LETTER

Reply to Coyne: Genomic analyses are unthwarted

In his comment on our PNAS article (1), Dr. Coyne suggests that statistical analysis is untenable when predictor variables are correlated and that it is important to control for potential confounding (2). These issues were each effectively addressed by the standard linear statistical models we used to quantify associations between leukocyte gene expression and well-being while controlling for potential confounders (exactly the approach recommended in Coyne's reference 3). In particular, the following issues are addressed:

i) Are hedonic and eudaimonic scale scores interchangeable? We addressed this possibility through exploratory and confirmatory factor analyses of the items measuring hedonic and eudaimonic well-being. Consistent with previous observations (e.g., references 6, 14, and 27 from original article), both analyses rejected a single common factor solution in favor of a two-factor solution (in the latter case, difference, $P < 0.0001$). Noninterchangability is also evident from the fact that ~92% of the total variance in each scale's scores represents systematic (true score) variance (Cronbach's $\alpha = 0.93$ for hedonic and 0.92 for eudaimonic), whereas the 0.79 correlation between scales implies that shared variance accounts for ~62% (r^2) of the variance on either scale alone. Thus, ~30% of the total variance in each scale's scores reflects unshared systematic variation. These results show that the two scales measure different things and that those two things are partially correlated under natural conditions.

ii) Might the correlation between hedonic and eudaimonic well-being lead to erroneous conclusions? We addressed this possibility in a reparameterized analysis of gene expression reported in the Results, paragraph 4 (1). If eudaimonic and hedonic scales were truly interchangeable, then only their shared variance (the sum, eudaimonic + hedonic) would systematically correlate with gene expression, and their unique/unshared variance (the difference, eudaimonic – hedonic) would reflect only random measurement error and would not correlate systematically with gene expression. Neither was the case. Gene expression associated only with the difference, and the sum and difference variables were not highly correlated (1). Even in the presence of correlated predictor variables and control for confounders, the general linear model parameter estimates we used are well established (3) to remain unbiased, and their *P* values remain accurate. [Correlated predictors and multiple covariates increase the sampling variability of point estimates, but their SEs adjust appropriately (3). Correlated predictors might potentially lead to conservative false-negative errors in statistical testing, but they would not induce false-positive errors.] Thus, there is no reason for concern that the standard multivariate analyses we used led to inaccurate conclusions.

iii) How were covariates selected? Covariates were selected a priori, and no other covariates were explored. Selection was based on previously observed associations with leukocyte gene expression profiles and inflammation (4–6) and the potential to associate with well-being in real-world contexts.

iv) Has this study "settled" the relative merits of hedonic and eudaimonic well-being? On this point, we agree with Coyne. No single investigation could do so. The Discussion notes that the present results are limited in several respects and should motivate additional research on the psychological and biological correlates of distinct facets of human well-being.

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The authors declare no conflict of interest.

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