A critical reanalysis of the relationship between genomics and well-being

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Edited by Burton H. Singer, University of Florida, Gainesville, FL, and approved June 26, 2014 (received for review April 21, 2014)

Fredrickson et al. [Fredrickson BL, et al. (2013) *Proc Natl Acad Sci USA* 110(33):13684–13689] claimed to have observed significant differences in gene expression related to hedonic and eudaimonic dimensions of well-being. Having closely examined both their claims and their data, we draw substantially different conclusions. After identifying some important conceptual and methodological flaws in their argument, we report the results of a series of reanalyses of their dataset. We first applied a variety of exploratory and confirmatory factor analysis techniques to their self-reported well-being data. A number of plausible factor solutions emerged, but none of these corresponded to Fredrickson et al.'s claimed hedonic and eudaimonic dimensions. We next examined the regression analyses that purportedly yielded distinct differential profiles of gene expression associated with the two well-being dimensions. Using the best-fitting two-factor solution that we identified, we obtained effects almost twice as large as those found by Fredrickson et al. using their questionable hedonic and eudaimonic factors. Next, we conducted regression analyses for all possible two-factor solutions of the psychometric data; we found that 69.2% of these gave statistically significant results for both factors, whereas only 0.25% would be expected to do so if the regression process was really able to identify independent differential gene expression effects. Finally, we replaced Fredrickson et al.'s psychometric data with random numbers and continued to find very large numbers of apparently statistically significant effects. We conclude that Fredrickson et al.'s widely publicized claims about the effects of different dimensions of well-being on health-related gene expression are merely artifacts of dubious analyses and erroneous methodology.

genomic perspectives | leukocytes | transcriptional response | epigenetics

In their article that has captured the attention and interest of the popular media, such as *The Economist* (1) and CNN (2), Fredrickson et al. (3) claimed to have shown that specific genomic factors for human health are differentially associated with "hedonic" and "eudaimonic" well-being, interpreting their results as suggesting that the way in which individuals seek happiness may have detrimental or beneficial effects on their physical health. Nowhere is this better expressed than in a press article that reported Fredrickson et al.'s findings as having demonstrated that "people who are happy but have little to no sense of meaning in their lives—proverbially, simply here for the party—have the same gene expression patterns as people who are responding to and enduring chronic adversity" (4, para 14). Given the apparent importance of their findings, which appeared to amount to nothing less than a true breakthrough in behavioral genomics research, we eagerly and with great earnest read the article with the hope that science might finally have been able to illuminate true pathways to "the good life" (or at least help to divert people from a not so good life). Unfortunately, what we encountered did not strike us as a breakthrough. In fact, after an extensive reanalysis of Fredrickson et al.'s data, we concluded that their study suffers from numerous problems that render its conclusions unfounded and potentially misleading. In this article, we would like to share our criticisms so that the reader can make an informed decision about the real meaning and value for science of the study of Fredrickson et al.

This article is organized into three sections. The first summarizes what we perceive as some of the theoretical and general methodological shortcomings of the study of Fredrickson et al. (3); it was our observation of these issues, and our consequent skepticism about the plausibility of the authors' findings, that led us to conduct our detailed reanalyses of their data. The second and third sections focus on two specific statistical problems: the factor analysis of the measure of well-being used by Fredrickson et al. and their use of multiply-iterated regressions to test for the differential relations of hedonic and eudaimonic well-being to gene expression. For the sake of brevity, in the present article, we limit our critique to that part of their article that Fredrickson et al. described as their primary analysis; i.e., the examination of the relationship between well-being and 53 conserved transcriptional response to adversity (CTRA) genes; we do not discuss their secondary analysis, where the Transcription Element Listening System (TELiS) database was used to derive information about purported differential effects of hedonic and eudaimonic well-being across the entire genome. We anticipate, however, that the publication of the present article might lead other researchers to examine this secondary analysis in detail; the *SI Appendix* contains the results of some preliminary examinations of one aspect of that part of the study of Fredrickson et al., which suggest that it may also have considerable problems.

Significance

This article critically reanalyzes the work of Fredrickson et al. [Fredrickson BL, et al. (2013) *Proc Natl Acad Sci USA* 110 (33):13684–13689], which claimed to show that distinct dimensions of psychological well-being are differentially correlated with levels of expression of a selection of genes associated with distinct forms of immune response. We show that not only is Fredrickson et al.'s article conceptually deficient, but more crucially, that their statistical analyses are fatally flawed, to the point that their claimed results are in fact essentially meaningless. We believe that our findings may have implications for the reevaluation of other published genomics research based on comparable statistical analyses and that a variant of our methodology might be useful for such a reevaluation.

Author contributions: N.J.L.B. and D.A.M. performed research; N.J.L.B. contributed new reagents/analytic tools; N.J.L.B. and D.A.M. analyzed data; and N.J.L.B., D.A.M., M.P.S., H.L.F., and J.C.C. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

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This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1407057111/-/DCSupplemental.

Theoretical and Methodological Issues

Based on their view that "psychological well-being has been shown to forecast future physical health above and beyond its association with current physical health. . .and above and beyond its association with reduced levels of stress, depression, and other negative affect states" (p. 13684), Fredrickson et al. set out in their study (3) to identify "molecular signaling pathways that transduce positive psychological states into somatic physiology" (p. 13684). Although we do not object to the basic intent of their study—in fact, we see their goals as laudable, because the emergent field of epigenetics has provided compelling reason to see behavior and experience as having a determining influence on gene expression (5)—we are critical of Fredrickson et al.'s vagueness in conceptualization and presumed directionality of effect. Other than abductively attributing possible evolutionary significance to a presumed link between positive psychological states and a set of candidate genes implicated in physiological stress response, the authors provided virtually nothing in terms of a theoretically informed directional model to guide their investigation (e.g., at the most basic level, there is no clear statement as to whether the researchers see positive states as determining gene expression or vice versa) and, ultimately, the interpretation of their results. For example, the claim made by Fredrickson et al. that hedonic well-being is associated with reports of subjective happiness but is, unbeknownst to people, tied to lack of well-being in other areas of functioning (e.g., physical well-being) is a finding that is actually consistent with research on positive illusions/self-serving bias/self-enhancement bias, a phenomenon that is well documented and has even been characterized as adaptive (6–8). Consequently, their project is reduced to a nebulous and largely exploratory correlational study without any solid founding in available theory and research.

More problematic, however, is the difficulty with the conceptualization of positive psychological states that Fredrickson et al. (3) defined in terms of eudaimonic and hedonic well-being. There are two salient weaknesses here. First, despite their assertion of conceptual uniqueness but concurrent acknowledgment of the correlatedness and reciprocal influence of eudaimonic and hedonic well-being on each other, they appeared to give little consideration as to whether well-being represents a state (i.e., a transient aspect of behavior and experience) or a trait (i.e., a more pervasive and stable aspect of behavior and experience) construct. Given our understanding of these constructs, eudaimonic well-being, generally defined (including by Fredrickson et al.) in terms of tendencies to strive for meaning, appears to be trait-like, because such striving for meaning is typically an ongoing life project, in the sense of Sartre (9). Conversely, hedonic well-being, typically defined in terms of a person's (recent) affective experiences, appears to be state-like; regardless of the level of meaning in one's life, everyone experiences good and bad days. Notwithstanding our speculation, the lack of clarity and precision regarding well-being as a state vs. trait is unfortunate because it readily translates into potential methodological challenges for a study on functional genomics. For example, if well-being is a state, then a person's level of well-being will change over time and perhaps at a very fast rate. If we only measure well-being at one time point, as Fredrickson et al. did, then unless we obtain a genetic sample at the same time, the likelihood that the well-being score will actually and accurately reflect level of genomic expression will be diminished, if not eliminated.

Second, even though the eudaimonic and hedonic well-being constructs have a venerable history in philosophy and psychology, they by no means capture the richness and complexity of the well-being construct domain as manifested in the extant literature. This conceptual limitation leads us to question whether there is a scientifically adequate definition and taxonomy of well-being on which to do research in the first place. The scope of this difficulty becomes painfully obvious when one considers the various incarnations of well-being concepts proffered by several researchers, including general well-being, subjective well-being, psychological well-being, ontological well-being, spiritual well-being, religious well-being, existential well-being, chaironic well-being, emotional well-being, and physical well-being, along with the various constructs that are treated as essentially synonymous with well-being, such as self-esteem, life satisfaction, and, lest we forget, happiness.

Departing from theoretical concerns and focusing briefly on methodological weaknesses, there are three things about the study of Fredrickson et al. (3) that seem to us to merit explicit mention here. First, the sample consisted of just 80, mostly white American adults. (The sample size in the publicly available dataset is, in fact, less than 80; the consequences of this are discussed in more detail in *SI Appendix*.) Although the authors acknowledged that "replication of these findings in other populations...will be required to gauge generality and consistency of these effects" (3, p. 13687), this potential lack of generality was not reported in the majority of reports of this work in major popular new outlets. Also, given the number and type of statistical analyses that were conducted and the number of variables involved, such a small sample size considerably limits the statistical power of the study, especially when running a large number (i.e., 53) of independent regressions with a large number (10) of predictor variables. Second, the assessment of well-being was completed through the single administration of one self-report measure, and biological samples were obtained at only one time for all participants. Ostensibly, such a state of affairs raises the specter of potential issues with response bias and confounding situational influences on both self-reported data and biological samples. To give just one example, we doubt whether an inventory of minor health problems over the preceding 2 wk constitutes an adequate control for the possible effects of an ongoing infectious condition on the expression of genes associated with immune system response. Third, the choice of 53 human genes out of some 20,000 potential candidates appears to be based almost exclusively on the prior opinion of one of the authors of the article by Fredrickson et al., who is also the author or a coauthor of all of the works cited by Fredrickson et al. in support of their selection of genes. In addition, the decision to apply a weighting of exactly 1.00 or −1.00 to the regression coefficients associated with each of these genes, thus assigning an identical magnitude of effect to every gene, seems to be completely arbitrary. A recent article (10) found the human transcriptome to be extremely complex, with >100,000 distinct transcripts coding for around 20,000 protein-coding genes. In that context, the gene expression model assumed by the authors appears to be rather simplistic.

We turn now to the first of two statistical aspects of the study of Fredrickson et al. (3) for which we performed an extensive reanalysis of their data: the factor analysis of the measure of well-being they used.

Problems with the Factor Structure of the Short Flourishing Scale

Fredrickson et al. (3) measured well-being using an instrument that they named the Short Flourishing Scale, although this seems to have previously been referred to in the literature as the Mental Health Continuum-Short Form (MHC-SF) (11). According to Keyes (12), the MHC-SF assesses three forms of well-being: emotional well-being (items SF1–SF3), social well-being (items SF4–SF8), and psychological well-being (items SF9–SF14). This 3D structure has been confirmed in empirical studies (11, 13). In an Appendix describing the technical details of the scoring of the MHC-SF, Keyes (12) applied the word "hedonic" to the first factor and "eudaimonic" (or "positive functioning") to the second and third, and indicated that a person's "flourishing" status depends on

how many items from each of these two groups are experienced with a minimum specific frequency. However, this split of the MHC-SF items into hedonic and eudaimonic categories appears to have been made principally to simplify the instructions for diagnosing persons as flourishing; we were not able to identify any published evidence supporting an underlying psychometric factor in which the previously empirically demonstrated emotional and social well-being factors combined into one. Indeed, we note that Keyes et al. (11) referred to these groupings of hedonic and eudaimonic items as "clusters," an ostensibly neutral term that seems to deliberately avoid the word "factor." Nevertheless, Fredrickson et al. (3) implied, and Cole and Fredrickson (14) stated explicitly, that a factor analysis of the psychometric data from the MHC-SF in their study revealed just two distinct factors (hedonic and eudaimonic), corresponding to Keyes' (12) "diagnostic question" categories (i.e., items SF1–SF3 for hedonic and SF4–SF14 for eudaimonic).

Even though the factor structure of the MHC-SF that Cole and Fredrickson (14) claimed to have obtained deviates from what has previously been reported for the scale in the published empirical literature and is thus already a cause for concern, what specifically raised a red flag for us is the high degree of correlation between the hedonic and eudaimonic factors (i.e., $r = 0.79$, $P < 0.0001$), as pointed out by Coyne (15). In conventional psychometric research, such a high intercorrelation would be interpreted as suggesting that the two constructs are essentially measuring the same thing. Interestingly, although acknowledging the high correlation, Cole and Fredrickson (14) argued, based on the observed reliabilities for the two factors, that about 30% of the variance of each factor is unique and can be used to explore the novel associations of the two forms of well-being to genomic expression. Unfortunately, although their use of their reliabilities to establish how much unique systematic variance remains is not in itself erroneous, their assumption that the 30% of variance is all reflective of meaningful construct variance may be seen as without solid footing. Research has demonstrated that method bias, which is systematic, is pervasive and can have deleterious effects on research findings (16).

Notwithstanding the above issues, we took it upon ourselves to use the data from the study of Fredrickson et al. (3) to complete our own exploratory and confirmatory factor analyses to examine the internal structure of the test. Although we only summarize our findings here, the results of these analyses are reported in detail in *SI Appendix*.

In the exploratory factor analyses (EFAs), which we ran using different extraction (e.g., principal axis, maximum likelihood) and rotation (orthogonal, oblique) methods, we found two factors with eigenvalues greater than 1 with all items producing a loading of 0.50 on at least one factor. Examination of factor loading coefficients consistently showed that the first factor was comprised of elevated loadings from items SF1, SF2, SF3, SF4, SF5, SF9, SF10, SF11, SF12, SF13, and SF14, whereas the second factor housed high loadings from items SF6, SF7, and SF8. Examination of item content to devise labels for the factors led us to name the first factor "personal well-being" (PWB) and the second factor—comprised of those MHC-SF items that ask for the respondent's opinions about society, rather than personal introspection "evaluative perception of the social environment" (EPSE). Thus, our EFA findings show that, although it appears that the MHC-SF does seem to emulate a two-factor structure, the distribution of high item loadings across the factors does not conform to what Cole and Fredrickson (14) reported, nor to what other published studies have found (11, 13).

Considering next our confirmatory factor analyses (CFAs), we tested one- and two-factor models to see if the construct of well-being as operationalized by the MHC-SF best fits different theoretically defendable expressions of well-being [e.g., general well-being vs. hedonic and eudaimonic well-being, with items assigned to each factor as per Cole and Fredrickson (14)]. In the two-factor model, the latent constructs of hedonic and eudaimonic well-being were permitted to intercorrelate. In all CFAs, factor loadings for all items were found to be statistically significant at $P < 0.05$ or lower. For the one-factor model, goodness-of-fit statistics indicated grossly inadequate fit [$\chi^2 = 227.64$, $df = 77$, goodness-of-fit index (GFI) = 0.73, comparative fit index (CFI) = 0.83, root-mean-square error of approximation (RMSEA) = 0.154]. Although the equivalent statistics for the correlated two-factor model were slightly better, they still came out as poor ($\chi^2 = 189.40$, $df = 76$, GFI = 0.78, CFI = 0.87, RMSEA = 0.135). Thus, even though our findings tended to support the view that well-being is best represented as at least a 2D construct, they did not confirm the claim of Fredrickson et al. (3) that the MHC-SF produces two factors conforming to hedonic and eudaimonic well-being. Extending from this, we are sure that the reader can appreciate the implications this holds for the study of Fredrickson et al.—if the only measure used to operationalize well-being does not demonstrate factorial validity in a manner consistent with the theory underlying the test, then any analyses and associated assertions based on those analyses are rendered highly suspect in their scientific value. As Ryff and Singer (17) put it, "Lacking evidence of scale validity and reliability, subsequent work is pointless" (p. 276).

As our last point of comment, and perhaps the most significant, we now consider the regression analyses performed by Fredrickson et al. (3).

Problems with the Regression Analyses

Fredrickson et al. (ref. 3, p. 13685 and pp. 1–2 of SI Text) described their method of analysis that led to their principal result—namely, that the expression of CTRA genes differs as a function of their two purported well-being dimensions—as follows:

> General linear model analyses quantified the association between expression of each of the 53 CTRA contrast genes and levels of hedonic and eudaimonic well-being [each well-being dimension treated as a continuous measure and adjusted for correlation with the other dimension of well-being and for age, sex, race/ethnicity, body mass index (BMI), smoking, alcohol consumption, recent minor illness symptoms, and leukocyte subset prevalence...]. Contrast coefficient-weighted association statistics were averaged to summarize the magnitude of association over the entire CTRA gene set.

Specifically, the sequence of operations constituting the procedure described above is the following:

i) For each of the 53 CTRA genes of interest (ref. 3, p. 1 of SI Text), an ordinary least-squares linear regression is performed with the gene expression value as the dependent variable. The predictor variables in this regression are, first, the seven demographic variables [age, sex, race (white/nonwhite), body mass index, alcohol consumption yes/no, smoking yes/no, and number of recent minor illness symptoms]; second, the expression levels of the eight control genes (*CD3D*, *CD3E*, *CD4*, *CD8A*, *CD19*, *FCGR3A*, *NCAM1*, and *CD14*); and third, the two standardized (*z*-scored) values of the purported hedonic (SF1–SF3) and eudaimonic (SF4–SF14) factors from the psychometric data.

ii) The above regression generates coefficients for each of the 17 predictor variables, of which the 2 of interest are those for the hedonic and eudaimonic factors. These two coefficients are independently summed, after having first been multiplied by −1 in the case of the 34 genes that are expected to be down-regulated in the CTRA.

iii) The average coefficient for the hedonic and eudaimonic factors—representing the difference in gene expression attributable to each of these factors—is determined by dividing the respective sums, obtained in step 2, by the number of CTRA genes (i.e., 53).

iv) The averaged coefficients from step 3 are tested for a statistically significant difference from zero using a one-sample *t* test. The null hypothesis is that there is no difference between the average gene expression differences attributable to hedonic and eudaimonic well-being (ref. 3, p. 2 of SI Text).

Our first reaction to this description was one of surprise that Fredrickson et al. apparently expected to generate meaningful results when analyzing 17 independent variables using just 80 cases. As Tabachnik and Fidell put it: "The cases–to–IVs ratio has to be substantial or the solution will be perfect—and meaningless" (ref. 18, p. 123). These authors give an equation ($50 + 8m$, where m is number of independent variables), suggesting that the minimum number of cases required in this study for would be at least 186.

We also consider this process—which we refer to henceforth as "RR53," for regression repeated 53 times—to be unnecessarily complicated. It seems to us that it would be far simpler to regress the scores for hedonic and eudaimonic well-being on the average expression of the 53 genes of interest, after changing the sign of the values of those genes that were expected to be down-regulated. This approach would appear to correspond closely to Fredrickson et al.'s (3) statement that "[T]he goal of this study is to test associations between eudaimonic and hedonic well-being and average levels of expression of specific sets of genes" (ref. 3 p. 1 of SI Text); it would also have the advantage of greatly reducing the number of dependent variables being predicted from the sample size of 80 participants. We conducted a number of such regressions, using different methods of evaluating the average level of expression of the 53 CTRA genes of interest (e.g., taking the mean of their raw values, or the mean of their *z*-scores), but in all cases, the model ANOVA was not statistically significant. We therefore set out to analyze and understand in more detail how the RR53 regression procedure could, in contrast to our naive regressions, be producing such highly significant results.

Our first step was to apply the RR53 procedure to reproduce Fredrickson et al.'s figure 2 (3), showing the associations between hedonic well-being and up-regulated CTRA genes, eudaimonic well-being and down-regulated CTRA genes, and the split of these two overall plots into three gene subsets. During this process, which we performed with SPSS version 18 (and calibrated against several other software packages; *SI Appendix*), we noticed that a substantial number of the regression models for the CTRA genes had a nonsignificant model ANOVA ($P > 0.05$ in 22 of 53 cases). Furthermore, the *t* tests for the regression coefficients corresponding to the predictor variables of interest, namely hedonic and eudaimonic well-being, were almost all nonsignificant ($P > 0.05$ in 104 of 106 cases; mean $P = 0.567$, SD = 0.251), and in the two remaining cases (gene *FOSL1*, for both hedonic, $P = 0.047$, and eudaimonic, $P = 0.030$), the overall model ANOVA was not statistically significant ($P = 0.146$). We believe that to draw any conclusions from these coefficients is inappropriate. (The RR53 procedure appears to be exquisitely sensitive to even the smallest variations in the data. Readers are invited to consult *SI Appendix* for further details.)

Having reproduced Fredrickson et al.'s principal result (3), and also having become aware of the alternative factor structure described in the previous section of the present article, we next proceeded to apply the same statistical techniques to the PWB/EPSE factor pair. We therefore created two new variables, which we named PWB (corresponding to items SF1–SF5 and SF9–SF14) and EPSE (corresponding to items SF6–SF8). When we applied Fredrickson et al.'s regression procedure using these variables as the two principal predictor variables of interest (replacing the hedonic and eudaimonic factor variables), we discovered that the effects of this factor pair were about twice as high as those for the hedonic and eudaimonic pair (PWB: up-regulation by 13.6%, $P < 0.001$; EPSE: down-regulation by 18.0%, $P < 0.001$; *SI Appendix*, Figs. S3 and S4). We found this result rather curious, as it suggests that the participants' genes are not only expressing "molecular well-being" (ref. 3, p. 13688), but apparently also, and even more vigorously, some other response that we presume Fredrickson et al. might call "molecular social evaluation."

Curious as to what else these genes might be able to tell us, we wrote a program in R to analyze the effect of applying the RR53 procedure to every possible way of splitting of the psychometric data items SF1–SF14 into two pseudofactors, which we then used in the RR53 procedure in place of the hedonic and eudaimonic factors from Fredrickson et al.'s original analysis (3). Excluding duplicates due to symmetry, there are 8,191 possible such combinations. Of these, we found that 5,670 (69.2%) gave statistically significant results using the method described on pp. 1–2 of SI Text of ref. 3 (i.e., the *t* tests of the fold differences corresponding to the two elements of the pair of pseudofactors were both significant at the 0.05 level), with 3,680 of these combinations (44.9% of the total) having both components significant at the 0.001 level. Furthermore, 5,566 combinations (68.0%) generated statistically significant pairs of fold difference values that were greater in magnitude than Fredrickson et al.'s (3, figure 2*A*) hedonic and eudaimonic factors.

Although one possible explanation of these results is that differential gene expression is associated with almost any factor combination of the psychometric data, with the study participants' genes giving simultaneous molecular expression to several thousand factors that psychologists have not yet identified, we suspected that there might be a more parsimonious explanation. Therefore, as a further test of the validity of the RR53 procedure, we replaced Fredrickson et al.'s psychometric data (3) with random numbers (i.e., every item/respondent cell was replaced by a random integer in the range 0–5) and reran the R program. We did this in two different ways. First, we replaced the psychometric data with normally distributed random numbers, such that the item-level means and SDs were close to the equivalent values for the original data. With these pseudodata, 3,620 combinations of pseudofactors (44.2%) gave a pair of fold difference values having *t* tests significantly different from zero at the 0.05 level; of these, 1,478 (18.0% of the total) were both statistically significant at the 0.001 level. (We note that, assuming independence of up- and down-regulation of genes, the probability of the latter result occurring by chance with random psychometric data if the RR53 regression procedure does indeed identify differential gene expression as a function of psychometric factors, ought to be—literally—one in a million, i.e., 0.001^2, rather than somewhere between one in five and one in six.) Second, we used uniformly distributed random numbers (i.e., all responses were equally likely to appear for any given item and respondent). With these white noise data, we found that 2,874 combinations of pseudofactors (35.1%) gave a pair of fold difference values having *t* tests statistically significantly different from zero at the 0.05 level, of which 893 (10.9% of the total) were both significant at the 0.001 level. Finally, we reran the program once more, using the same uniformly distributed random numbers, but this time excluding the demographic data and control genes; thus, the only nonrandom elements supplied to the RR53 procedure were the expression values of the 53 CTRA genes. Despite the total lack of any information with which to correlate these gene expression values, the procedure generated 2,540 combinations of pseudofactors (31.0%) with a pair of fold difference values having *t* tests statistically significantly different from zero at the 0.05 level, of which 235 (2.9% of the total) were both significant at the 0.001 level.

Thus, in all cases, we obtained far more statistically significant results using the methods of Fredrickson et al. (3) than would be predicted by chance alone for truly independent variables (i.e.,

$0.05^2 \times 8{,}191 \sim 20$), even when the psychometric data were replaced by meaningless random numbers. To try to identify the source of these puzzling results, we ran simple bivariate correlations on the gene expression variables, which revealed moderate to strong correlations between many of them, suggesting that our significant results were mainly the product of shared variance across criterion variables. We therefore went back to the original psychometric data, and scrambled the CTRA gene expression data, reassigning each cell value for a given gene to a participant selected at random and thus minimizing any within-participants correlation between these values. When we reran the regressions with these data, the number of statistically significant results dropped to just 44 (0.54%).

To summarize, even when fed entirely random psychometric data, the RR53 regression procedure generates large numbers of results that appear, according to these authors' interpretation, to establish a statistically significant relationship between self-reported well-being and gene expression. We believe that this regression procedure is, simply put, totally lacking in validity. It appears to be nothing more than a mechanism for producing apparently statistically significant effects from nonsignificant regression coefficients, driven by a high degree of correlation between many of the criterion variables. In particular, there is no reason to believe that the result shown in Fredrickson et al.'s figure 2*A* (3) demonstrates any relationship between hedonic and eudaimonic well-being on the one hand and differential gene expression on the other.

Conclusion

In this article, we highlighted the myriad problems with the study of Fredrickson et al. (3), which range from theory and conceptualization, to measurement, and to statistics and interpretation of findings. As we said at the beginning, we do not fault these authors for wanting to study the relationship of psychological constructs with functional genomics. However, given the remarkable claims made by Fredrickson et al., as well as the attention their findings have garnered in the popular media, we believe it is vitally important that researchers, practitioners, and laypersons alike should be made aware of the deficiencies of their study and, in particular, of their statistical analyses, which appear to have conjured nonexistent effects out of thin air. For positive psychology to move into the health arena in a responsible way (19), the research on which advice is based must be rigorous and must avoid giving false hope or even causing iatrogenic harm. It seems to us that Fredrickson et al.'s study falls far short of the level of responsible scholarship required in promoting human health and well-being.

ACKNOWLEDGMENTS. We thank Dr. Jim Coan, Dr. Nora Egan Demers, Dr. Andy Field, Dr. Tanya Hart, Neuroskeptic, Dr. Stuart J. Ritchie, and Dr. Rob Summers for valuable contributions to the discussions that took place before and during the writing of this article, as well as a number of researchers who preferred to remain anonymous. We also thank Dr. Steven Cole for his prompt reply to our request for clarification of some issues in Fredrickson et al.'s article and SI Text. This research was not supported by any public or private grants.

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