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Positive Mental Well-Being and Immune Transcriptional Profiles in Highly Involved Videogame Players

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Abstract

Previous research has identified a link between experiencing life as meaningful and purposeful—what is referred to as "eudaimonia"—and reduced expression of a stress-induced gene profile known as the "conserved transcriptional response to adversity" (CTRA). In the current study, we examine whether similar links between eudaimonic well-being and CTRA reduction occur in a sample of 56 individuals with a particularly strong engagement with virtual worlds: avid online videogame players. Results consistently linked higher eudaimonic wellbeing, and more specifically the social well-being subdomain of eudaimonia, to lower levels of CTRA gene expression. That favorable psychobiological relationship between eudaimonia and CTRA appeared most strongly among individuals reporting high levels of positive psychosocial involvement with gaming. Findings are consistent with the hypothesis that committed social/recreational activity may help damp CTRA expression especially among persons who are already experiencing some kind of threshold of positive eudaimonic experience.

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Keywords

Social genomics; online games; eudaimonia; well-being; biocultural anthropology

1. Introduction

Previous research has identified a link between experiencing life as meaningful and purposeful—*eudaimonia*—and reduced expression of a stress-induced gene profile known as the "conserved transcriptional response to adversity" (CTRA) (Fredrickson et al., 2015, 2013). The CTRA profile is induced in immune cells (leukocytes) by activation of fight-or-flight stress responses from the sympathetic nervous system (Heidt et al., 2014; McKim et al., 2018; Powell et al., 2013), and involves up-regulated expression of genes involved in inflammation and down-regulation of genes linked to innate antiviral responses and antibody production (Cole, 2014, 2017, 2019). In the current study, we examine whether similar links between eudaimonic wellbeing and CTRA reduction occur in a population of individuals with a particularly strong engagement with virtual worlds: avid online videogame players.

Beyond Frederickson et al.'s research, other subsequent studies set the stage for our own inquiry by having identified in various settings associations between higher eudaimonic well-being and reduced CTRA, including in the context of individuals' sense of the meaning of their work and increased feelings of social interdependence in a Tokyo-based IT firm (Kitayama et al., 2016); in a population-representative sample of older American adults (Cole, Levine, et al., 2015); in breast cancer survivors initiating a stress-reduction program (Boyle et al., 2019); and in Southern Californian adults experimentally assigned to undertake pro-social "acts of kindness" toward specific others compared to individuals in a neutral control group (Nelson-Coffey et al., 2017). Differential CTRA activity may potentially contribute to the favorable health effects associated with positive psychological well-being, as eudaimonic dimensions such as having purpose in life and experiencing personal growth have also been linked to increased longevity across adult life (Hill and Turiano, 2014; Steptoe et al., 2015; Zaslavsky et al., 2014). More broadly, these findings are also consistent with research connecting reduced CTRA to other positive psychological processes including cognitive-behavioral stress management (Antoni et al., 2012), and to lifestyle practices such as yoga, meditation, mindfulness, and Tai Chi (Black et al., 2013; Bower et al., 2014; Creswell et al., 2012; Irwin et al., 2014). Such research suggests that experiencing life and social relationships as meaningful might favorably affect health, particularly given that elevated CTRA is associated with increased risk of several disease states (Cole, 2013, 2019; Cole, Capitanio, et al., 2015; Knight et al., 2016; Simons et al., 2017). Notably, throughout this research literature, only the "eudaimonic" rather than "hedonic" dimensions of positive psychological well-being—i.e., well-being involving transcendence of immediate self-gratification toward purposeful, meaningful, and pro-social goals, rather than simply high positive emotion and felt happiness (Kahneman et al., 1999; Ryan and Deci, 2001; Steptoe et al., 2015)—have been reliably linked to this reduction in CTRA expression.

Positive engagement with highly valued goals in the context of belonging to a community of online videogamers who share those goals has also been shown to constitute a key path to enhanced eudaimonic well-being (Carras et al., 2018; Jones et al., 2014). Of direct relevance to eudaimonia, gamers report that their play gives them the feeling of belonging to something bigger than themselves (McGonigal, 2011), with a "gamer" identity often perceived as central to players' self-concepts and sense of purpose in life (Castronova, 2008; Nardi, 2010; Snodgrass et al., 2012, 2017a; Taylor, 2009; Turkle, 2011). In some cases, gaming worlds allow gamers to pursue alternate gendered, racial, sexual, and appearance- and age-based identities that are somewhat (though not entirely) separated from so-called "real life" (Yee, 2014), providing players with cathartic breaks from the stresses and strains of offline existence (Snodgrass, Dengah, Lacy, & Fagan, 2013; Snodgrass et al., 2012, 2014; Yee, 2006a, 2006b, 2006c). Such identity, purpose, and stress relief typically unfold in the context of gaming-specific social relationships, which give players a sense of connection that can relieve loneliness (Schiano, Nardi, Debeauvais, Ducheneaut, & Yee, 2014; Snodgrass, Bagwell, et al., 2018). As such, some researchers have proposed that online games can have the same role as taverns or coffeehouses that came before by serving as congregational "third places" between the first space of home and the second of work (Steinkuehler and Williams, 2006). Gaming with offline friends has also been shown to be associated with more positive online gaming experiences (Snodgrass, Lacy, Francois Dengah, & Fagan, 2011), as has belonging to in-game social groupings ("guilds") common in some games (Longman, O'Connor, & Obst, 2009; Nardi, 2010; Snodgrass, Batchelder, et al., 2016; Snodgrass, Lacy, et al., 2016). Summing up concisely this and other videogame research, one group put it recently: "We propose that videogames, by their very nature, have design elements aligned with attributes of well-being, and that playing videogames can provide opportunities for flourishing mental health" (Jones et al., 2014, p. 3).

In the current study, we hypothesized that gamers who generally experience higher *endaimonic* well-being in their lives will show lower levels of CTRA (H1), and, following current theory, that we'd find distinctive contributions from both *social* (H1a) and *psychological* (H1b) dimensions of eudaimonia (Fredrickson et al., 2015, 2013; Keyes, 2009; Lamers et al., 2011; Turkle, 2011). Related, research shows that gaming challenges leads to feelings of accomplishment and positive emotions, which contribute to online games' *hedonic* fun and pleasures (Charlton & Danforth, 2007; Koster, 2013; McGonigal, 2011; Snodgrass et al., 2013, 2012; Snodgrass, Lacy, Dengah II, Fagan, & Most, 2011; Yee, 2006b, 2006c). However, based on the Frederickson et al. (2013, 2015) studies—and also on subsequent research identifying relationships only between eudaimonia and CTRA, and not between hedonia and CTRA—we did not expect hedonic well-being to be associated with CTRA decreases in our gaming context (H2). Finally, given that gaming itself can produce eudaimonic feelings of meaning and social connection, we explored in a research question whether the negative (i.e., favorable) association between eudaimonia and CTRA would be stronger for more heavily involved gamers (RQ1). That is, we anticipated something like a "dosage" effect, with more intensive forms of online gaming involvement associated with greater improvements in CTRA. We didn't frame this as a hypothesis given that no current study had yet to identify associations specifically between *internet- or gaming-related eudaimonia* and reduced CTRA.

Overall, the present study aims to expand our understanding of how the biological correlates of eudaimonia might appear among individuals who participate in intensive recreational subcultures such as videogaming. Such activity is widespread among contemporary young adults, and for a substantial proportion forms the center of their social lives and (“gamer”) identity (e.g., Jones et al., 2014; Schiano et al., 2014; Snodgrass et al., 2018a, 2016a; Steinkuehler and Williams, 2006), just as recreations like music, athletics, hiking, and so forth do for others. As such, videogaming may be associated with psychosocial conditions that link to mental and physical well-being. As discussed above, previous scholarship on well-being and CTRA has focused on individuals’ involvements in personally and socially meaningful activity—work, pro-social acts of kindness, lifestyle practices such as yoga, meditation and mindfulness. We wanted to test whether eudaimonic activity experienced in online play-based environments—of substantial importance as a contemporary form of recreation and personal expression—also manifest in similarly altered immune system regulation.

2. Materials and Methods

2.1. Participants

In the context of a study of avid videogamers, we interviewed and drew blood from 58 gamers who had reported a range of positive and negative play experiences (Snodgrass, Dengah II, et al., 2018). We recruited them from among the respondents to a prior questionnaire study of ours (N=404) conducted in Colorado and Utah by identifying and contacting individuals in that sample who scored in the top and bottom quartiles (N=202) on a previously developed Positive and Negative Gaming Experiences Scale (PNGE-42) (Snodgrass et al., 2017a). By drawing from both ends of the continuum, this procedure was intended to maximize variability in participants’ gaming experiences. We invited all persons in those top and bottom quartiles to provide blood and to meet with us for additional interviewing. We met with and obtained data from 58 out of 202 persons who responded positively to our invitation. The original survey respondents had been previously recruited from local internet gaming clubs and other networks of ethnographic informants in two university communities in Utah and Colorado between January 2016 and October 2016. All participants provided informed consent prior to participation, and all procedures were approved by the Institutional Review Board of Colorado State University. Two blood-draw individuals were later eliminated due to inadequate transcriptome data, as described further below.

2.2. Blood Spot Collection Protocol

Standard dried blood spot collection procedures were used (McDade et al., 2007). Researchers conducted the blood collection and in-person interviews at a time and location of the participant’s choosing (e.g., homes, libraries, offices, university labs, etc.). Lancets were used to prick the ring or middle fingertips, and draw approximately 5 drops of blood (~50μL) that were collected onto Whatman (#903) filter paper cards. The blood was allowed to dry onto the filter paper before being stored in an airtight plastic bag, with a desiccant to complete the drying process. Blood spot samples were stored in a secure freezer (−30°C) until being shipped to the UCLA Social Genomics Core Laboratory for gene expression analysis.

2.3. Transcriptome Profiling

We conducted genome-wide transcriptional profiling of dried blood spots using methods previously described (Snodgrass, Dengah II, et al., 2018) and validated as showing good correspondence to results from gold standard venipuncture blood samples for the bioinformatic quantities analyzed here (e.g., CTRA profile) (Kohrt et al., 2016; McDade et al., 2016). Briefly, RNA was mobilized out of filter papers using a standard RNA stabilization buffer (Qiagen RLT), extracted using standard methods (Qiagen RNeasy), converted to fluorescent cDNA (NuGEN PicoSL), and hybridized to Illumina Human HT-12 v4 BeadArrays following the manufacturer's standard protocol in the UCLA Neuroscience Genomics Core Laboratory. Two participants' samples yielded insufficient RNA and were dropped from further analyses. The remaining 56 samples were assayed in a single batch and yielded valid results according to standard quality assurance methods (e.g., median probe fluorescence intensity >80 units). The microarray-based transcriptome profiling approach used here did not require any normalization to a specific internal housekeeping control because the quantile-based data normalization employed at the outset of data analysis (see below) standardizes total assayed RNA levels across samples at the level of the whole transcriptome (Bolstad et al., 2003).

2.4. Other Measures

Measurements other than the transcriptome data (including self-reports of gaming experiences) were collected as part of participants' initial online survey, with additional information (such as mental well-being and BMI) collected in face-to-face meetings along with the blood-draw.

2.5. Regression Analysis

2.5.1. CTRA indicator genes—The primary outcome analyzed in this study was a contrast computed over 53 previously specified CTRA indicator genes (Fredrickson et al., 2015, 2013), including 19 pro-inflammatory genes (*IL1A, IL1B, IL6, IL8, TNF, PTGS1, PTGS2, FOS, FOSB, FOSL1, FOSL2, JUN, JUNB, JUND, NFKB1, NFKB2, REL, RELA, RELB*) that serve as positive indicators of the CTRA profile, and 34 genes involved in Type I interferon responses (*GBP1, IFI16, IFI27, IFI27L1-2, IFI30, IFI35, IFI44, IFI44L, IFI6, IFIH1, IFIT1-3, IFIT5, IFIT1L, IFITM1-3, IFITM4P, IFITM5, IFNB1,IRF2, IRF7-8, MX1-2, OAS1-3, OASL*) and antibody synthesis (*IGJ, IGLL1, IGLL3*), which were reverse-scored to reflect their role as inverse indicators of the CTRA profile (Fredrickson et al., 2015, 2013). Quantile-normalized transcript abundance values for each gene were $\log_2$-transformed to stabilize variance, sign-adjusted as noted above to reflect the CTRA profile, and summed to create a single composite CTRA indicator score (Fredrickson et al., 2015, 2013). Random variations in Illumina BeadArray production resulted in missing determinations of *IL1B, IFI15,* and *IFITM1* RNA levels for some samples (Illumina Inc., 2011), so we conservatively deleted all data for these genes (rather than attempting to impute missing values), resulting in a 50-gene CTRA score in the confirmation study.

2.5.2. Mental well-being measures—Mental well-being, our main predictor, was assessed with the Mental Health Continuum-Short Form (MHC-SF), a 14-item self-report measure (Keyes, 2009; Lamers et al., 2011). This scale has been widely used in research on well-being in general, as well as its more specific relation to CTRA, and was specifically designed to measure the hedonic and eudaimonic dimensions of mental well-being. Respondents are asked to rate the frequency they experienced various positive cognitions on a 6-point Likert scale (1=never, 2=once or twice, 3=approximately once per week, 4=two or three times per week, 5=almost every day, and 6=every day). While the 14 items function satisfactorily as together as a scale, it also includes 3 correlated dimensions: 1.) 3-item *hedonic* well-being (happiness, interest in life, life satisfaction) and 2.) 11-item *eudaimonic* well-being, with the latter composed of i.) 5-item *social* well-being (respondents feel that they contribute to society, that they belong to a community, that society is becoming a better place, that people are good, and that society makes sense) and ii.) 6-item *psychological* well-being measure (respondents feel that they like most parts of their personality, are good at managing daily responsibilities, have warm and trusting relationships with others, have challenging growth experiences, are confident thinking and expressing their own ideas and opinions, and that their lives have direction and meaning). In our analyses, following common practices in previous work (e.g., Fredrickson et al., 2015, 2013), these items were was scored in three different ways: 1.) total mental well-being (14 items), defined by the sum of all items' scores: hedonic (3 items), social (5 items), and psychological (6 items) well-being; 2.) eudaimonic well-being (11 items), scored as the sum of social (5 items) and psychological (6 items) well-being; 3.) separately scored subscales of hedonic (3 items), social (5 items), and psychological (6 items) well-being. All scale scores—that is, the MHC-SF-14 and all its subscales—possessed acceptable reliability as assessed by Cronbach's alpha coefficients>.80.

2.5.3. Positive Videogame Involvement—To explore how videogame involvement might change the relationship between CTRA and mental well-being (assessed via the MHC-SF's various sub-scales), we categorized individuals as belonging to either a high (N = 13) or low (N = 43) "Positive Gaming Involvement" group. This grouping was based on four factors, the first of which was an ethnographically developed Gaming Involvement 15-item scale, which is theoretically grounded in Yee's tripartite motivational framework and grew out of an earlier systematic interview analysis (Snodgrass et al., 2017). The 15 involvement items included three questions for each of Yee's gamer motivations (*achievement*, *social*, and *immersion*), to which we had originally added additional questions about general *involvement* (commitment of time, energy, and effort to gaming) and also what we referred to as "*engagement*" (motivated and passionate gaming). Based on triangulation with our ethnographic and interview data, we included individuals in the high Positive Gaming Involvement group who: 1.) Scored in the top tercile of our 15-item Gaming Involvement scale; 2.) Played at least 10 hours per week; 3.) Assessed their play as overall positive (as a balance of 21 self-reported positive compared to 21 negative gaming experiences (Snodgrass et al., 2017, 2018b)); and 4.) Did not qualify as overly "addicted" to videogames, i.e., did not have scores 28 or above on the Internet Gaming Disorder Scale, short form of 9-items (IGDS-SF9) (Pontes and Griffiths, 2015; Snodgrass et al., 2018b). The low Positive Gaming Involvement group included individuals not meeting all four of these criteria, and who thus were less intensively and less positively involved with videogames.

2.5.4. Covariates—Standard covariates used in our regression analysis were collected from participants after the blood draw, including gender, age, and state of residence (Utah=0, Colorado=1). Estimated body mass index was collected through self-reported height and weight. Alcohol consumption was collected as recalled reports of daily consumption during an average week, coded as either more than two drinks per day vs. fewer.

2.5.5. Analytical procedures—Following the approach of previous studies, CTRA gene expression composite scores were used as response variables in linear model analyses quantifying the associations of CTRA gene expression with key predictors (MHC-SF and Positive Videogame Involvement) and controls (gender, age, BMI, and alcohol consumption). We first examined relationships between CTRA indicator genes and mental well-being (H1 and H2), followed by analysis of whether the relationship between CTRA and the mental well-being indicators was stronger for more heavily involved gamers (RQ1). Given our relatively limited sample size, it was advisable to limit the number of covariates in linear model analyses, in order to minimize biases due to model overfitting.

2.6. Ancillary Analysis

To better understand the composition of our high and low Positive Gaming Involvement groups (and thus the nature of the RQ1 interaction effects described above), we compared these two groups' levels of self-reported social support, using data collected from their original survey responses. Here, we adapted a 4-item version of a previously validated Interpersonal Support Evaluation List (ISEL), with us asking respondents if they had people they could turn to offline and online for help with their problems, for advice, conversation, or with whom they simply enjoyed spending time (Cohen and Hoberman, 1983). This created two 4-item scales, one for offline support, the other for online support, with items in each rated along a 5-point scale (1=strongly disagree, 2=disagree, 3=neutral, 4=agree, and 5=strongly agree). Each scale was summed first separately, and then together, with higher values indicating greater perceived social support. The Offline Social Support scale showed good internal consistency with a Cronbach's alpha of 0.91. Similarly, Online Social Support had an alpha of 0.84, and the combined Offline and Online Social Support scale an alpha of 0.85.

Further, we assessed whether respondents felt societal support or lack of support for their videogame play. For this, we asked respondents whether they agreed that mainstream society, the media, gamer and non-gamers friends, family members, significant others, and various other categories of persons they knew supported gaming as a "positive and even healthy" activity (for each item, 1=strongly disagree, 2=disagree, 3=neutral, 4=agree, and 5=strongly agree). These 10 questions were summed into a Social Norm Support scale, with higher scores showing more perceived social support for gaming (alpha=0.66). (See Appendix A for more detail on our study's measures.)

3. Results

3.1. Descriptive Statistics

Table 1 gives descriptive statistics for key control and mental well-being variables considered in our analysis, first for the sample as a whole and then separately for each of the study's two involvement groups (high/low Positive Gaming Involvement). There, we see that location (Utah vs. Colorado) had no relation to high/low Positive Gaming Involvement. Nor did this location variable show significant bivariate correlations with our key predictors, and it was thus excluded from further analysis. By contrast, we see modest associations between participant gender, age, and BMI and Positive Gaming Involvement, with each of these controls, along with alcohol consumption, included in analyses reported here. (None of our controls showed bivariate relationships with the MHC-SF scale and various sub-scales).

3.2. Regression Analyses: Mental Well-Being and CTRA

3.2.1. Total mental well-being and CTRA—Among the 58 individuals from whom we collected blood samples, 56 yielded valid transcriptome profiles and had data available for all indicator variables analyzed. Of primary interest in this study are differences in expression of the 50-gene CTRA indicator score in relationship to our key measures of mental well-being, which appear in Table 2. Model 1 shows relationships to gender, age, BMI, and alcohol consumption, which were weak in our sample. Controlling for these four variables, total mental well-being (MHC-SF-14 items) was associated with significantly reduced CTRA expression (Table 2: Model 2). (Note that all continuous predictor variables as well as the CTRA outcome were used in standardized form in the regression models, facilitating their interpretation). Thus, in Model 2, we see that a one SD change in MHC-SF-14 was associated with a little over a one-third of a SD reduction in predicted CTRA.

3.2.2. Eudaimonic and hedonic well-being and CTRA (H1 and H2)—To determine whether these associations reflected the eudaimonic or hedonic well-being items, or both, follow-up analyses examined CTRA associations with the 11-item eudaimonia scale (combined social and psychological well-being) and the 3-item hedonia scale entered as separate variables. Results supported H1 in linking lower levels of CTRA gene expression to general eudaimonic well-being (Table 2: Model 3). In that analysis, a one SD change in the 11-item eudaimonia measure was associated with more than a half a SD decrease in CTRA (Model 3). By contrast, this analysis revealed no reliable association of CTRA gene expression with hedonic well-being (also Model 3), supporting H2.

3.2.3. Social and psychological dimensions of eudaimonia and CTRA (H1a, H1b, and H2)—In more detailed follow-up analyses (Table 2: Models 4-7), we wanted to clarify relationships between CTRA and the mental well-being sub-scales. We first examined CTRA's associations with the 3-item hedonic well-being scale, the 5-item social well-being scale, and the 6-item psychological well-being scales analyzed simultaneously along with the controls (Table 2: Model 4). In that analysis, the social well-being measure's standardized coefficient (−0.358) was largest among those three sub-scales, though its p-value (p=0.077) was above a conventional 0.05 level.[1] The hedonia and psychological well-being sub-scales' standardized coefficients in that analysis were comparatively less substantial (0.192 and −0.216 respectively), and did not show statistical significance, again in part due to these scales' intercorrelations (also Model 4).

We then examined relationships between CTRA and the 3-item hedonia measure, alongside the controls, finding this relationship to be insubstantial (B=−0.153 (non-sig), Adj R^2= −0.03) (Table 2: Model 5). By contrast, when considered alongside the controls and hedonia, the social well-being measure displayed a strong relationship with CTRA (B=−0.429, Adj R^2=0.09) (Table 2: Model 6), as did the psychological well-being sub-scale, though it was less substantial (B=−0.377, Adj R^2=0.03) (Table 2: Model 7).[2]

Overall, these analyses pointed to the stand-alone importance of both the social and psychological dimensions of eudaimonia in predicting CTRA (H1a and H1b), though with a stronger contribution from social eudaimonia in this particular context. Throughout these follow-up analyses, we again found no reliable association of CTRA gene expression with hedonic wellbeing (Models 4-7), consistent with H2.

3.3. Social Well-Being, Positive Gaming Involvement, and CTRA (RQ1)

To test RQ1, we examined the interaction of the 5-item social eudaimonia scale (as the previous results indicated it as driving eudaimonia's relationship to CTRA) with Positive Videogame Involvement, with CTRA as the outcome. Comparing Models 4 and 5 in Table 3, we see that allowing for a different association between Social Well-Being and CTRA, depending on level of Positive Gaming Involvement (INV), as in Model 5, fit the data much better, more than doubling the value of the R^2 The regression coefficients indicated a weak and negative association of Social Well-Being with CTRA when Positive Gaming Involvement (INV) was low (−0.161 + [−0.789 * INV=0] = −0.161), but a substantial

[1]The 5-item social and 6-item psychological sub-scales of eudaimonia are highly correlated with each other (R^2=0.592, p<<.001), and also with hedonia (respectively, R^2=0.523, p<<.001 and R^2=0.676, p<<.001), as would be expected given these three sub-scales were developed to assess related dimensions of overall mental well-being (measured via the MHC-SF-14). However, we monitored the effects of multicollinearity using variance inflation factors (VIFs) and none exceeded the standard threshold for significant multicollinearity (typically 10 in the statistical literature) (Chatterjee and Hadi, 2012). We show here a table of variance inflation factors (VIF) for key predictors, calculated using the predictors of Model 4, Table 2. Neither the largest VIF of 2.43 nor the mean VIF of 1.56 indicate a problem, following common rules of practice (Chatterjee and Hadi, 2012).

Variable	VIF
Psych WB	2.43
Hedonic WB	2.20
Social WB	1.75
Alcohol	1.22
Age	1.16
BMI	1.11
Male	1.10
Mean VIF	1.56

[2]For example, compared to Table 2's Model 5, including the social component of eudaimonia alongside the controls and hedonia added substantial explanatory power to the model (Table 2: Model 6), as did the inclusion of psychological well-being with hedonia and the control variables (Table 2: Model 7). However, the inclusion of social compared to psychological eudaimonic well-being was larger both in terms of the social eudaimonia sub-scale's relationship to CTRA (B=−0.429 compared to −0.377) and the model's overall explained variance (0.09 vs. 0.03, or 3X the explained variance).

negative (i.e., favorable) association in the high Positive Gaming Involvement group (−0.161 + [−0.789 * INV=1] = −0.95) (Table 3: Model 5). The effect of being in either the high or low Positive Gaming Involvement groups was also quite small when levels of Social Well-Being (SWB) were near the (standardized) mean of zero (−0.09 + [−0.789 * SWB=0] = −0.09), indicating that at low (+/−) levels of Social Well-Being, Positive Gaming Involvement had little effect on CTRA levels. But at values of Social Well-Being that departed from the mean, high Positive Gaming Involvement did show marked association with CTRA. For example, if Social Well-Being was at 1.0 SD *below* the mean, persons in the high as opposed to low Positive Gaming Involvement group were predicted to have CTRA *elevated* about 0.7 SD (−0.09 + [−0.789 * SWB=−1.0] = +0.7). At the other end, among persons with Social Well-Being at 1.0 SD *above* the mean, persons in the high as opposed to low Positive Gaming Involvement group were predicted to have a CTRA score *reduced* by 0.88 SD (−0.09 + [−0.789 * SWB=1.0] = −0.88).

Figure 1 shows the bivariate relationship of Social Well-Being with CTRA separately for the low/high Positive Gaming Involvement groups, with scatterplots showing actual CTRA scores in the two groups. (Note that analysis without the outlier seen in the bottom right of Figure 1 continued to yield similar parameter estimates and effect sizes, although statistical significance declined to p=0.070 after removing this most probative test of the RQ1 hypothesis.[3])

3.4. Ancillary Analysis: Positive Gaming Involvement and Social Support

Finally, returning to Table 1, in ancillary analysis, we see that the high and low Positive Gaming Involvement groups had comparable scores on *all* the mental well-being scales. Because of how we constructed high and low Positive Gaming Involvement, the high involvement group scored higher on that involvement measure and also on hours gamed per day, positive gaming experiences, and balance of positive compared to negative gaming experiences. However, those two groups showed no substantial differences in either negative or addictive gaming experiences, as assessed via our ethnographically developed scale and the IGDS-SF9, thus auguring against the possibility that the CTRA-involvement relation reflects the role of addictive experience. A noteworthy difference is that the high Positive Gaming Involvement group reported experiencing substantially more Online Social Support, combined Offline and Online Social Support, and also Social Norm Support related to their gaming, which might plausibly be linked to CTRA expression.

4. Discussion

Research links life stress and mental disorders such as depression and PTSD to compromised and dysregulated immune function (Mehta et al., 2018; Ross et al., 2019), including to *increased* CTRA (Chiang et al., 2019a, 2019b). Research has also begun to

[3]In analysis without that case, regression coefficients continued to show a weak and negative association of Social Well-Being with CTRA when Positive Gaming Involvement (INV) was low (−0.159), but a substantial negative association in the high Positive Gaming Involvement group (−0.646). Thus, for the high Positive Gaming Involvement individuals in this analysis, a one SD change in Social Well-Being was associated with an almost two-thirds SD reduction in predicted CTRA—a substantial effect, even after having removed this individual who provides particularly relevant test of the research question (RQ1). Further, this case does not appear to represent an outlier due to measurement error because qualitative interview data verified that this individual was healthy, well-adjusted, and socially active, with highly involved videogame play contributing positively to his mental well-being.

show how *positive* practices can instill resilience to the negative linked psychological and genomic responses to stress (Mason et al., 2019; Panter-Brick et al., 2019). In the present study, in a sample of young adults deeply engaged in a play-based subculture (videogaming), we confirm a small but growing body of research that links high levels of positive mental well-being specifically to *reduced* expression of CTRA indicator genes (Boyle et al., 2019; Cole et al., 2015b; Fredrickson et al., 2015, 2013; Kitayama et al., 2016; Nelson-Coffey et al., 2017). In our study, that favorable psychobiological relationship appeared among individuals reporting high levels of positive psychosocial involvement with gaming (i.e., high subjective achievement, social connection, immersion, commitment of time, energy, and effort, and passion/motivation). Among those with low levels of positive involvement with videogames, eudaimonic well-being showed a weaker and nonsignificant negative association with CTRA gene expression. Viewed more broadly, these findings would be consistent with committed social/recreational activity having desired damping effects on CTRA expression only among persons who are already experiencing some kind of threshold level of positive eudaimonic experience.

Also of interest is that the specific subdomain of eudaimonia that showed this pattern most substantially involved *social* well-being, or individual perceptions of their surrounding socio-cultural milieu as one they belong to and understand, find positive and improving, and to which they can personally contribute. This is consistent with previous evidence on the importance of social involvement for CTRA gene expression (e.g., Kitayama et al., 2016; Nelson-Coffey et al., 2017), and research indicating the intensely social aspect of positive engagement in videogame subculture (Snodgrass et al., 2017, 2018b). In that sense, the socio-cultural modification of individual psycho-biological relationships in the American videogamers sampled here could be seen as a kind of recreational analogue to the workplace patterns of eudaimonic experience and its relation to CTRA among Japanese IT workers (Kitayama et al., 2016).

Further analysis of differences between the high and low Positive Gaming Involvement groups showed that the high positive involvement gamers reported that they experienced more online and overall social support, and also were more likely to perceive that those around them judged videogaming to be a generally positive and healthy activity. This echoes a growing body of research pointing to the typically social nature of online play (Carras et al., 2018; Jones et al., 2014; McGonigal, 2011; Schiano et al., 2014; Snodgrass et al., 2011; Snodgrass et al., 2018a, 2016a, 2016b; Steinkuehler and Williams, 2006). In our view, this ancillary analysis, along with prior research, helps explain the high positive gaming involvement group’s greater CTRA “sensitivity” to social well-being: for this group, finding gaming personally meaningful may sensitize them to the favorable effects of external social support and positive social evaluation on their own internal “molecular well-being” (i.e., making positive social evaluation more personally meaningful, and perhaps also enhancing the impact of negative social evaluation, relative to individuals who invest less personal value in gaming involvement, although the latter dynamic is more speculative in these data; Figure 1).

Some have argued that connections between videogaming and flourishing mental health (Jones et al., 2014)—and specifically the way they “provide users with eudaimonic benefits of confidence, social connection, personal growth, and opportunities for employment or even leadership” (Carras et al., 2018, p. 7)—could offer benefits for mental health treatment, in particular for veterans suffering from PTSD (Carras et al., 2018). Our study provides evidence that the eudaimonic well-being some videogamers experience might be linked to somatic and immunological changes as well, and thus at least potentially to reduced disease risks. However, we would not claim evidence for videogaming as a clinical tool, as do others in related research (Carras et al., 2018; Jones et al., 2014). In the current study, enhancement of CTRA advantages was most pronounced among high-involvement videogamers experiencing relatively *high* social well-being, but the latter is likely to be compromised among persons suffering from PTSD or some other clinical disorder (Hinton and Good, 2015; Young, 1997). As shown in our Figure 1, increases in social well-being are strongly associated with reduced CTRA only among *high* involvement videogame players. By contrast, at the *low* end of social well-being, high compared to low involvement videogamers actually have *higher* absolute levels of CTRA, and thus more *compromised* “molecular well-being.”

These findings parallel a well-known phenomenon whereby many psychological or emotional treatments are most effective to persons already experiencing some kind of emotional or cognitive advantage, which has been described elsewhere in the context of internet use and online videogaming as a “rich-get-richer” and “poor-get-poorer” effect (Desjarlais & Willoughby, 2010; Kraut et al., 2002, 1998; Selfhout, Branje, Delsing, ter Bogt, & Meeus, 2009; Snodgrass, Bagwell, et al., 2018; Snodgrass et al., 2014; Valkenburg & Peter, 2009). In fact, research suggests that for poorly functioning individuals the time spent in intensive gaming might take away from their ability to improve their lives, by connecting to offline others, for example (Snodgrass et al., 2011). For such psychosocially distressed individuals, intensive videogaming can signal distress (Kardefelt-Winther, 2014; Snodgrass et al., 2014)—and even an “addiction” that further erodes one’s well-being (Griffiths et al., 2016; Snodgrass et al., 2019)–rather than a potential therapeutic device. Overall, our study is consistent with the idea that videogaming as a therapeutic device would be most effective among the psychosocially healthy, with diminished and even reversed effects for those already suffering psychosocially.

4.1. Limits

This study is subject to several limitations, including a correlational study design, which precludes drawing definitive conclusions about the causal relationship among the variables examined. In fact, causality could be bidirectional or even reversed from the supposition that social play reduced CTRA expression. That is, higher CTRA might compromise the experience of mental well-being, and persons with lower CTRA might be psychosomatically healthy in ways that allow them to improve their social relations and thus also their eudaimonic well-being. Other limits include use of a convenience sampling strategy (rendering uncertain the generalizability of the present findings to the population in general or to other gamer subcultures) and absence of long-term follow-up on disease outcomes (so the health significance of the present gene expression effects remains to be defined in future research). Also, a limited sample size precludes any exploratory/discovery-oriented analysis of the genome-wide transcriptomic data and is only sufficient to test a priori-specified genomic hypotheses such as the association of a single pre-specified CTRA composite score with the psychosocial factors examined here. The sample size also meant that regression coefficients were somewhat less statistically reliable in the more exploratory analysis of interactions between social well-being, positive gaming involvement, and CTRA after having removed one individual with particularly high Social Well-Being scores and particularly low CTRA gene expression values. Despite these limitations, this study adds to an existing literature linking eudaimonia to measures of molecular well-being by underscoring the key role of play-based subcultures as a context for promoting the social aspects of eudaimonia that seem to play a central role in its biological impacts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

Higher gamer eudaimonia links to less genomic dysregulation of immune function (CTRA)

Social well-being is particularly strongly associated with reduced expression of CTRA

The eudaimonia CTRA association is strongest among the most highly involved players

Play may damp CTRA expression among persons already above a well-being threshold

The study is the first to link Internet-related wellness to immune system regulation

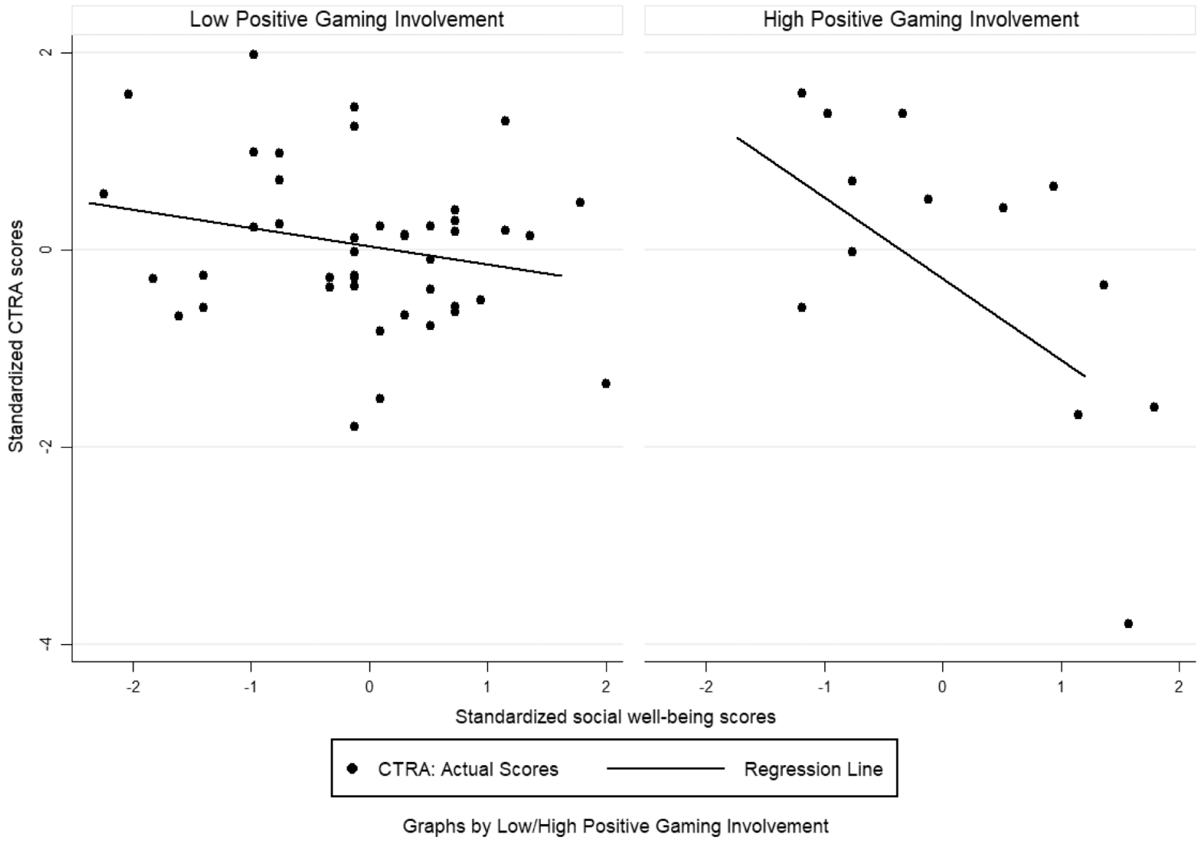

Figure 1:
Graph of CTRA (adversity) as a function of social well-being, by low/high positive gaming involvement.

Table 1:

Key variables: total sample; high/low positive gaming involvement.

Factor	Level	Total Sample	High Involvement	Low Involvement	p-value*
N		56	13	43	
Location	UT	23 (41%)	5 (38%)	18 (42%)	0.83
	CO	33 (59%)	8 (62%)	25 (58%)	
Regression Covariates					
1=Male	0	20 (36%)	2 (15%)	18 (42%)	0.081
	1	36 (64%)	11 (85%)	25 (58%)	
Age, mean (SD)		23.79 (4.15)	21.69 (2.29)	24.42 (4.40)	0.037
BMI, mean (SD)		24.38 (4.56)	26.34 (5.40)	23.79 (4.16)	0.076
1=Two or more drinks per day	0	52 (93%)	13 (100%)	39 (91%)	0.25
	1	4 (7%)	0 (0%)	4 (9%)	
Mental Well-Being Scales					
SWB-14, mean (SD)		62.13 (10.38)	61.54 (10.07)	62.30 (10.58)	0.82
SWB-11, mean (SD)		47.80 (8.58)	47.54 (8.95)	47.88 (8.57)	0.90
SWB-5 (social), mean (SD)		19.57 (4.73)	20.31 (5.22)	19.35 (4.62)	0.53
SWB-6 (psych), mean (SD)		28.23 (4.82)	27.23 (4.62)	28.53 (4.89)	0.40
SWB-3 (hedonia), mean (SD)		14.32 (2.39)	14.00 (1.78)	14.42 (2.56)	0.58
High/Low Positive Gaming Involvement Variables					
Involvement-15, mean (SD)		51.77 (13.22)	62.46 (2.73)	48.53 (13.44)	<0.001
Hours gaming/day, mean (SD)		2.96 (1.69)	4.08 (1.32)	2.63 (1.66)	0.006
Positive gaming XP-21, mean (SD)		75.27 (18.87)	92.54 (4.96)	70.05 (18.41)	<0.001
Negative gaming XP-21, mean (SD)		49.32 (15.38)	44.69 (7.00)	50.72 (16.94)	0.22
Positive - Negative XP-42, mean (SD)		25.95 (21.19)	47.85 (7.60)	19.33 (19.44)	<0.001
IGDS-SF9, mean (SD)		19.82 (7.57)	18.92 (3.48)	20.09 (8.44)	0.63
Ancillary Analyses					
Offline SS-4, mean (SD)		17.68 (3.52)	18.54 (1.85)	17.42 (3.87)	0.32
Online SS-4, mean (SD)		12.02 (5.07)	14.62 (4.91)	11.23 (4.91)	0.034
Offline + Online SS, mean (SD)		29.70 (7.28)	33.15 (5.13)	28.65 (7.55)	0.050
Social Norm Support, mean (SD)		31.09 (5.11)	33.54 (4.14)	30.35 (5.19)	0.048

*For all group tests, p-values are from Pearson's chi-squared (categorical variables) and ANOVA (continuous variables).

Table 2:

CTRA (adversity) gene expression as a function of covariates and mental well-being.

	Model 1 CTRA	Model 2 CTRA	Model 3 CTRA	Model 4 CTRA	Model 5 CTRA	Model 6 CTRA	Model 7 CTRA
Male (=1)	0.385(0.279)	0.333(0.279)	0.413(0.259)	0.411(0.263)	0.334(0.287)	0.393(0.257)	0.383(0.285)
Age	0.074(0.116)	0.112(0.118)	0.107(0.120)	0.109(0.122)	0.089(0.119)	0.109(0.113)	0.094(0.129)
BMI	−0.034(0.137)	−0.022(0.123)	0.015(0.134)	0.017(0.137)	−0.045(0.135)	0.010(0.138)	−0.017(0.130)
Alcohol (high=1))	−0.617(0.415)	−0.355(0.398)	−0.334(0.395)	−0.304(0.433)	−0.535(0.427)	−0.284(0.438)	−0.498(0.384)
MHC-SF (Total WB) (14 items)		−0.348(0.144)**					
Eudaimonia (Soc+Psy WB) (11 items)			−0.527(0.195)***				
Hedonia (3 items)			0.217(0.164)	0.192(0.169)	−0.153(0.126)	0.072(0.138)	0.122(0.173)
Soc WB (5 items)				−0.358(0.203)*		−0.429(0.185)**	
Psy WB (6 items)				−0.216(0.177)			−0.377(0.177)**
Constant	−0.203(0.209)	−0.187(0.209)	−0.249(0.201)	−0.248(0.202)	−0.172(0.211)	−0.232(0.193)	−0.218(0.219)
Adjusted R^2	−0.03	0.08	0.11	0.10	−0.03	0.09	0.03
N	56	56	56	56	56	56	56

* $p<0.1$;

** $p<0.05$;

*** $p<0.01$

[a] Cell entries represent the resulting linear model coefficients, with standard errors in parentheses. Standard errors were derived from a bootstrap procedure with 10,000 repetitions and used to calculate p-values from a t-statistic. In addition, CTRA and all continuous predictor variables have been standardized. Thus, all coefficients for continuous variables are interpretable as fully standardized slopes. Binary variables have not been standardized, so their coefficients are interpretable as y-standardized only.

Table 3:

CTRA (adversity) gene expression as a function of covariates and social well-being and positive gaming involvement, with the two key predictors considered in isolation from each other, together, and interacting.

	Model 1 CTRA	Model 2 CTRA	Model 3 CTRA	Model 4 CTRA	Model 5 CTRA
Male (= 1)	0.385(0.279)[a]	0.371(0.265)	0.452(0.281)	0.404(0.270)	0.404(0.244) *
Age	0.074(0.116)	0.113(0.112)	0.032(0.123)	0.091(0.115)	0.110(0.110)
BMI	−0.034(0.137)	0.001(0.131)	0.007(0.139)	0.021(0.138)	0.027(0.141)
Alcohol (high=1)	−0.617(0.415)	−0.278(0.426)	−0.663(0.418)	−0.309(0.417)	−0.537(0.375)
Soc WB (5 items)		−0.392(0.160) **		−0.383(0.155) **	−0.161(0.125)
Pos Gaming INV (high=1)			−0.305(0.481)	−0.153(0.410)	−0.090(0.367)
Pos Gaming INV X Soc WB (5 items)					−0.789(0.400) **
Constant	−0.203(0.209)	−0.216(0.198)	−0.171(0.207)	−0.199(0.201)	−0.168(0.190)
Adjusted R^2	−0.03	0.11	−0.04	0.09	0.21
N	56	56	56	56	56

* $p<0.1$;

** $p<0.05$;

*** $p<0.01$

[a] Cell entries represent the resulting linear model coefficients, with standard errors in parentheses. Standard errors were derived from a bootstrap procedure with 10,000 repetitions and used to calculate p-values from a t-statistic. In addition, CTRA and all continuous predictor variables have been standardized. Thus, all coefficients for continuous variables are interpretable as fully standardized slopes. Binary variables have not been standardized, so their coefficients are interpretable as y-standardized only.