



Cultures under stress: A cross-national meta-analysis of cortisol responses to the Trier Social Stress Test and their association with anxiety-related value orientations and internalizing mental disorders

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ABSTRACT

Acute cortisol changes are physiological indicators (i.e., biomarkers) of psychosocial stress that have been repeatedly assessed using standardized laboratory protocols like the Trier Social Stress Test (TSST). Despite this methodological standardization, however, cortisol stress responses vary considerably across different studies. Based on multilevel meta-analyses of 237 TSST studies ($n = 8487$ individuals), we demonstrate that ~25% of this variability is actually attributable to systematic differences between countries. Particularly North American and European studies show a remarkable effect disparity ($d = 0.45$ vs. $d = 0.73$, respectively).

Specifically, in-depth analyses suggested that the cultural orientation towards anxiety-related values in English-speaking countries (incl. the UK and Ireland) was associated with decreased cortisol stress responses. This finding was further supported by associations with the regionally varying prevalence of internalizing mental disorders (e.g., major depression or post-traumatic stress disorder) as reported by the WHO World Mental Health Surveys, a larger inequality of family incomes, larger population growth, larger expenses for health and the military, and lower tax rates. The size of these effects is comparable to the most important moderators of cortisol stress responses known to date, that is, male sex and higher age.

Based on these observations, we argue that the cortisol stress response may reflect the persistent threats in the sociocultural environment an individual is accustomed too. Highly competitive cultures emphasize the individuals' responsibility for socioeconomic prosperity, but simultaneously increase the collective population stress and thus lower sustainable ontogeny and resilience towards unexpected environmental adversity.

1. Background

The investigation of the predictors and health sequelae of psychological stress responses in humans was particularly facilitated by the development of standardized laboratory protocols during the last 50 years. In this regard, the Trier Social Stress Test (TSST, Kirschbaum et al., 1993) and its derivatives have arguably become the most popular tool for stress induction (e.g., Allen et al., 2014; Kudielka et al., 2007). This popularity of the TSST relates to its capability to reliably increase the secretion of pituitary-adrenal hormones such as cortisol, which is nowadays considered the major physiological indicator of psychosocial stress (Koolhaas et al., 2011).

Despite their methodological standardization, the numerous TSST studies published to date display a considerable degree of variability in their observed cortisol responses between different participant populations (Zänkert et al., in press). While part of this variability is

necessarily attributable to the mere randomness of participant sampling, a major portion of variance is caused by moderating factors that generate true variability (i.e., heterogeneity) of the cortisol response in the various TSST studies. With regard to substantial moderators, male sex and older age are the strongest predictors of larger cortisol stress responses known to date (Liu et al., 2017; Miller et al., 2018; Otte et al., 2005). With regard to methodological moderators, the mixed-sex composition of the TSST committee and their withholding of evaluative feedback robustly predict larger cortisol stress responses, but still the majority of between-study heterogeneity cannot be explained (Goodman et al., 2017). A specific manifestation of heterogeneity, that is, North American studies seem to report attenuated cortisol responses as compared to European studies, was recently discussed at the 44th annual conference of the International Society of Psychoendocrinology in Montréal (2014). Several factors such as the exposure to endocrine disrupting chemicals or other micropollutants (as for instance indicated

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by their regionally varying concentrations in municipal wastewater; Bolong et al., 2009; Luo et al., 2014) were mentioned as further candidate moderators that might drive these differences.

Surprisingly, however, the debate disregarded the possibility that cortisol responses to psychosocial stress exposure could as well be moderated by geo-cultural factors. Thus, the heterogeneity of the cortisol stress response could have been caused by a selection bias (e.g., Grimes and Schulz, 2002) that either attenuates or enhances the effectiveness of the TSST as a function of cultural variability across different study populations.

In order to enable a quantitative mapping of such geocultural similarities and differences, we started searching for reference data and discovered the cultural value orientations of Schwartz (2006). In addition to two cultural value dimensions postulated similarly in competing value theories, Schwartz (2006) reported data suggesting the existence of a third value dimension. This dimension reflects the tendency to organize social coexistence on the basis of harmony vs. values of power (see Section 2 for details) and uniquely discriminates between a preference of achievement- and power-oriented values in English-speaking countries and Israel as compared to the preference for the rather universalistic and benevolent values in many countries on the European mainland incl. Sweden, Finland, Germany, Italy, or the Czech Republic (Schwartz, 2006). Accordingly, these cultural reference data provided a suitable basis to derive predictions about the amplitude of cortisol stress response in TSST studies from culturally different populations.

2. Cultural value orientations in different countries

In general, values are defined as persistent and affect-laden beliefs that determine goals and motivate actions across different situations. Although each individual has its own preference for particular values, these values are commonly not independent from those of other individuals of the same social group. Thus, values can also serve as social norms that change very slowly across time. Concerning this particular function of values, the theory of cultural value orientations as proposed by Schwartz (2006) relies on and extends the two dominant intercultural value frameworks (cf. Hofstede, 2003; Inglehart and Baker, 2000). Due to the subtle nuances regarding its distinction to the cross-cultural theory of individual values (see Schwartz, 2011, for details), this section does not focus on the theorizing underlying the different cultural value orientations, but concisely presents the results of a large-scale international survey that provided evidence in favor of this theory. Thus, we emphasize that the herein chosen terms might deviate from those reported in the relevant literature and shall exclusively aid the interpretation of cultural values at the level of the populations that have been concurrently surveyed by Schwartz and exposed to the TSST.

The reference data for cultural values orientations that this article relies on were informed by the Schwartz Value Survey (SVS). From 1988 and 2007, the SVS was administered to students and schoolteachers from 80 different countries, who rated the relative importance of 56–57 annotated items describing guiding principles of their lives (e.g., humility, social justice, order, ambition). Based on 45 of these items, Schwartz (2006) compiled statistical evidence confirming seven different cultural value orientations that were predicted by his theorizing. Schwartz (2006) further proposed that these seven cultural value orientations could be mapped onto three non-orthogonal dimensions indicating that a cultural preference for specific values tends to be accompanied by a cultural depreciation of rather opposing values. He labeled these three cultural value dimensions:

(1) Autonomy (pleasure, exciting life, curiosity, creativity, freedom)¹

¹ Although Schwartz (2006) proposed that the autonomy pole of this dimension was primary indicated by value orientation towards affective

vs. Embeddedness (security, social order, politeness, obedience)
 (2) Egalitarianism (equality, responsibility, honesty, social justice, helpfulness) vs. Hierarchy (authority, humility, wealth, social power)
 (3) Harmony (environmental protection, peace, world of beauty, unity with nature) vs. Mastery (ambition, influence, daring, social recognition, independence)

The circular configuration of mutually opposing cultural value orientations along these value dimensions is illustrated in Fig. 1. Similar dimensions were also reported by other value theorists. For instance, dimension (1) primarily reflects the variance shared by the secular-rational + self-expression values vs. the tradition + survival values of Inglehart and Baker (2000). Thus, it reflects for the sociocultural transition from developing countries to industrial countries that is accompanied by higher economic performance (Inglehart and Baker, 2000). Dimension (2) covers additional variance of the self-expression vs. survival values, that is incrementally predictive of democratization and household size (Schwartz, 2006). Proceeding from these findings, the 21 countries in which TSST studies were conducted (Goodman et al., 2017) arguably form a rather selective sample of affluent, industrialized countries that similarly emphasize egalitarian and autonomy values (as indicated by the opaque vs. transparent flags in Fig. 1).

Dimension (3), by contrast, taps into cultural values that are not represented by other theoretical frameworks. These values are fairly uninformative of the socioeconomic trench represented by dimension (1) but reflect the endogenous cultural variation among the countries that afforded experimental stress research using the TSST (Fig. 1). There is a remarkable spread with regard to cultural values that scatter along the harmony-mastery dimension: Most countries on the European mainland (e.g., Finland, Sweden, Germany, Italy, France, Spain) plus French Canada combine their emphasis of egalitarianism and autonomy with a preference for harmony values. By contrast, English-speaking countries (e.g., Anglo Canada, the United States, the United Kingdom, and Ireland), Japan, and the German-speaking part of Switzerland cluster together because they rather seem to prefer mastery values.

In this regard, we considered it remarkable that the mastery pole of dimension (3) seems to be indicative of those egocentric values that supposedly “serve to cope with anxiety due to uncertainty in the social and physical world” (Schwartz, 2012). In other words, a preference for mastery values is adaptive group strategy that deals with an increased exposure to environmental threat by promoting individual power and accountability. This proposition is particularly interesting with respect to the likely between-country differences in the cortisol stress response, because it directly concerns those determinants of psychosocial stress that render the TSST an effective stress-induction protocol (Dickerson and Kemeny, 2004). Accordingly, a cultural preference for mastery values should also enable individuals to actively dampen their cortisol responses in stressful situations.

3. Anxiety and internalizing psychopathology in different countries

Blunted cortisol stress responses are often considered as indicative of a maladaptive coping with environmental threat based on repeated observations of decreased cortisol secretion in stressed participants suffering from anxiety disorders and major depression (i.e. internalizing psychopathology; Zorn et al., 2017). Given that cortisol stress responses probably vary systematically across countries, it would be reasonable to expect that the same applies to the prevalence of internalizing

(footnote continued)

autonomy, we decided to combine it with intellectual autonomy as both of these cultural value orientations highly correlated across the cultures in the reference dataset ($r = 0.76$).

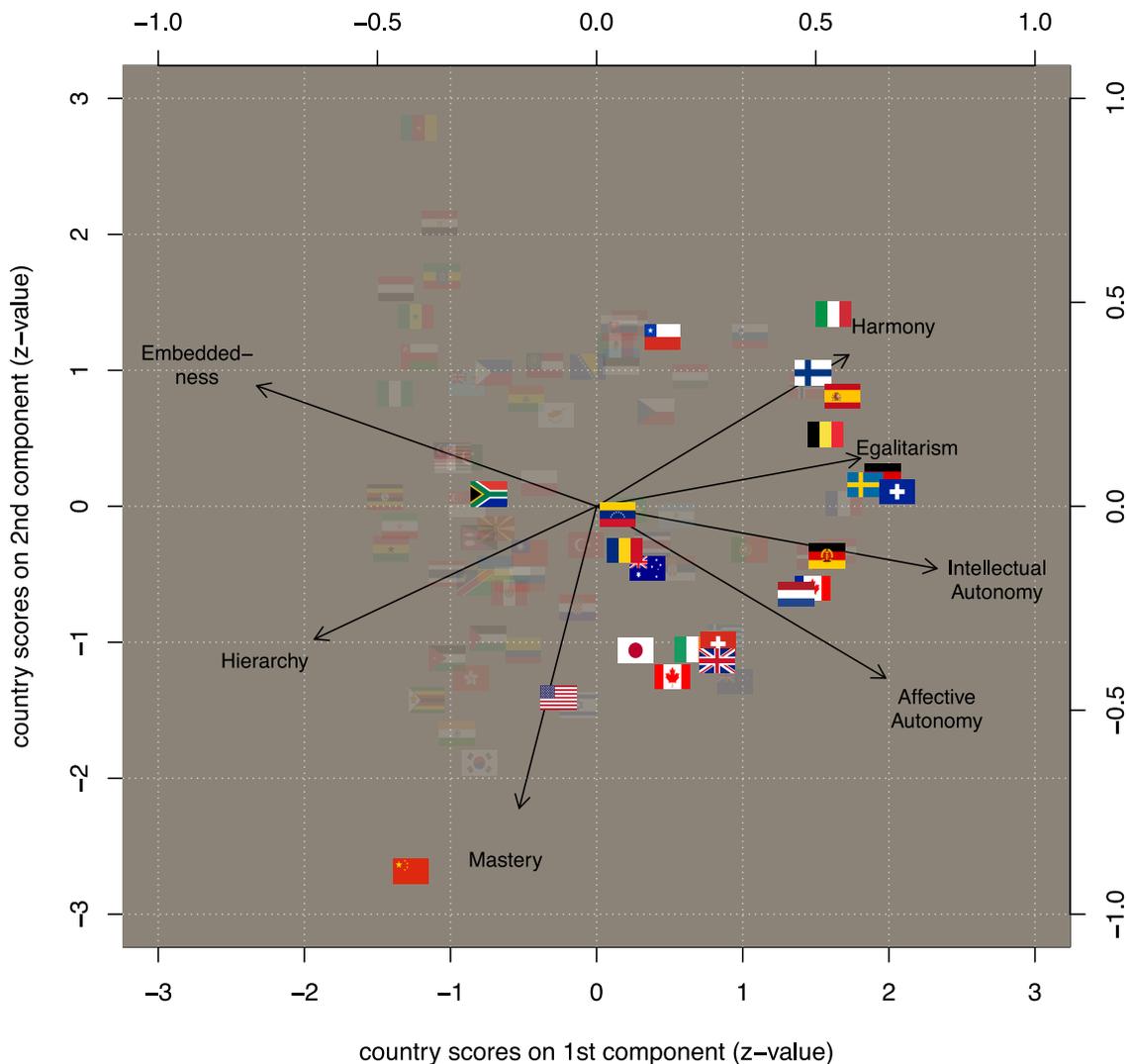


Fig. 1. Principal component biplot (Gabriel and Odoroff, 1990) based on reference data for the seven cultural value orientations compiled by Schwartz (2006). Flags represent the reference data of all 80 countries. Transparency indicates the countries for which no TSST data was available. French Canada and French Switzerland are indicated by blue coloring of the Canadian and the Swiss flag, respectively. Eastern Germany is indicated by the obsolete flag of the German Democratic Republic (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

psychopathology with higher rates in countries that emphasize anxiety-related mastery values (see Section 2). Consistent with this expectation, World Mental Health Surveys (Kessler and Ustun, 2014) recently reported higher prevalence rates for internalizing mental disorders in English-speaking countries (compiled in Table 1) that could mirror the population differences contributing to between-study heterogeneity in the TSST. A negative association of physiological stress responses and self-reported mental disorders would fit well to a decreased effectiveness of TSST in North America, but also suggests that the corresponding transition from blunted and very pronounced cortisol secretion may proceed gradually. Specifically, countries with an intermediate prevalence of internalizing symptomatology like the Netherlands, Belgium, or France, should report moderate cortisol stress responses. By contrast, countries with a low prevalence of internalizing symptomatology such as Germany, Italy, or China should report the largest cortisol stress responses. More importantly, however, such a finding would suggest that social norms have substantial implications for the burden of mental disorders around the world.

4. Meta-analysis of differences in cortisol responses to the TSST

Based on the data of Goodman et al. (2017) and Schwartz (2006), we set out to investigate the contribution of geo-cultural factors to the large between-study heterogeneity in cortisol responses to the TSST. Specifically, we first strived to confirm the anecdotal reports of heterogeneity in the cortisol response due to the country (or cultural region) of the TSST-conducting studies (see Section 1). Second, we hypothesized that such systematic between-country differences could be predicted by shared anxiety-based cultural values in the source population of the respective study (see Section 2). These analyses were complemented by inspecting the association of cortisol responses to the TSST and political, economic, and mental health characteristics of the contributing countries that also reflect variability in cultural values. In this regard, we also investigated the association between cortisol stress responses and the internationally varying prevalence of internalizing mental disorders (see Section 3).

Table 1
Selected 12-month prevalence (sorted by MDD in %) of various internalizing mental disorders as reported by the WHO Mental Health Surveys.

Country	MDD	PD	SAD	SP	GAD	PTSD
Romania*	1.5	–	1.0	3.3	0.2	0.4
Poland	1.6	–	0.9	2.5	0.5	–
China*	2.0	0.2	0.4	1.7	0.6	0.2
Japan*	2.4	0.3	0.7	2.3	1.2	0.4
Italy*	2.9	0.7	1.1	3.9	0.6	0.4
Germany*	3.1	0.7	1.5	6.9	0.5	0.5
Spain*	3.8	0.6	0.7	3.8	0.8	0.4
Australia*	4.8	1.8	4.2	–	3.6	–
Netherlands*	4.9	1.3	1.3	5.4	1.0	1.2
Belgium*	5.2	0.9	1.2	5.0	0.9	0.6
France	5.6	1.0	2.6	7.7	2.1	1.4
New Zealand	5.7	1.7	5.3	7.6	3.1	2.1
Israel	5.9	0.6	–	–	3.1	0.4
United States*	6.7	2.7	7.1	9.1	4.0	2.5
United Kingdom* (Northern Ireland)	8.8	–	4.0	7.2	2.8	3.8

Note. MDD = Major Depressive Disorder (Kessler et al., 2015), PD = Panic Disorder (De Jonge et al., 2016), SAD = Social Anxiety Disorder (Stein et al., 2017), SP = Specific Phobia (Wardenaar et al., 2017), GAD = Generalized Anxiety Disorder (Ruscio et al., 2017), PTSD = Post-Traumatic Stress Disorder (Karam et al., 2014), * at least one study reported TSST data from this country (Goodman et al., 2017).

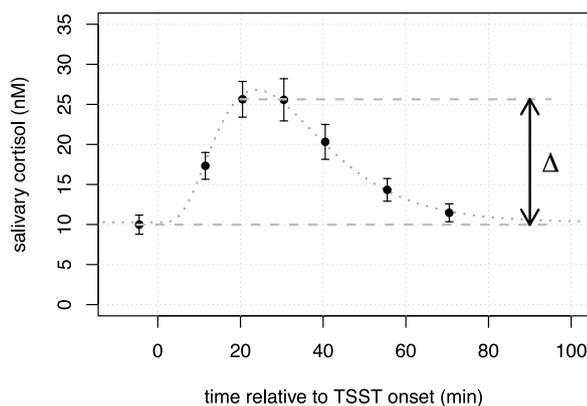


Fig. 2. Illustration of cortisol change in response to the TSST ($n = 100$ males; Miller et al., 2018). The unstandardized distance $\Delta = 15.7$ nM indicates the mean amplitude of the cortisol stress response in the sampled population. The differential scaling of cortisol concentrations across studies is accounted for by the standardization of Δ to the pooled between-subject variability $d = \Delta / SD = 1.79$.

4.1. Methods

4.1.1. Data extraction

To investigate between-country differences in cortisol stress responses to the TSST, we first updated² the meta-dataset compiled by Goodman et al. (2017). This dataset is comprised of aggregated cortisol data from a total number of $k = 237$ (sub)samples that were nested in $n = 186$ TSST studies. The outcome variable of these samples was defined as the standardized cortisol difference d between pre-TSST and post-TSST sampling occasions (baseline vs. peak levels; see Fig. 2). Missing information about the portion of males and the mean and dispersion of age in the respective sample were extracted from the

²Based on the original dataset, we repeated the extraction of sampling variances for samples with conspicuously large effects ($d > 2.5$). This reanalysis suggested that some of these large effects were inflated due to the standardization of the raw cortisol difference (Δ) by standard errors instead of standard deviations. Thus, we updated the corresponding effect estimates.

original study reports or imputed if possible (Hozo et al., 2005). Thereafter, we coded the continent, country, and region of all samples based on (a) explicit reports or (b) the affiliation of the respective corresponding authors.

We merged the resulting dataset with the reference data for the seven cultural value orientations provided by Schwartz (2006). The three cultural value dimensions were calculated as (1) mean of intellectual and affective autonomy minus embeddedness orientations, (2) egalitarianism minus hierarchy orientations, and (3) harmony minus mastery orientations as proposed by Schwartz (2006). Additionally, cross-cultural estimates of the 12-month prevalence of major depression (Kessler et al., 2015), panic disorder (De Jonge et al., 2016), social anxiety disorder (Stein et al., 2017), specific phobia (Wardenaar et al., 2017), generalized anxiety disorder (Ruscio et al., 2017), and post-traumatic stress disorder (Karam et al., 2014) were compiled based the WHO World Mental Health Surveys (Kessler and Ustun, 2004). Finally, we extracted the following country-level information from the World Factbook of the United States Central Intelligence Agency (CIA, 2016) that supposedly also reflect endogenous cultural differences between countries: population growth rate (%), birth rate (births per 1000 citizens), life expectancy at birth (years), prevalence of obesity in adults (%), gross domestic product (USD per capita), tax rate (% of GDP), public expenditures (% of GDP) for (a) health, (b) education, (c) military, inequality of the family income distribution (Gini index; Milanovic, 1997), and energy generated from renewable sources (% of total installed capacity).

4.1.2. Analytical methods

The sampling variances σ^2 of the compiled effect sizes d were estimated as outlined by Morris and DeShon (2002) assuming a correlation of $r = 0.5$ between baseline and peak cortisol concentrations. Based on these data, multilevel meta-analyses were performed using the *metafor* package (Viechtbauer, 2010) with R 3.4.2 statistical software (R Core Team, 2017).

Initially, we obtained a basic estimate of the mean TSST-related cortisol responses d that was adjusted for small-study effects (e.g., publication or measurement bias) by meta-regression on the sampling variance σ^2 (PEESE; Stanley and Doucouliagos, 2014). According to Carter et al. (2018), this method results in conservative effect estimates under conditions of very severe publication bias and questionable research practices. To account for further well-known sources of between-study heterogeneity in TSST studies, d was thereafter additionally regressed on the mean age of the sample (Miller et al., 2016; Otte et al., 2005), the relative portion of males (Liu et al., 2017), and the year of publication (Jennions and Møller, 2002). The full baseline model is given below where i denotes the respective study sample:

$$d_i \sim N(X\beta + u_i, \sigma_i^2)$$

$$X\beta = \beta_0 + \beta_1\sigma_i^2 + \beta_2AGE_i + \beta_3SEX_i + \beta_4YEAR_i$$

$$u_i \sim N(0, \tau^2)$$

The different residual sources of between-study heterogeneity τ^2 were quantified using restricted maximum likelihood estimation (REML): First, the dependency of different subsamples from the same study (due to shared study-level characteristics) was accounted by modeling a compound symmetric covariance structure. Second, the country-related portion of between-study heterogeneity was estimated and tested for significance.

Based on these analyses, a multistage gatekeeping procedure was used in combination with Bonferroni adjustments for multiplicity (Dmitrienko et al., 2008) to separately test for (1) differences in the cortisol stress response between North American vs. European countries, (2) associations with the seven cultural value orientations (Schwartz, 2006), and (3) the corresponding three cultural value dimensions. Moreover, associations between the cortisol stress response

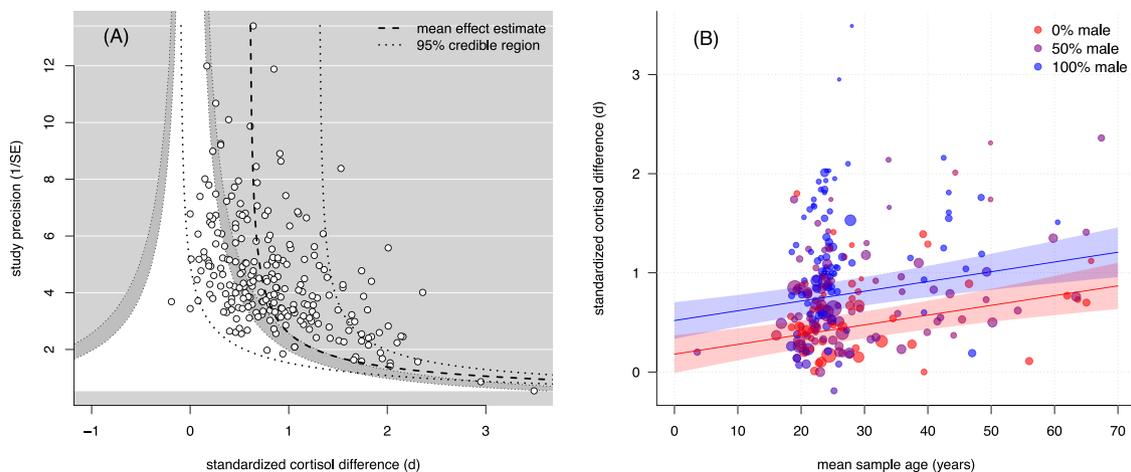


Fig. 3. (A) Contour-enhanced funnel plot (Peters et al., 2008) of the TSST-induced cortisol responses against the precision of the respective subsample. The likely publication bias (as indicated by the severe asymmetry of the funnel) is accounted for meta-regression. The credible region is supposed to encompass 95% of all possible effect scenarios given the pronounced between-study heterogeneity. (B) Dependency of the cortisol stress response on the mean age and the portion of males investigated in the respective subsample. Dot size indicates the relative precision. Shaded regions represent the 95% confidence intervals for male- and female-only studies.

and the above listed country characteristics extracted from the World Mental Health Surveys (Kessler and Ustun, 2014) and the World Factbook (CIA, 2016) were exploratory investigated. All of these nested models were also comprised of the four baseline covariates. The corresponding analytical scripts and data can be accessed on the Open Science Framework (<https://osf.io/qxf5t>).

4.2. Results

4.2.1. Between-study heterogeneity in the cortisol stress response

The basic meta-analysis replicated the substantial between-study heterogeneity in the cortisol stress response to the TSST ($d = 0.60$, $CI_{95\%}: 0.53 - 0.67$, $\tau^2 = 0.13$), even after accounting for small-study effects ($\beta_1 = +2.68$, $CI_{95\%}: 1.99 - 3.38$, see Fig. 3A). There was a strong correlation of cortisol stress responses in subsamples of the contributing studies ($r = 0.57$). The heterogeneity of the cortisol responses was further reduced ($F(4,232) = 27.45$, $p < 0.001$, $R^2 = 18.8\%$) by adjusting for the mean age ($\beta_2 = +0.21$ per 10 years, $CI_{95\%}: 0.11 - 0.31$) and the portion of males ($\beta_3 = +0.37$ in fully male vs. fully female samples, $CI_{95\%}: 0.24 - 0.51$) in the respective study, but not by the time that had passed since the TSST was introduced ($\beta_4 = -0.01$ per 10 years, $CI_{95\%}: -0.14 - 0.12$). The increase of the cortisol stress response with higher mean age and a larger portion of males in the respective study is visualized in Fig. 3B.

To investigate if the residual between-study heterogeneity in cortisol stress responses could be related to differences between countries, we enriched the meta-regression model by an additional variance component and were thereby able to account for 25.5% of the remaining between-study heterogeneity. This model with additional between-country heterogeneity predicted the observed cortisol responses significantly better ($\chi^2(1) = 23.47$, $p < 0.001$, $AICc = 237.13$) as compared to the baseline model without between-country heterogeneity ($AICc = 258.44$).

4.2.2. Country-related differences in the cortisol stress response

To illustrate the between-country heterogeneity in more detail, the conditional estimates of the cortisol stress response in the different TSST-conducting studies are shown in Fig. 4A. Overall, the depicted effect pattern seems to confirm the previously raised suspicion that the TSST induces lower cortisol stress responses when conducted in North America as compared to Europe. This difference was confirmed by formal hypothesis testing ($F(1,219) = 28.11$, $p < 0.001$) with European studies reporting a mean cortisol stress response of $d = 0.73$ as

compared to $d = 0.45$ in North American studies. Furthermore, it should be noted that descriptively those countries / regions with many pro-socialist oriented and post-soviet societies (incl. Scandinavia, Eastern Europe, the former German Democratic Republic, Italy, China) tended to report larger cortisol stress responses as compared to English-speaking countries (i.e., Anglo Canada, the United States, the United Kingdom, Ireland) and the Netherlands. To our surprise, however, Japan and some Latinian country regions (incl. Spain, French Canada, and French Switzerland) also suggestively reported rather low cortisol responses.

4.2.3. Cultural values and the cortisol stress response

The regression of the between-country differences on the seven cultural value orientations revealed a significant positive association of the cortisol stress response with harmony values ($\beta = +0.08$ per SD, $CI_{95\%}: 0.04 - 0.11$, $p < 0.001$), whereas embeddedness values ($\beta = -0.13$ per SD, $CI_{95\%}: -0.21 - -0.04$, $p = 0.003$) and mastery values ($\beta = -0.12$ per SD, $CI_{95\%}: -0.19 - -0.04$, $p = 0.003$) were associated with decreased cortisol responses. Accordingly the harmony-mastery dimension was also reliably associated with the cortisol stress response ($\beta = +0.16$ per SD, $CI_{95\%}: 0.08 - 0.25$, $p < 0.001$), whereas the autonomy-embeddedness dimension ($\beta = -0.17$ per SD, $CI_{95\%}: -0.36 - 0.03$, $p = 0.096$) and the egalitarianism-hierarchy dimension ($\beta = -0.05$ per SD, $CI_{95\%}: -0.17 - 0.08$, $p = 0.454$) were not associated. When accounting for all value dimensions simultaneously, this finding corresponded to a predicted effect of $d = 1.13$ in the countries scoring high on the harmony-mastery dimension (e.g., Germany), as compared to $d = 0.54$ in countries that score low on this dimension (e.g., the United States). Fig. 4B illustrates the relation between the harmony-mastery dimension and the cortisol stress response. Although the remaining value associations did not exceed the Bonferroni-adjusted significance threshold, it should be noted that all cultural value orientations in the subset of contributing countries were higher associated (median $r = 0.79$, IQR: 0.67 – 0.89) as compared to the reference data of Schwartz (2006; median $r = 0.48$, IQR: 0.37 – 0.56). This highlights, that the geo-cultural variance among the TSST-conducting studies is insufficient to fully disentangle the specific contribution of the different cultural value orientations. Overall, the cultural value dimensions were able to account for $R^2 = 15.2\%$ in the effect heterogeneity across the different TSST studies ($F(3,229) = 7.94$, $p < 0.001$).

4.2.4. Mental disorders and further exploratory associations

Table 2 lists the exploratory associations between various

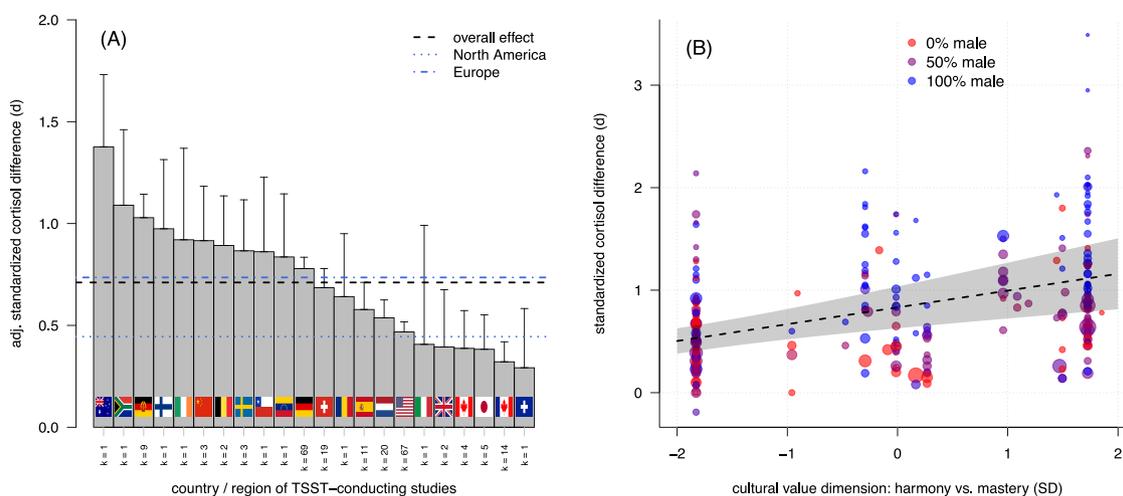


Fig. 4. (A) Estimated country-specific cortisol stress responses, adjusted for sample age, portion of male participants, publication year, and small-study effects. Bars indicate standard errors. (B) Dependency of the cortisol stress response on the harmony-mastery. Dot size indicates the relative precision. The shaded region represents the 95% confidence interval.

characteristics of the contributing countries and the cortisol stress response. Except for the prevalence of specific phobia, we observed pronounced associations between all considered internalizing mental disorders (i.e., major depression, generalized anxiety disorder, panic disorder, social anxiety disorder, post-traumatic stress disorder) and the cortisol stress response. On average, the stress-related cortisol increase in those countries with the lowest vs. highest prevalence of internalizing mental disorders differed by $d = -0.25$ SD, that is, higher prevalence rates were associated with a blunted cortisol responses. Increased TSST-related cortisol secretion was most strongly associated with lower population growth and birth rates, higher tax rate, lower public expenditures for healthcare and the military, and an overall lower inequality of family incomes.

5. Discussion

Beyond the mere confirmation of the hypothesis that between-country differences actually contribute to the heterogeneity of cortisol responses across different participant populations, the present study

aimed to investigate the specific characteristics that might have driven this heterogeneity. In this regard, we found that a major portion of country-related heterogeneity in cortisol stress responses could be attributable to variability in cultural values. The size of this pronounced cultural effect was comparable to that of the strongest known moderators of stress-related cortisol secretion, that is, participant sex and age (Liu et al., 2017; Otte et al., 2005). Specifically, the data suggest that the harmony-mastery dimension of cultural values is the most important geo-cultural moderator of the cortisol stress response. This result aligns excellently with the notion that values at the mastery pole of this cultural value dimension serve to cope with the anxiety-inducing properties of the social and physical environment a group of individuals lives in (Schwartz, 2012). Conversely, a devaluation of mastery values (by emphasizing harmony values) will only be beneficial when the social group is able and willing to cooperatively alleviate most of these anxiety-inducing properties. Based on this reasoning, the uncontrollability and threat components of the TSST (Dickerson and Kemeny, 2004) might be identically implemented in different populations so that purely methodological moderators of the cortisol stress response would

Table 2

Regression of cortisol stress response (scaled in SD) on different country characteristics (CIA World Factbook 2016) and 12-month prevalence of internalizing mental disorders (WHO World Mental Health Surveys).

Characteristic	Unit	Range	k	β	SE(β)	CI _{2.5%}	CI _{97.5%}	p
<i>CIA World Factbook</i>								
Population growth rate	% per year	-0.3 – 1.3	237	-0.254	0.061	-0.375	-0.133	< 0.001
Birth rate	per 1000 citizens + year	1.3 – 2.4	237	-0.410	0.138	-0.682	-0.137	0.003
Life expectancy at birth	years	63.1 – 85.0	237	-0.022	0.016	-0.053	0.009	0.157
Obesity in adults	% of citizens	5.0 – 33.0	237	-0.008	0.004	-0.016	0.001	0.088
Gross domestic product (GDP)	5000 USD per citizen	2.7 – 13.9	237	-0.037	0.017	-0.069	-0.004	0.028
Tax rate	% of GDP	18.1 – 53.7	237	0.009	0.002	0.004	0.014	< 0.001
Public Expenditures								
Health	% of GDP	4.6 – 17.9	237	-0.029	0.008	-0.045	-0.013	< 0.001
Education	% of GDP	3.8 – 7.0	237	0.005	0.062	-0.118	0.127	0.940
Military	% of GDP	0.55 – 4.35	237	-0.061	0.019	-0.098	-0.023	0.002
Inequality of income	Gini index (0 – 100)	21.5 – 62.5	237	-0.013	0.003	-0.020	-0.006	< 0.001
Renewable energy	% of total capacity	7.1 – 97.3	237	0.001	0.001	-0.001	0.004	0.229
<i>WHO World Mental Health Survey</i>								
Major Depression	% of citizens	1.5 – 8.8	182	-0.069	0.018	-0.104	-0.034	< 0.001
Panic Disorder	% of citizens	0.2 – 2.7	179	-0.121	0.033	-0.186	-0.055	< 0.001
Social Anxiety Disorder	% of citizens	0.4 – 7.1	183	-0.038	0.011	-0.060	-0.016	0.001
Specific Phobia	% of citizens	1.7 – 9.1	181	-0.028	0.017	-0.061	0.004	0.090
Generalized Anxiety Disorder	% of citizens	0.2 – 4.0	183	-0.071	0.019	-0.109	-0.033	< 0.001
Post-Traumatic Stress Disorder	% of citizens	0.2 – 3.8	182	-0.127	0.031	-0.189	-0.065	< 0.001

be hardly detectable (which is consistent with the findings of Goodman et al., 2017). Nonetheless, the cortisol responses to the TSST are supposed to vary considerably because it less likely affects individuals who are used to operate in highly competitive and potentially threatening environments.

Although it should be highlighted that the above discussed result may be confounded with other hidden moderators (e.g., the TSST situation could be perceived more or less aversive in different countries), the above proposed interpretation gains additional plausibility by its neat fit into Max Weber's concept of protestant work ethics (see Furnham, 1984, for details). Such work ethics are particularly prominent in Anglo-Frisian countries, which have been essentially shaped by the Protestant notion that any person who lacks socioeconomic prosperity probably shows insufficient diligence and can therefore be held responsible for his/her own situation. Please note, that important components of this moral principle are shared by Confucian cultures (Zhang et al., 2012). However, only the Japanese but not the Chinese studies reported low cortisol responses to the TSST. By contrast, many countries on the European mainland rely on the secular humanist conviction that unindebted hardship can happen to anyone at any time and should therefore be borne by society as a whole. Accordingly, the anxiety of socioeconomic insecurity is alleviated in these countries, which enables them to emphasize cultural values promoting peaceful coexistence and sustainability. Thus, the TSST probably becomes an effective trigger of high cortisol stress responses due to the induction of a rather unusual state of psychosocial challenge in these cultures. Put more bluntly, such a causal mechanism would imply that capitalist societies show lower cortisol stress responses as compared to social-liberal societies because people are more frequently confronted with threatening situations (cf. Prins et al., 2015). Although, we would also like to remark that the suggestive pattern of intermediate cortisol responses in some Latinian countries (in particular Spain, French Switzerland, and French Canada) and high cortisol responses in Australia and South Africa are not fully compatible, their association with other factors reflecting harmony values (e.g., higher tax rate, lower public expenditures for the military, and lower inequality of family income³ are associated with larger cortisol responses, see Table 2) essentially support our interpretation.

Irrespective of the specific reason for the association between the cortisol stress response and cultural values, an interindividual variability in value-related coping strategies for countering environmental challenge may also have contributed to the previously reported findings of attenuated cortisol stress responses in internalizing mental disorders (Zorn et al., 2017). Consistently, citizens of the United States, Northern Ireland, France, Spain, and the Netherlands show lower cortisol stress responses and seem to suffer substantially more often from major depression as compared to many other European countries (e.g., Italy and Germany; Kessler et al., 2014). Considering their preference for mastery values, China and Japan form the only exceptions from this effect pattern, which could be either due to a cultural measurement bias in the WHO World Mental Health Surveys or unobserved confounding factors.

5.1. Limitations

We would like to highlight, that the suggested link between varying cultural values and stress-related psychiatric disorders is only probabilistic, that is, there is a considerable amount of residual heterogeneity in different studies that needs to be explained by other factors. Regarding the cortisol stress response, we found in this regard that some heterogeneity is attributable to small-study effects (i.e., less precise studies are more prone to bias and report larger cortisol responses

³ Buttrick and Oishi (2017) recently reviewed the psychological consequences of income inequality including status competition, lower social cohesion, mistreatment, and increased anxiety.

to the TSST). Accordingly, remarkably large and small TSST effects in specific countries should be interpreted with caution when they are only informed by a small number of studies (e.g., South Africa, Australia, or French Switzerland; see Fig. 4A). Conversely, the large portion of studies from the United States and Germany also yields a considerable bias potential for confounding the impact of the cultural values in these two particular countries with other hidden moderators.

Heterogeneity in the cortisol responses may also explain why other stress-induction protocols (e.g., Dedovic et al., 2005; Reinhardt et al., 2012; Schwabe et al., 2008; Smeets et al., 2012) often failed to match the original TSST. While these findings could be interpreted as inferior capability of the protocols to induce psychosocial stress (Skoluda et al., 2015), the present meta-analyses also highlights that population differences need to be taken into account when between-study differences in the cortisol stress response are interpreted. While the meta-analytical approach used in this article allowed us to investigate such population differences, it simultaneously suffered from an inability to assess potential within-population associations between cultural values and the cortisol stress response. As these complementary approaches may not necessarily yield the same conclusions (e.g., Cooper and Patall, 2009), our findings require confirmation by studies that capture value orientations at the participant level.

Finally, we want to emphasize that the compiled data on cultural value orientations and cortisol stress responses were obtained from young student samples, whereas the prevalence rates for mental disorders were derived for population-representative samples. Accordingly the above outlined connection between value-related strategies for stress coping and internalizing psychopathology partly relies on the assumption that between-country differences in mental disorders are similarly reflected by young subpopulations of the World Mental Health Surveys.

5.2. Conclusion

The present study was able to formally confirm between-country differences in cortisol responses to the TSST with English-speaking countries showing the lowest stress responses. To explain these differences, we argue for and demonstrate robust associations between mean cortisol stress responses and anxiety-related values in the corresponding cultures. Cross-cultural differences in the prevalence of internalizing mental disorders (incl. anxiety disorders and major depression) and attenuated cortisol stress responses in individuals suffering from these disorders provide converging evidence for the proposed hypothesis. Based on the notion that values do not only serve as social norms but also as individual traits, our findings could finally contribute to explaining why individuals respond so differently to stress exposure.

Conflict of interest

None declared.

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