



HHS Public Access

Author manuscript

Transl Issues Psychol Sci. Author manuscript; available in PMC 2024 June 01.

Published in final edited form as:

Transl Issues Psychol Sci. 2023 June ; 9(2): 123–136. doi:10.1037/tps0000349.

Stress, Coping, and Physical Health in Caregiving

Melissa Zajdel,

Tracy Swan,

Taylor Robinson,

Krystyna R. Keller,

Lindsey Mountcastle,

Laura M. Koehly

Social Network Methods Section, Social and Behavioral Research Branch, National Human Genome Research Institute

Abstract

Informal caregivers experience a great deal of stress due to care-related duties and responsibilities. Caregiving stress has the ability to impact caregivers' physical health, but has been largely understudied in caregivers of children with a chronic illness. In this study, we examine the associations of stress to both caregiver self-rated health and biomarkers of the hypothalamic-pituitary-adrenal (HPA) axis and immune systems (arginine vasopressin, c-reactive protein, tumor necrosis factor alpha). We also examine whether coping style (proactive, avoidant, support coping) buffers the links of stress to health across two different stressor contexts: caregiving for a child with a rare or undiagnosed disease ($n = 101$) and caregiving for a typically developing child ($n = 69$). Results indicated perceived stress was linked to worse self-rated health, however, stress was only linked to biological markers of health for caregivers of typically developing children. Results also suggest that coping style may moderate some of the links of stress to health, as proactive coping was linked to lower arginine vasopressin. However, models also suggested the role of coping style may differ based on caregiving context, as support coping was linked to better health only for caregivers of typically developing children, and more proactive coping overall was observed in the rare disease context. Future research should continue to examine how stress and coping interact within different caregiving contexts to protect caregiver health and well-being.

Keywords

caregiving; coping; stress; health; HPA axis; immune system

In 2020, about 53 million adults reported providing care to a friend or family member who was unable to care for themselves (National Alliance for Caregiving [NAC] & AARP, 2020). These individuals are 'informal caregivers,' or those who provide regular, unpaid care or assistance to family or friends with a disability or illness (CDC, 2020). Caregivers adopt a variety of responsibilities such as providing care (e.g., feeding, dressing), making care-

related decisions for the care recipient, and supporting other informal caregivers (Pelentsov et al., 2015). The accumulation of these responsibilities and the stressors associated with caregiving are known as ‘caregiving burden’ and often result in poorer health for caregivers (Pinquart & Sörensen, 2003).

Caregivers of children with chronic health conditions in particular experience a great deal of psychological stress associated with the caregiving process (see Cousino & Hazen, 2013 for review). This stress results from sources such as financial strains, difficulties coordinating services, advocating for the care recipient, providing activities of daily living, and inadequate social support (Murphy et al., 2007; Pelentsov et al., 2015). Moreover, the stress from caregiving has been robustly shown to impact psychological health, as caregivers have higher rates of anxiety and depression (Murphy et al., 2007), posttraumatic stress disorder (Kazak & Barakat, 1997), and lower subjective well-being (Pinquart & Sörensen, 2003).

However, a multitude of research suggests that stress impacts more than psychological health: stress can “get under the skin” to impact both short- and long-term physical health (see O’Connor et al., 2021 for a review). For instance, perceived stress has been linked to both self-reported cold symptoms and clinical indicators of illness (e.g., mucus weight) after viral exposure (Cohen et al., 1991). Reviews have also consistently linked increased stress levels to weakened immune responses and poorer antibody responses after vaccination (see Cohen et al., 2001 for a review). Additionally, stress has been linked to poor health outcomes including worse self-rated health (Cohen et al., 2015) and increased risk of premature death (Chiang et al., 2018). Caregiving stress specifically has been linked to similar health outcomes. For example, informal caregivers of family members with Alzheimer’s disease or related dementias (ADRD) produced lower antibody responses (Glaser et al., 2000), had higher mortality risk (Schulz & Beach, 1999) and reported worse self-rated health than non-caregiving controls (von Kanel et al., 2019).

Given these links of stress to physical health, research has sought to identify the physiological processes that can lead to poor distal health outcomes. A number of pathways through which stress can impact physiological health have been identified, including health behavior changes, neuroendocrine impacts, genomic interactions, and autonomic function (O’Connor et al., 2021). In the current report, we examine the impact of stress on self-rated health, a metric that captures an individual’s assessment of their health and is related to more objective markers of health such as immune function and chronic illness (e.g., Cohen et al., 2015; Idler & Benyamini, 1997). We also examine the impact of stress on health through a set of physiological biomarkers—arginine vasopressin (AVP), tumor necrosis factor- α (TNF α), and c-reactive protein (CRP)—that reflect functioning of primary physiological systems such as the immune and inflammatory systems, as well as the HPA axis, which have bidirectional effects on each other. Biomarkers of the immune and inflammatory systems—TNF α and CRP—play a role in preparing the body to fight illnesses and stimulating the body’s reaction to stressful stimuli (Noushad et al., 2021). Instances of heightened immune responses, such as extended times of stress, are characterized by increased levels of pro-inflammatory cytokines (e.g., TNF α). The HPA axis is also activated by both acute and chronic stressors and operates through a network of hormones including AVP, which is

a primary stimulatory biomarker that initiates further HPA axis activation (Spencer & Deak, 2017). The HPA axis is critical for overall health as it influences respiratory, cardiovascular, and metabolic functioning (O'Connor et al., 2021). Dysregulation of both the HPA axis and immune systems are associated with poor health, such as increased risk of cardiovascular disease, obesity, insulin resistance, hypertension, sleep disorders, and autoimmune disorders (see O'Connor et al., 2021 for a review; see Steptoe et al., 2007 for a review).

In the caregiving domain, there is evidence to suggest that the HPA axis and immune function may be impacted in caregivers of adults with chronic illnesses. For example, caregivers of individuals with ADRD were found to have elevated levels of TNF α compared to control participants, while duration of caregiving was linked to CRP; these levels also dropped after the death of the care recipient (von Kanel et al., 2012). Additionally, caregivers of patients with cancer showed an increase in inflammation—assessed via CRP—during the year following diagnosis, while CRP did not increase for non-caregiver control participants (Rohleder et al., 2009). Similarly, caregivers of patients with ADRD had higher TNF α compared to control participants (Damjanovic et al., 2007). Finally, a review found caregivers demonstrated higher levels of cortisol relative to non-caregivers, but found inconsistent evidence for differences in other biomarkers of the HPA axis (e.g., ACTH) and immune system (e.g., CRP, TNF α) (Allen et al., 2017).

The negative impact of stress on physical health is not immutable though, as there are factors that can disrupt these links to preserve health. According to the caregiving stress process model and stress buffering hypotheses, various coping behaviors can impact the link between stress and health, as coping can either attenuate or exacerbate these links (Cohen & Wills, 1985; Pearlin et al., 1990; see Fairfax et al., 2019 for a review). These frameworks suggest that certain types of coping (e.g., proactive coping or support coping) can serve as a protective buffer under high levels of stress. There is also empirical evidence that exemplifies this pattern. In the caregiving domain specifically, indirect or avoidant coping styles (e.g., anger, impatience, anxiety, avoidance) have been associated with worse physical health for people with a chronic illness (e.g., type 2 diabetes) as well as worse self-reported physical health in caregivers of individuals with ADRD (Kim et al., 2007; Peyrot & McMurry, 1992). In contrast, direct or proactive coping styles (e.g., positive reappraisal) led to better physical health outcomes for individuals with a chronic illness and caregivers of individuals with ADRD (Kim et al., 2007; Peyrot & McMurry, 1992). Additionally, individuals with multiple stressful life events (e.g., financial difficulties) report fewer psychological and physical symptoms when they use proactive coping (Toussaint et al., 2014). Finally, proactive coping strategies (e.g. reframing) have been positively associated with better quality of life for caregivers, while avoidant strategies (e.g. denial) were associated with poorer quality of life (see Fairfax et al., 2019 for a review).

There are a variety of factors that can influence how one copes with stress, including the type of stressor, additional life events, and available social support (Cohen and Wills, 1985; Pearlin et al., 1981). Whether coping buffers stress may also depend on the type of stressor an individual encounters. For instance, less common stressful life events or uncontrollable types of stress may require different coping and self-regulation strategies than more normative stressful life events (Roth & Cohen, 1986; Wrosch & Freund, 2001). Thus,

we directly examine whether stress and coping impact health similarly across two different caregiving contexts: parents caring for a typically developing child—a more normative type of stress—as well as parents caring for a child with a rare or undiagnosed disease—a less common type of stress (Berg et al., 2021). Because a rare or undiagnosed disease is a uniquely stressful context, the traditional mechanisms linking stress and coping to physical health may not be observed and we examine caregiving context as a potential moderator of the links of stress and coping to health.

As the reviewed literature demonstrates, there is very little research that examines physical health outcomes for informal caregivers of children with a chronic health condition; most research focuses on either the psychological burden caregivers of children with a chronic illness experience or the physical health of caregivers of adults (e.g., spouses of individuals with ADRD). However, caring for a child with a chronic illness is uniquely stressful because care in this context often requires a lifetime commitment that includes changes in income, domestic responsibilities, illness-specific health literacy, and specialized caregiving skills (Pelentsov et al., 2015). The number of pediatric caregivers within the U.S. is also increasing—from 10.2 million in 2015 to 14.1 million in 2020—making this context particularly important to investigate (NAC & AARP, 2020). Here, we explore how stress and coping style impacts physical health for both caregivers of typically developing children and caregivers of children with a rare or undiagnosed illness, allowing us to examine whether stress and coping operate similarly across contexts.

First, we examine the links of stress to physical health, as assessed by both physiological biomarkers as well as self-rated health and hypothesize stress will be linked to worse physical health. We also examine whether links vary by caregiving context—whether the associations are similar across caregivers of children with rare or undiagnosed conditions and caregivers of typically developing children. Second, we examine the direct effects of coping style on physical health—as well as moderation by caregiving context—to examine how coping style impacts health. However, given the lack of empirical evidence directly exploring the role of stress and coping across stressor contexts—and the lack of research on caregiving in rare diseases in general—we examine moderation by caregiving context without directional hypotheses. Third, we examine whether coping style moderates the links of stress to physical health, hypothesizing that certain coping styles (e.g., proactive coping) may be more adaptive under conditions of stress than other coping styles (e.g., avoidant coping).

Methods

Participants

Participants were 404 self-identified informal caregivers—defined as those who provide regular, unpaid care or assistance to family or friends with a disability or illness (CDC, 2020)—of either 1) children with rare or undiagnosed diseases or 2) age-matched typically developing children that participated in the Inherited Diseases, Caregiving, and Social Networks study at the National Human Genome Research Institute. Participants were recruited through ongoing studies, illness-specific advocacy groups, and the National Institutes of Health Clinical Center Office of Patient Recruitment and consented via phone.

The first participant ($n = 205$) was able to refer additional kin and non-kin members ($n = 199$) over the age of 18 who are part of the caregiving process to participate in the study—though participants do not have to be primary caregivers. Therefore, some families have multiple participants who enrolled in the study. All procedures were approved by the IRB (Protocol 12-HG-0022) and preregistered on [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01498263): NCT01498263.

Caregivers ($n = 404$) were caring for children ($n = 205$) with inborn errors of metabolism (*child* $n = 119$; *caregiver* $n = 252$), undiagnosed diseases (*child* $n = 15$; *caregiver* $n = 40$), neurodegenerative diseases (*child* $n = 8$; *caregiver* $n = 13$), or typically developing children (*child* $n = 63$; *caregiver* $n = 99$). There was only one participant for 88 families, two participants for 67 families, 3 participants for 27 families, four participants for 16 families, five participants for 5 families, and six participants for 2 families. Participants identified as women (68.1%), were primarily mothers/step-mothers (46.0%) or fathers/step-fathers (25.5%), and the majority were married (80.4%). About 28.5% of the sample had a non-parental relationship to the child (e.g., grandparents, siblings). Caregivers ranged from 18 to 79 years of age (mean = 43.76, $SD = 12.27$), caring for children who were an average of 9.88 years of age ($SD = 8.68$). See Supplemental Table 1 for full demographics. All caregivers in the study completed survey questionnaires either online or via phone.

Caregivers that 1) were a parent or guardian of the care recipient and 2) were planning a visit to the National Institutes of Health were also invited to participate in a sub-study that involved provided blood while onsite. From the larger study, 184 participants from 127 families provided blood samples. After collection, 2 unusable samples were excluded and an addition 12 samples were not analyzed because caregivers did not complete the survey measures. This resulted in a final sample size of 170 caregivers from 122 families. In this subset, there was one participant for 75 families, two participants for 46 families, and 3 participants for one family. Demographics are provided in Table 1. Participants were sent the self-report questionnaire ahead of the biospecimen collection visit and were able to complete the questionnaire within several weeks of biospecimen collection—median time between assessments was 7 days.

Up to 33mL of blood was collected and 20mL were processed to the serum/plasma level. Samples were stored in a -80°C freezer and aliquots (600 μL) were sent in batches to SBH Sciences. As quality control, 10% of the samples were re-analyzed to ensure there were no major batch effects. There were no major batch effects, so we used the values from the first assay. To estimate intra-assay and inter-assay CVs standard controls with known concentrations of analyte (e.g., high, medium, low) were included to assess analytic precision. CRP was analyzed by R&D Duoset ELISA Development Kit Cat #DY1707 with a minimal detection level of > 330 ng/ml at 1:8000 dilution, within run precision of 1.7% ng/ml at medium concentration and run to run precision at 3.0% ng/ml at medium concentration. TNFa samples were analyzed using the Miliplex, Millipore HCYTOMAG-60K Kit, with a minimal detection level of < 6 pg/ml, within run precision 8.8% pg/ml, run to run precision 5.8% pg/ml at high concentration and 14.5% pg/ml at low concentration. AVP was analyzed using the abcam Arg8-Vasopressin ELISA Kit GR306845-2 with a minimal detection level of > 400 pg/ml at 1:20 dilution, within run

precision 6.2% pg/ml at medium concentration, run to run precision at 18.8% pg/ml at medium concentration.

Measures

Coping—The BriefCOPE is a 28-item questionnaire designed to measure the ways individuals cope with a stressful life event (Carver et al., 1997). Example items include: “I’ve been concentrating my efforts on doing something about the situation I’m in” and “I’ve been blaming myself for things that happened.” Items were rated on a scale from 1 = I haven't been doing this at all to 4 = I've been doing this a lot. The 14 two-item subscales within the Brief COPE are: (1) self-distraction, (2) active coping, (3) denial, (4) substance use, (5) use of emotional support, (6) use of instrumental support, (7) behavioral disengagement, (8) venting, (9) positive reframing, (10) planning, (11) humor, (12) acceptance, (13) religion, and (14) self-blame. Mean scores were used for each of the 14 scales. Missing data ranged from 10.6% to 13.9% in the subscales in the full dataset and from 2.4% to 7.6% in the subset of caregivers who contributed biological data. Additional psychometric information can be viewed in the results section.

Perceived Stress Scale—The Perceived Stress Scale is a 10-item scale that measures the degree of stress experienced in the last month (e.g., How often have you been upset because of something that happened unexpectedly?) (Cohen et al., 1983). Items were rated on a scale from 0 = never to 4 = very often and summed to create a composite score as suggested in the literature. The scale showed good reliability in the full sample ($\alpha = .90$) and in the subset of caregivers with biological data ($\alpha = .90$). There were no missing data in perceived stress in the subset of caregivers with biological data; the mean score was 16.40 ($SD = 7.34$; range 2-36).

Physical Health

Biological Outcomes.: Three biomarkers were collected from the blood serum: CRP, TNFa, AVP. All biomarkers were natural log transformed; skewness and kurtosis were acceptable after transformation (skewness < 2.0; kurtosis < 4.0). Higher numbers represent higher circulating biomarkers and worse physical health. There was 2.9% missing data for CRP, 1.2% for TNFa, and no missing data for AVP. The mean score after natural log transformation for CRP was 7.11 ng/ml ($SD = 1.49$, range = 1.68-10.20), for TNFa was 2.76 pg/ml ($SD = .96$; range = .48-7.38), and for AVP was 8.03 pg/ml ($SD = .53$; range = 6.93-9.57).

Self-Rated Physical Health (SRH).: The physical component score of the Short-Form Health Survey (SF-12) are 6 self-report items designed to measure health-related quality of life (Ware et al., 1996). This survey assesses health across domains including limitations in activities due to health problems, limitations in usual role activities due to physical health problems, bodily pain, and general health perceptions. Reliability was good ($\alpha = .78$). There were no missing data in self-rated health in the subset of caregivers with biological data; the mean score for the sample was 83.00 ($SD = 17.50$; range 14.30-100).

Overview of Analyses

First, we conducted an exploratory factor analysis to examine general coping styles in the full sample ($n = 404$). Because past literature suggests factor analyses benefit from larger sample sizes (e.g., Comrey, 1988; McNeish, 2017), we opted to conduct the factor analysis in the full sample to both reduce bias and maximize power. To determine the best solution, we examined the screeplot, eigenvalues > 1.00 , parallel analysis, optimal coordinates, and acceleration factor in R statistical software (v4.0.2) using the nFactors package (Raiche & Magis, 2020). We ran a factor analysis using the stats package in R, which employs maximum likelihood estimation to examine the items and constrained the number of factors based on the above metrics. We used a Promax rotation which allows for correlation across coping factors given that it is likely a person who engages in one type of coping may be likely to engage in another type of coping.

Second, we conducted a series of preliminary analyses including: 1) examination of group differences in primary study variables and demographics by caregiving context (see Table 1), correlations among primary study variables (see Supplemental Table 2), and covariate selection. Covariate selection was determined by examining the relationships of theoretically relevant variables (caregiving context, participant age, gender, marital status, income, BMI, alcohol use, caffeine consumption, age of the child, and batch effects) to the independent variables (stress, coping styles). Caregiving context (rare disease vs. typically developing), caregiver age, caregiver gender, and batch were related to at least one independent variable. Therefore, models were constructed with these covariates and backwards selection based on BIC was employed to refine model fit; final models were determined when either the BIC did not improve with covariate removal or all covariates were related to the outcome of interest.

Third, we fitted a series of hierarchical linear models to examine the association of stress and coping with physical health in the context of caregiving in the subset of caregivers that contribute biological data ($n = 170$).¹ All models used hierarchical linear models and the nlme package in R (Pinheiro et al., 2020) to account for the nesting of individual caregivers within families with restricted maximum likelihood. The first set of models examined the direct links of perceived stress to each physical health outcome (CRP, TNFa, AVP, and SRH); we then examined whether caregiving context moderated the links of stress to health outcomes. The second set of models examined the direct links of coping style (proactive, avoidant, support) to physical health (CRP, TNFa, AVP, and SRH) with all three mean-centered coping styles in a single model for each outcome; we then examined whether caregiving context moderated the links of coping style to health. The third set of models then added the interaction between stress and coping style to assess the potential stress buffering effect of coping on health. We ran models with interactions between stress and all three mean-centered coping styles in a single model for each outcome to reduce the number of models examined. For both the second and third sets of models, if any interaction was significant, we re-ran the models retaining only the individual coping style to determine if

¹Because self-rated health (SRH) was assessed in the full sample we re-ran models in the full dataset and the results were largely the same.

significance holds without the influence of the other coping styles; we interpret only those that retain significance when examined on their own because coping styles are correlated and we do not want to overfit the data. Missing data was minimal (see Methods); thus, we imputed mean scores for missing data in the independent variables, though results were largely the same when we ran models without imputing scores.

Results

Coping Styles Factor Analysis

Optimal numbers of factors varied by metric: screeplot (3), eigenvalues (4), parallel analysis (3), optimal coordinates (3), and acceleration factor (1). We chose a three-factor solution based on the majority of metrics and consistent with our predictions and past research (see Krägeloh, 2011 for a review). The three factors represented 1) proactive coping: planning (.86), acceptance (.57), active coping (.71), reframing (.53), and religion (.40); 2) avoidant coping: disengagement (.72), blaming (.67), distraction (.50), denial (.45), and venting (.44); and 3) support coping: use of emotional support (.93) and use of instrumental support (.75). These three factors are consistent with past research evident in the coping literature, and represent proactive coping or approach-focused strategies, avoidant coping or emotion-focused coping, and leveraging social support (Carver et al., 1989; Pearlin et al., 1990). Humor and substance use did not load on any factor (loading $< .40$) and were dropped. Loadings can be seen in Supplemental Table 3. Mean composite scores were created and had good reliability: proactive coping ($\alpha = .83$), avoidant coping ($\alpha = .79$), and support coping ($r = .63$). Mean composite factors were correlated: proactive and support coping ($r = .50, p < .001$), proactive and avoidant coping ($r = .43, p < .001$), and avoidant and supportive coping ($r = .20, p = .01$).

Direct Effects of Stress and Coping on Physical Health

Model results with beta coefficients, standard errors, and confidence intervals can be seen in Table 2. Results indicated that stress was linked to worse SRH ($B = -.72, p < .001$), but was not linked to any biomarker: CRP, TNFa, or AVP. However, caregiver context moderated the links of stress to TNFa ($B = -.04, p < .05$) and AVP ($B = -.02, p < .05$). Simple slopes analyses suggested a significant positive association between stress and TNFa for caregivers of typically developing children ($B = .04, SE = .02, p < .05$), but not caregivers of children with a rare or undiagnosed disease ($B = -.004, SE = .01, p = .70$) (Supplemental Figure 2). Similarly, stress was positively associated with AVP for caregivers of typically developing children ($B = .02, SE = .01, p < .05$), but not caregivers of children with a rare disease ($B = -.004, SE = .01, p = .53$) (Supplemental Figure 2). Caregiving context did not moderate the links of stress to CRP or SRH.

Proactive coping was not linked to physical health: CRP, TNFa, AVP, or SRH, nor were these links moderated by caregiving context. Avoidant coping was linked to worse SRH ($B = -11.10, p < .001$), but was not linked to: CRP, TNFa, AVP, nor were there interactions with caregiving context. Finally, support coping was not directly linked to health: CRP, TNFa, AVP, or SRH. The links of support coping to TNFa and SRH were moderated by caregiving context when all three interactions were entered into the same model, however,

without proactive coping and avoidant coping in the model, the links to TNFa were no longer significant ($B = -.30$, $SE = .18$, $p = .09$, 95% CI: $[-.66, .05]$). The links of the interaction between support coping and caregiving context to SRH were still significant with removal of proactive and avoidant coping ($B = -8.23$, $SE = 3.58$, $p = .03$, 95% CI: $[-15.45, -1.02]$). Simple slopes suggested support coping was linked to higher SRH for caregivers of typically developing children ($B = 5.76$, $SE = 2.75$, $p < .05$), but not caregivers of children with a rare or undiagnosed disease ($B = -2.47$, $SE = 2.48$, $p = .32$) (Supplemental Figure 3). Caregiving context did not moderate the links of support coping to CRP or AVP.

Stress-Buffering by Coping Style

Results indicated proactive coping moderated the link of stress to AVP in full models (Table 2) and when only proactive coping was entered in the model ($B = -.02$, $SE = .01$, $p < .05$, 95% CI: $[-.03, -.0001]$). Simple slopes suggest higher levels of stress were linked to more AVP at low levels of proactive coping ($B = .02$, $SE = .01$, $p < .05$), but not at average ($B = .01$, $SE = .01$, $p = .23$) or high levels of proactive coping ($B = -.003$, $SE = .01$, $p = .66$) (see Supplemental Figure 4). The interaction of stress and proactive coping was not linked to CRP or SRH and was only linked to TNFa in full models, not when proactive coping was entered alone ($B = -.02$, $SE = .01$, $p = .14$, 95% CI: $[-.04, .01]$). There were no buffering effects of avoidant coping on CRP, TNFa, AVP, or SRH. The interaction of stress and support coping was linked to AVP only when all coping styles were in the model, but when proactive and avoidant coping were removed from the model this effect was not seen ($B = .01$, $SE = .01$, $p = .48$, 95% CI: $[-.01, .02]$). The stress and support coping interaction was not linked to CRP, TNFa, or SRH.

Discussion

Stress has long been associated with physical health, but within this process there are intervening factors that can either mechanistically lead to worse physical health or buffer against negative impacts. We investigated links of stress and coping to physical health for caregivers and examine the impact of normative stress (i.e. parenting) to the uniquely stressful experience of caregiving for a child with a rare or undiagnosed disease. Briefly, we found that higher stress and avoidant coping were linked to worse self-rated health, but context may moderate some associations between stress and coping to health. We also found some evidence for stress-buffering, as proactive coping mitigated increased AVP associated with stress. Below we review the findings and discuss implications.

Before delving into the main models, we examined whether there were differences across stress, coping, and physical health between rare disease caregivers and caregivers of typically developing children in order to gain a greater understanding of whether these types of caregiving differed in the stress process. Interestingly, there were no overall differences in health based on caregiving context for either the biomarkers of interest or self-rated health. While some studies do find differences between caregivers of children with a chronic illness and caregivers of children without a chronic illness (e.g., see Dijkstra-de Neijs et al., 2020 for a review), we view the lack of findings here as a positive pattern—that caregiving for a child with a chronic illness can be associated with resiliency and not necessarily poor

health. We did find that rare disease caregivers reported more stress overall, but as we talk about in more depth below, stress was not linked to physiological biomarkers of health in this group—suggesting these caregivers may have adapted to the daily management of their child’s illness. Finally, there were no differences in the use of avoidant or support coping, but rare disease caregivers reported using more proactive coping than caregivers of typically developing children. Given past literature suggests that proactive coping is linked to positive health outcomes (e.g., see Taylor & Stanton, 2007 for a review)—and the findings here that suggest proactive coping may buffer deleterious findings of stress on health—the use of this coping style to address rare disease stressors may be particularly impactful for caregivers.

The first main goal of this paper was to examine the links of perceived stress to physical health both through self-rated health and via biological markers. Interestingly, caregiver perceived stress was not directly linked to biomarkers; it was only linked to worse self-rated health. Poor health is consistent with the limited previous research that examines caregivers of children with a chronic condition (e.g., Dijkstra-de Neijs et al., 2020), and holds implications for other health outcomes. For example, self-rated health is linked to weakened immune function (Cohen et al., 2015) and is an indicator of mortality even after inclusion of health indicators and relevant covariates (e.g., Idler & Benyamini, 1997). Caregiving can be highly stressful, and it is critical for clinicians and researchers to know stress is linked to worse self-rated health for both caregivers of children with rare or undiagnosed conditions and typically developing children.

While stress was not directly linked to biomarkers, caregiving context moderated the association such that stress was linked to enhanced TNF α and AVP for caregivers of typically developing children—biomarkers that may lead to or be indicative of worse physical health. Indeed, dysregulation of the HPA axis and immune systems—as indicated by elevated levels of TNF α and AVP—have been linked to adverse health outcomes such as blood glucose dysregulation, metabolic dysfunction, cancer, anxiety, and depression (Kiecolt-Glaser & Glaser, 1995; Mavani et al., 2015; O’Connor et al., 2021). These results reveal a misalignment between perceived and biological health under conditions of stress for rare disease caregivers, since perceived psychological stress was not linked to physiological biomarkers. One potential explanation is that rare disease caregivers may have adapted to stress at a physiological level, but perceive that caregiving negatively interferes with the ability to maintain their physical health (e.g., competing time demands). Indeed, some research suggests prolonged stress may lead to resilience, thus, rare disease caregivers may still perceive caregiving as stressful, but show greater resilience as evidence by a lack of association to physiological outcomes (Rutter, 2012).

Future research may want to examine how length of time as a caregiver—or time since diagnosis—may impact the links of stress to physiological health as there is rationale for multiple hypotheses. First, it may be the case that caregivers of a child with a rare disease experience greater stress temporally close to the diagnosis, as their realities shift, caregiving responsibilities are added, and fear for their child’s future health are heightened, but over time they adapt to this stress. Conversely, it might be the case that the impact of stress on biological outcomes may occur more slowly over time and have a cumulative effect on physical health. In contrast, caregivers of typically developing children may not encounter

the same level of daily stress and burden and thus, more traditional associations of stress to health were observed. Past research that links caregiving to dysregulated physiological biomarkers is largely conducted in caregivers of adults with chronic illnesses—primarily ADRD (e.g., Damjanovic et al., 2007; von Kanel et al., 2012). However, this type of caregiving may be relatively normative from a life-course perspective because chronic illness is more likely to occur in older age (Berg et al., 2021; Brody, 1985). Additionally, caregiving for older individuals may be shorter in duration than pediatric disorders, as the average duration of care is 3-11 years after diagnosis with ADRD (Alzheimer's Association Report, 2022), whereas management of rare diseases is often a lifetime commitment. In contrast, caring for a child with an illness—especially a rare disease—may be particularly stressful, and is characterized by unique stressors such as a lack of resources, information, and support (Pelentsov et al., 2015).

In addition to examining the links of stress to physical health, we examined the role of coping style in managing stress. While past literature has identified a number of coping styles, the ones identified in this study—proactive, avoidant, and support coping—are consistent with strategies outlined by traditional models of stress and coping (Carver et al., 1989; Pearlin et al., 1990). For example, these factors represent approach-focused strategies or coping styles designed to modify the stressor context, avoidance type coping styles or those that are aimed at reducing distress in the moment, and support coping which represents leveraging resources from available network members to address a stressor (e.g., Lazarus & Folkman, 1984; Pearlin et al., 1990).

Contrary to hypotheses, when we examined the links of these coping styles to health, we found very few associations. The one exception was a link between avoidant coping and self-rated health such that more avoidant coping was associated with worse self-rated health. This is consistent with past research that states avoidant coping may be worse for health (Kim et al., 2007; Peyrot & McMurry, 1992). However, findings also suggested that the impact of coping style may depend on stressor context, as support coping was linked to better self-rated health only for caregivers of typically developing children, not for caregivers of children with a rare disease. Support coping is characterized by mobilizing either instrumental resources or emotional reassurance from social network members (Cohen & Wills, 1985)—both of which may be more difficult for network members in a rare disease context. Social network members may be less knowledgeable about rare diseases and how to help, either instrumentally or emotionally. Because caring for a child with a rare or undiagnosed disease is uniquely stressful, the impact of coping style may depend on caregiving context; coping may not be universally positive or negative under conditions of chronic or unique stress. Indeed, the controllability and longevity of the stressor may influence the effectiveness of coping style, and it is possible that under instances of uncontrollable stress, coping strategies such as avoidance or disengagement may not be wholly negative (Roth & Cohen, 1986; Taylor & Stanton, 2007). Future research should continue to examine coping styles across different stressor contexts to continue to explore these hypotheses.

In this study, we also sought to examine whether coping style moderates the links of stress to physical health outcomes in line with both the stress-buffering hypothesis and the stress

process model (Cohen & Wills, 1985; Pearlin et al., 1981). Contrary to hypotheses, coping largely did not buffer the links of stress to health—either self-rated health or biomarkers. The only exception was a stress buffering effect of proactive coping on the association between stress and AVP, such that the links of stress to AVP were evident at low levels of proactive coping, but higher proactive coping buffered this link. While we do not want to overinterpret this link, this is consistent with past literature that has demonstrated the benefits of proactive coping (Toussaint et al., 2014) and is interesting because AVP is a stimulatory hormone of the HPA axis, as it is produced by stimulation of corticotropin-releasing hormone neurons and plays a role in the subsequent release of ACTH (Spencer & Deak, 2017). In comparison, TNF α and CRP are inflammatory and immune-related biomarkers that may result from chronic stress (Noushad et al., 2021). Thus, there may be utility in engaging in proactive coping strategies early in the stress process or at heightened levels of stress to mitigate the subsequent stimulation of the HPA axis. Future longitudinal research should examine this possibility as the data in this study are cross sectional in nature. Research that continues to examine the observed discrepancy between biological and self-rated health in rare disease caregivers—and the possibility that stress may differentially impact physical health based on the type of stress experienced—is also warranted.

While these findings advance the current state of the literature, there are limitations to address. First, while we examined the differences in rare disease caregiving and typically developing caregiving, the results do not separate diagnoses within the rare disease context and future research should examine whether these patterns exist across rare diseases (e.g., neurodegenerative disorders, inborn errors of metabolism), undiagnosed diseases, and perhaps more common childhood illnesses (e.g., type 1 diabetes). Second, we acknowledge that our measures reflect more general, trait level variables and may not capture more immediate in-the-moment levels of stress or styles of coping. Third, this study is cross-sectional, and future research should incorporate longitudinal designs to examine the impact of stress on health over time and the potential intervening impact of coping style. Finally, there were some differences in demographics between groups, with caregivers of typically developing children reporting more racial/ethnic diversity and higher levels of educational attainment than rare disease caregivers.

This study is among the first to examine the links of psychological stress and coping to physical health in caregivers of children with a chronic illness and given our unique sample, we were able to determine whether these patterns generalized across stressor context. Overall, we saw patterns that challenged traditional paradigms of stress and coping—namely that typically described patterns were only observed in the context of parenting a typically developing child, while stress and coping may function differently for caregivers facing less common, chronic stressors such as rare diseases. More broadly, this study holds implications for healthcare as it is clear caregivers would benefit from resources to mitigate the physical and psychological effects of stress. Healthcare and research alike should focus efforts to develop interventions, support groups, and strategies to teach adaptive coping strategies to caregivers in order to mitigate the negative impacts of stress. In sum, this study found that caregiving stress may indeed be linked to poor health for caregivers of children with and without chronic illnesses, but caregiving type may impact the mind-body connection in context-dependent ways. Thus, it is important that future research and clinicians consider

both caregiver context and type of stress to fully understand the impact on physical health via research or translating findings to interventions for caregivers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research was supported by funding from the Intramural Research Program of the National Human Genome Research Institute (Grant ZIAHG200395). The data that support the findings of this study are available from the senior author upon reasonable request. The authors thank Drs. Peter McGuire, Cynthia Tift, and Charles Venditti for referring the participants in this study. Finally, we thank the participants and their families for their involvement in this study.

References

- Allen AP, Curran EA, Duggan Á, Cryan JF, Chorcorain AN, Dinan TG, ... & Clarke G (2017). A systematic review of the psychobiological burden of informal caregiving for patients with dementia: Focus on cognitive and biological markers of chronic stress. *Neuroscience & Biobehavioral Reviews*, 73, 123–164. 10.1016/j.neubiorev.2016.12.006 [PubMed: 27986469]
- Alzheimer's Association Report (2022). 2022 Alzheimer's disease facts and figures. 10.1002/alz.12638
- Berg CA, Kelly CS, & Utz RL (2021). Family care exchanges across the life span. In *Handbook of the Psychology of Aging* (pp. 263–274). Academic Press.
- Brody EM (1985). Parent care as a normative family stress. *The Gerontologist*, 25(1), 19–29. 10.1093/geront/25.1.19 [PubMed: 3920124]
- Carver CS, Scheier MF, & Weintraub JK (1989). Assessing coping strategies: A theoretically based approach. *Journal of Personality and Social Psychology*, 56(2), 267–283. 10.1037/0022-3514.56.2.267 [PubMed: 2926629]
- Carver CS (1997). You want to measure coping but your protocol is too long: Consider the brief cope. *International Journal of Behavioral Medicine*, 4(1), 92–100. 10.1207/s15327558ijbm0401_6 [PubMed: 16250744]
- Centers for Disease Control and Prevention. (2020). Caregiving for family and friends—a public health issue. <https://www.cdc.gov/aging/agingdata/docs/caregiver-brief-508.pdf>
- Chiang JJ, Turiano NA, Mroczek DK, & Miller GE (2018). Affective reactivity to daily stress and 20-year mortality risk in adults with chronic illness: Findings from the National Study of Daily Experiences. *Health Psychology*, 37(2), 170–178. 10.1037/hea0000567 [PubMed: 29154603]
- Cohen S, Kamarck T, and Mermelstein R (1983). A global measure of perceived stress. *Journal of Health and Social Behavior*, 24, 386–396.
- Cohen S, & Wills TA (1985). Stress, social support, and the buffering hypothesis. *Psychological Bulletin*, 98(2), 310–357. 10.1037/0033-2909.98.2.310 [PubMed: 3901065]
- Cohen S, Tyrrell DA, & Smith AP (1991). Psychological stress and susceptibility to the common cold. *New England Journal of Medicine*, 325(9), 606–612. 10.1056/NEJM199108293250903 [PubMed: 1713648]
- Cohen S, Miller GE, & Rabin BS (2001). Psychological stress and antibody response to immunization: a critical review of the human literature. *Psychosomatic Medicine*, 63(1), 7–18. 10.1097/00006842-200101000-00002 [PubMed: 11211068]
- Cohen S, Janicki-Deverts D, & Doyle WJ (2015). Self-rated health in healthy adults and susceptibility to the common cold. *Psychosomatic Medicine*, 77(9), 959–968. 10.1097/PSY.0000000000000232. [PubMed: 26397938]
- Comrey AL (1988). Factor-analytic methods of scale development in personality and clinical psychology. *Journal of Consulting and Clinical Psychology*, 56(5), 754–761. 10.1037/0022-006X.56.5.754

- Cousino MK, & Hazen RA (2013). Parenting stress among caregivers of children with chronic illness: a systematic review. *Journal of Pediatric Psychology*, 38(8), 809–828. 10.1093/jpepsy/jst049 [PubMed: 23843630]
- Damjanovic AK, Yang Y, Glaser R, Kiecolt-Glaser JK, Nguyen H, Laskowski B, ... & Weng NP (2007). Accelerated telomere erosion is associated with a declining immune function of caregivers of Alzheimer's disease patients. *The Journal of Immunology*, 179(6), 4249–4254. 10.4049/jimmunol.179.6.4249 [PubMed: 17785865]
- Dijkstra-de Neijs L, Leenen PJM, Hays JP, van der Valk ES, Kraaij R, van Rossum EFC, & Ester WA (2020). Biological consequences of psychological distress in caregivers of children with autism spectrum disorder and its potential relevance to other chronic diseases including cancer. *Current Epidemiology Reports*, 7(3), 139–148. 10.1007/s40471-020-00237-2
- Glaser R, Sheridan J, Malarkey WB, MacCallum RC, & Kiecolt-Glaser JK (2000). Chronic stress modulates the immune response to a pneumococcal pneumonia vaccine. *Psychosomatic Medicine*, 62(6), 804–807. 10.1097/00006842-200011000-00010 [PubMed: 11139000]
- Fairfax A, Brehaut J, Colman I, Sikora L, Kazakova A, Chakraborty P, & Potter BK (2019). A systematic review of the association between coping strategies and quality of life among caregivers of children with chronic illness and/or disability. *BMC Pediatrics*, 19, Article 215. 10.1186/s12887-019-1587-3 [PubMed: 31262261]
- Idler EL, & Benyamini Y (1997). Self-rated health and mortality: a review of twenty-seven community studies. *Journal of Health and Social Behavior*, 21–37. 10.2307/2955359 [PubMed: 9097506]
- Kazak AE, & Barakat LP (1997). Brief report: parenting stress and quality of life during treatment for childhood leukemia predicts child and parent adjustment after treatment ends. *Journal of Pediatric Psychology*, 22(5), 749–758. 10.1093/jpepsy/22.5.749 [PubMed: 9383934]
- Kiecolt-Glaser JK & Glaser R (1995). Psychoneuroimmunology and health consequences: data and shared mechanisms. *Psychosomatic Medicine*, 57(3), 269–274. 10.1097/00006842-199505000-00008 [PubMed: 7652127]
- Kim J-H, Knight BG, & Longmire CVF (2007). The role of familism in stress and coping processes among African American and White dementia caregivers: Effects on mental and physical health. *Health Psychology*, 26(5), 564–576. 10.1037/0278-6133.26.5.564 [PubMed: 17845108]
- Krägeloh CU (2011). A systematic review of studies using the brief cope: Religious coping in factor analyses. *Religions*, 2(3), 216–246. 10.3390/re12030216
- Mavani GP, DeVita MV, & Michelis MF (2015). A Review of the nonpressor and nonantidiuretic actions of the hormone vasopressin. *Frontiers in Medicine*, 2(19), 1–11. 10.3389/fmed.2015.00019 [PubMed: 25654080]
- McNeish D (2017). Exploratory factor analysis with small samples and missing data. *Journal of Personality Assessment*, 99(6), 637–652. 10.1080/00223891.2016.1252382 [PubMed: 27929657]
- Murphy NA, Christian B, Caplin DA, & Young PC (2007). The health of caregivers for children with disabilities: caregiver perspectives. *Child: care, health and development*, 33(2), 180–187. 10.1111/i.1365-2214.2006.00644.x [PubMed: 17291322]
- National Alliance for Caregiving & AARP (2020). *Caregiving in the United States 2020*. Washington, DC: AARP. 10.26419/ppi.00103.001
- Noushad S, Ahmed S, Ansari B, Mustafa UH, Saleem Y, & Hazrat H (2021). Physiological biomarkers of chronic stress: A systematic review. *International journal of health sciences*, 15(5), 46–59. [PubMed: 34548863]
- O'Connor DB, Thayer JF, & Vedhara K (2021). Stress and health: A review of psychobiological processes. *Annual Review of Psychology*, 72, 663–688. 10.1146/annurev-psych-062520-122331
- Pearlin LI, Menaghan EG, Lieberman MA, & Mullan JT (1981). The Stress Process. *Journal of Health and Social Behavior*, 22(4), 337–356. 10.2307/2136676 [PubMed: 7320473]
- Pearlin LI, Mullan JT, Semple SJ, & Skaff MM (1990). Caregiving and the stress process: An overview of concepts and their measures. *The Gerontologist*, 30(5), 583–594. 10.1093/geront/30.5.583 [PubMed: 2276631]
- Pelentsov LJ, Laws TA, & Esterman AJ (2015). The supportive care needs of parents caring for a child with a rare disease: A scoping review. *Disability and Health Journal*, 8(4), 475–491. 10.1016/j.dhjo.2015.03.009 [PubMed: 25959710]

- Peyrot MF, & McMurry JF Jr (1992). Stress buffering and glycemic control. The role of coping styles. *Diabetes Care*, 15(7), 842–846. 10.2337/diacare.15.7.842 [PubMed: 1516502]
- Pinheiro J, Bates D, DebRoy S, Sarkar D, R Core Team (2020). nlme: Linear and Nonlinear Mixed Effects Models. <https://CRAN.R-project.org/package=nlme>
- Pinquart M, & Sörensen S (2003). Differences between caregivers and noncaregivers in psychological health and physical health: a meta-analysis. *Psychology and Aging*, 18(2), 250–267. 10.1037/0882-7974.18.2.250 [PubMed: 12825775]
- Raiche G & Magis D (2020). nFactors: Parallel Analysis and Other Non Graphical Solutions to the Cattell Scree Test. <https://CRAN.R-project.org/package=nFactors>
- Rohleder N, Marin TJ, Ma R, & Miller GE (2009). Biologic cost of caring for a cancer patient: dysregulation of pro-and anti-inflammatory signaling pathways. *Journal of Clinical Oncology*, 27(18), 2909–2915. 10.1200/JCO.2008.18.7435 [PubMed: 19433690]
- Roth S, & Cohen LJ (1986). Approach, avoidance, and coping with stress. *American Psychologist*, 41(7), 813–819. 10.1037/0003-066X.41.7.813 [PubMed: 3740641]
- Rutter M (2012). Resilience as a dynamic concept. *Development and Psychopathology*, 24(2), 335–344. doi:10.1017/S0954579412000028 [PubMed: 22559117]
- Schulz R, & Beach SR (1999). Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. *JAMA*, 282(23), 2215–2219. 10.1001/jama.282.23.2215 [PubMed: 10605972]
- Spencer RL, & Deak T (2017). A users guide to HPA axis research. *Physiology & Behavior*, 178, 43–65. 10.1016/j.physbeh.2016.11.014 [PubMed: 27871862]
- Steptoe A, Hamer M, Chida Y (2007). The effects of acute psychological stress on circulating inflammatory factors in humans: A review and meta-analysis. *Brain, Behavior, and Immunity*, 21(7), 901–912. 10.1016/j.bbi.2007.03.011 [PubMed: 17475444]
- Taylor SE, & Stanton AL (2007). Coping resources, coping processes, and mental health. *Annual Review of Clinical Psychology*, 3(1), 377–401. 10.1146/annurev.clinpsy.3.022806.091520
- Toussaint L, Shields GS, Dorn G, & Slavich GM (2016). Effects of lifetime stress exposure on mental and physical health in young adulthood: How stress degrades and forgiveness protects health. *Journal of Health Psychology*, 21(6), 1004–1014. 10.1177/1359105314544132 [PubMed: 25139892]
- von Känel R, Mills PJ, Mausbach BT, Dimsdale JE, Patterson TL, Ziegler MG, ... & Grant I (2012). Effect of Alzheimer caregiving on circulating levels of C-reactive protein and other biomarkers relevant to cardiovascular disease risk: a longitudinal study. *Gerontology*, 58(4), 354–365. 10.1159/000334219 [PubMed: 22133914]
- von Känel R, Mausbach BT, Dimsdale JE, Ziegler MG, Mills PJ, Allison MA, ... & Grant I (2019). Refining caregiver vulnerability for clinical practice: determinants of self-rated health in spousal dementia caregivers. *BMC Geriatrics*, 19(1), 1–11. 10.1186/s12877-019-1033-2 [PubMed: 30606112]
- Ware JE Jr, Kosinski M, & Keller SD (1996). A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Medical Care*, 220–233. 10.1097/00005650-199603000-00003 [PubMed: 8628042]
- Wrosch C, & Freund AM (2001). Self-regulation of normative and non-normative developmental challenges. *Human Development*, 44(5), 264–283. 10.1159/000057066

Public Significance Statement

In this study, perceived stress and avoidant coping were linked to worse self-rated health for caregivers of both typically developing children and children with rare diseases, while proactive coping buffered the links of stress to physiological biomarkers. However, some aspects of traditional stress and coping frameworks may not apply under unique stress contexts such as rare disease caregiving, as results indicated stress was only linked to physiological biomarkers of health for caregivers of typically developing children, and these caregivers were the only ones to benefit from social support coping.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1.

Demographics

	Rare and Undiagnosed Diseases (Child <i>n</i> = 63) (Caregiver <i>n</i> = 101)	Typically Developing (Child <i>n</i> = 59) (Caregiver <i>n</i> = 69)	Total (Child <i>n</i> = 122) (Caregiver <i>n</i> = 170)
Caregiver Gender (n, %)			
Woman	57 (56.4%)	46 (66.7%)	103 (60.6%)
Man	44 (43.6%)	23 (33.3%)	67 (39.4%)
Care Recipient Gender (n, %) *			
Girl	20 (31.7%)	35 (59.3%)	55 (45.1%)
Boy	43 (68.3%)	24 (40.7%)	67 (54.9%)
Caregiver Age (Mean, SD) *	38.30 (6.06)	40.40 (7.34)	39.1 (6.86)
Care Recipient Age (Mean, SD)	7.33 (4.48)	7.83 (4.46)	7.57 (4.46)
Education (n, %) *			
Less Than HS	4 (4.0%)	1 (1.4%)	5 (2.9%)
HS Diploma/GED/Technical	16 (15.8%)	4 (5.8%)	20 (11.8%)
Some College	23 (22.8%)	9 (13.0%)	32 (18.8%)
Bachelor's Degree	39 (38.6%)	19 (27.5%)	58 (34.1%)
Post-Grad Degree	18 (17.8%)	36 (52.2%)	54 (31.8%)
Missing	1 (1.0%)	0 (0%)	1 (0.6%)
Marital Status (n, %)			
Married/Cohabiting	91 (90.1%)	56 (81.2%)	147 (86.5%)
Not Married	8 (7.9%)	13 (18.8%)	21 (12.4%)
Missing	(2.0%)	0 (0%)	2 (1.2%)
Relationship to CR (n, %)			
Father	43 (42.6%)	22 (31.9%)	65 (38.2%)
Mother	56 (55.4%)	44 (63.8%)	100 (58.8%)
Step-father	1 (1.0%)	0 (0%)	1 (0.6%)
Step-mother	1 (1.0%)	2 (2.9%)	3 (1.8%)
Grandparent	0 (0%)	1 (1.4%)	1 (0.6%)
Caregiver Race/Ethnicity (n, %) *			
Asian	4 (4.0%)	9 (13.0%)	13 (7.6%)
Black or African American	1 (1.0%)	11 (15.9%)	12 (7.1%)
Native Hawaiian/Pacific Islander	0 (0%)	1 (1.4%)	1 (0.6%)
Other	8 (7.9%)	6 (8.7%)	14 (8.2%)
White	87 (86.1%)	41 (59.4%)	128 (75.3%)
Missing	1 (1.0%)	1 (1.4%)	2 (1.2%)
Perceived Stress *	17.57 (7.11)	14.68 (7.39)	16.40 (7.34)
Coping Style			
Proactive Coping *	2.63 (.52)	2.32 (.82)	2.50 (.67)
Avoidant Coping	1.73 (.48)	1.62 (.55)	1.69 (.51)

	Rare and Undiagnosed Diseases (Child <i>n</i> = 63) (Caregiver <i>n</i> = 101)	Typically Developing (Child <i>n</i> = 59) (Caregiver <i>n</i> = 69)	Total (Child <i>n</i> = 122) (Caregiver <i>n</i> = 170)
Support Coping	2.28 (.75)	2.26 (.83)	2.28 (.78)
Physical Health			
CRP	7.02 (1.57)	7.25 (1.36)	7.11 (1.49)
TNFa	2.79 (.97)	2.70 (.94)	2.76 (.96)
AVP	8.08 (.49)	7.97 (.58)	8.03 (.53)
Self-Rated Health	82.12 (18.02)	84.27 (16.69)	82.99 (17.47)

Note:

* indicates a difference between rare disease caregivers and caregivers of typically developing children

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2.

Direct Links of Stress & Coping to Physical Health

	CRP (B, SE, CI)	TNF-a (B, SE, CI)	AVP (B, SE, CI)	SRH (B, SE, CI)
Links of Stress (Step 1):				
Perceived Stress (PSS)	.00 (.02) [-.03, .03]	.01 (.01) [-.01, .03]	.01 (.01) [-.01, .02]	-.72 (.19) [-1.11, -.33] ***
Stress by CG Context (Step 1.1):				
Rare Disease (RD)	.39 (.58) [-.76, 1.53]	.76 (.33) [1.11-1.42]*	.49 (.20) [10, .88]*	-3.29 (6.51) [-16.17, 9.60]
Perceived Stress	.02 (.03) [-.03, .08]	.04 (.02) [.01, .07]*	.02 (.01) [.003, .04]*	-.82 (.29) [-1.40, -.24]**
RD *PSS	-.04 (.03) [-.10, .03]	-.04 (.02) [-.08, -.01]*	-.02 (.01) [-.05, -.002]*	.19 (.37) [-.56, .93]
Links of Coping (Step 2):				
Proactive Coping	-.17 (.22) [-.61, .27]	-.15 (.12) [-.39, .10]	-.02 (.07) [-.17, .13]	1.66 (2.57) [-3.53, 6.85]
Avoidant Coping	.02 (.26) [-.51, .54]	.00 (.15) [-.31, .31]	.04 (.09) [-.14, .22]	-11.10 (2.96) [-17.09, -5.12]***
Support Coping	-.23 (.17) [-.58, .12]	.04 (.09) [-.15, .23]	-.09 (.06) [-.20, .03]	1.48 (2.05) [-2.67, 5.63]
Coping by CG Context (Step 2.1):				
Rare Disease (RD)	-.08 (.25) [-.57, .42]	.21 (.17) [-.21, .55]	.13 (.09) [-.06, .32]	-1.08 (2.79) [-6.59, 4.45]
Proactive Coping	-.37 (.35) [-1.08, .34]	-.43 (.20) [-.83, -.02]*	-.06 (.12) [-.30, .18]	-.28 (3.97) [-8.33, 7.76]
Avoidant Coping	.62 (.43) [-.25, 1.48]	.22 (.26) [-.31, .75]	.15 (.15) [-.15, .45]	-15.03 (4.88) [-24.90, -5.16]**
Support Coping	.02 (.31) [-.60, .64]	.38 (.17) [.05, .72]*	-.01 (.10) [-.21, .19]	8.04 (3.47) [1.01, 15.07]*
RD *Proactive Coping	.15 (.47) [-.81, 1.10]	.31 (.26) [-.22, .83]	-.04 (.16) [-.36, .28]	.88 (5.38) [-10.01, 11.77]
RD *Avoidant Coping	-.95 (.54) [-2.04, .14]	-.28 (.32) [-.92, .37]	-.17 (.19) [-.55, .21]	7.28 (6.13) [-5.12, 19.68]
RD *Support Coping	-.35 (.37) [-1.10, .41]	-.47 (.20) [-.88, -.07]*	-.11 (.12) [-.35, .14]	-10.37 (4.22) [-18.91, -1.83]*
Stress Buffering by Coping Style (Step 3):				
Perceived Stress	.01 (.02) [-.03, .05]	.01 (.01) [-.01, .03]	.01 (.01) [-.002, .02]	-.44 (.23) [-.89, .02]
Proactive Coping	-.13 (.23) [-.59, .32]	-.13 (.12) [-.39, .12]	-.02 (.07) [-.17, .13]	1.60 (2.61) [-3.70, 6.89]
Avoidant Coping	.01 (.32) [-.64, .66]	-.07 (.18) [-.44, .29]	-.03 (.11) [-.24, .18]	-9.25 (3.60) [-16.53, -1.96]*
Support Coping	-.30 (.19) [-.68, .07]	-.04 (.10) [-.25, .16]	-.14 (.06) [-.26, -.02]*	2.71 (2.13) [-1.61, 7.03]
Stress *Proactive Coping	-.01 (.03) [-.07, .05]	-.03 (.02) [-.06, -.002]*	-.03 (.01) [-.05, -.01]**	.20 (.32) [-.45, .85]
Stress *Avoidant Coping	-.02 (.04) [-.10, .05]	.003 (.02) [-.04, .04]	.004 (.01) [-.02, .03]	.65 (.43) [-.22, 1.53]

	CRP (B, SE, CI)	TNF- α (B, SE, CI)	AVP (B, SE, CI)	SRH (B, SE, CI)
Stress *Support Coping	.03 (.03) [-.02, .08]	.02 (.01) [-.003, .05]	.02 (.01) [.002-.03] *	-.39 (.29) [-.98, .19]

Note: All models reported are 2-level hierarchical linear models with caregiver nested within family. RD refers to rare disease (vs. typically developing), PSS refers to perceived stress. Covariates not shown.

[†] $p < .10$

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$.