of preventative medicine. Emphasizing the importance of play in our lives is captured eloquently by Brian Sutton in his masterful study of play.

> What is adaptive about play . . . may be not only the skills that are part of it but also the skillful belief in acting out one's own capacity for the future. The opposite of play, in these terms, is not a present reality or work, it is vacillation, or worse, it is depression. (Sutton-Smith, 1997, p. 198)

The eudaimonic understanding of happiness emphasizes the importance of meaning and purpose in our lives. The meaningful life does not consist in simply satisfying our basic primal instincts for food, shelter, and sex. In her examination of what constitutes positive psychological functioning, Carol Ryff (1989; see also Chapter 4, in this volume) identified the following six theory-guided dimensions of well-being:

> *Self-acceptance*: Holding positive attitudes toward oneself emerges as a central characteristic of positive psychological functioning.

> *Positive relations with others*: Self-actualizers are described as having strong feelings of empathy and affection for all human beings and as being capable of greater love, deeper friendship, and more complete identification with others.
>
> *Autonomy*: Self-determination, independence, and the regulation of behavior from within.
>
> *Environmental mastery*: One's ability to advance in the world and change it creatively through physical or mental activities.
>
> *Purpose in life*: The definition of maturity also emphasizes a clear comprehension of life's purpose, a sense of directedness, and intentionality.
>
> *Personal growth*: Such an individual is continually developing and becoming rather than achieving a fixed state wherein all problems are solved (Ryff, 1989, p. 1071).

These points are reinforced by Seligman and Csikszentmihalyi in their summary of the field of positive psychology.

> The field of positive psychology at the subjective level is about valued subjective experiences: well-being, contentment, and satisfaction (in the past); hope and optimism (for the future); and flow and happiness (in the present). At the individual level, it is about positive individual traits: the capacity for love and vocation, courage, interpersonal skill, aesthetic sensibility, perseverance, forgiveness, originality, future mindedness, spirituality, high talent, and wisdom. At the group level, it is about the civic virtues and the institutions that move individuals toward better citizenship: responsibility, nurturance, altruism, civility, moderation, tolerance, and work ethic. (Seligman & Csikszentmihalyi, 2000, p. 5)

The average person's life could be substantively improved when their pursuit of happiness is informed by positive psychology and when the general culture is shaped by the prescriptions of the eudaimonic conception of well-being. Living a life of self-acceptance, healthy relationships, autonomy, environmental mastery, purpose, and personal growth versus a life spent pursuing the insatiable consumption ideals perpetuated by capitalism has the potential to substantively improve our well-being. A culture that celebrates something as basic as play—physical, social, and imaginative—across the human life span, and prosocial activities like

philanthropy and volunteerism, could significantly improve the happiness and well-being of its population. For these reasons positive psychology and related approaches, such as humanistic psychology, ought to be considered an integral element of well-ordered science for the twenty-first century.

Conclusion

Science is concerned with creating, and disseminating knowledge. And this knowledge is then the foundation upon which new innovations can be developed to improve human health and happiness. The virtue epistemological construal of knowledge as "success from ability" (Greco, 2010) is useful because it emphasizes the fact that knowledge is always *context-dependent*. Our success in improving human health and happiness will depend on the circumstances of the threats to our health and happiness. The challenges facing human populations in a world dominated by infectious disease and severe poverty are very different from the challenges facing populations living to late life and (at least in developed countries) having access to an excess of material goods.

Historically it made sense for human populations to conceive well-ordered science through the lens of negative biology. Prioritizing the question "What causes disease?" in a world dominated by extreme poverty and infectious diseases (like smallpox) was both a rational and sensible prescription. But now positive biology deserves to take its rightful place within an account of well-ordered science for the twenty-first century. Positive biology encourages us to explore both the proximate and evolutionary causes of exemplary positive phenotypes. Rather than fixating solely on the causation of pathology, positive biology encourages the study of the biology of centenarians, the emotional resilience of those who experience growth and development from adversity (vs. those who become depressed or develop addiction), and the genetic and environmental factors that contribute to self-esteem, healthy relationships, and secure attachment, etc.

What steps need to be taken to ensure that positive biology plays a prominent role in science today? I believe many different courses of action are needed. Conceptually we must overcome the observational bias implicit in

negative biology; that is, the assumption that the most important things to explain are the negative outcomes of morbidity and mortality. Science should celebrate a "curiosity-driven" mindset rather than one that predominantly focuses on the prevention and treatment of specific diseases. The success stories of positive biology (e.g., healthy aging, high IQ, emotional resilience, etc.) also deserve serious scientific attention. Elsewhere (Farrelly, 2012b), I argued that the NIH should create a new Institute of Positive Biology, which would help researchers facilitate the novel interdisciplinary research that positive biology can offer. The creation of such an innovative institute would also ensure that research on positive phenotypes can compete on a more level playing field against research on disease. The latter currently enjoys the lion's share of research support. By transcending negative biology's fixation on negative phenotypes, positive biology may be able to yield significant insights and technological advances that help the human populations of the twenty-first century flourish in spite of the fact that we face a potentially precarious and uncertain future.

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