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Effects of relationship functioning on the biological experience of stress and physical health

Allison K Farrell and Jeffry A Simpson

In this paper, we outline how relationship functioning affects the biological experience of stress and its consequences for physical health. Negative relationship perceptions and processes, such as attachment insecurity, hostility, and frequent conflict, tend to heighten stress responses and generate worse health over time, whereas positive relationship perceptions and processes, such as responsiveness, support, and intimacy, are generally associated with reduced or buffered stress responses and improved health (with some caveats). Future research should focus on the mechanisms behind these effects, the extent to which they can be changed or reversed, incorporating developmental perspectives, and consider the effects of individual differences on these processes.

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Current Opinion in Psychology 2016, 13:xx-yy

This review comes from a themed issue on Relationships and stress

Edited by Gery C Karantzas, Marita P McCabe and Jeffry A Simpson

doi:10.1016/j.copsyc.2016.04.014

2352-250/Published by Elsevier Ltd.

Beneficial effects of close relationships for helping people cope with stressors are widely documented for not only mental well-being, but also for physical health [1]. Relationships, however, can also be a source of stress, generating deleterious health effects. In this article, we describe the biological experience of stress and its effects on physical health, review evidence regarding the impact of relationship functioning throughout this process, and discuss future research directions.

Biological experience of stress and physical health

The biological stress pathway and its effects on physical health are outlined in Figure 1. When individuals experience a stressor, the hypothalamus initiates a hormone cascade resulting in the release of cortisol [2]. Cortisol bonds to glucocorticoid receptors (GRs), which launches DNA transcription. Genes regulated in this process serve many functions, particularly immune system suppression and inflammation.

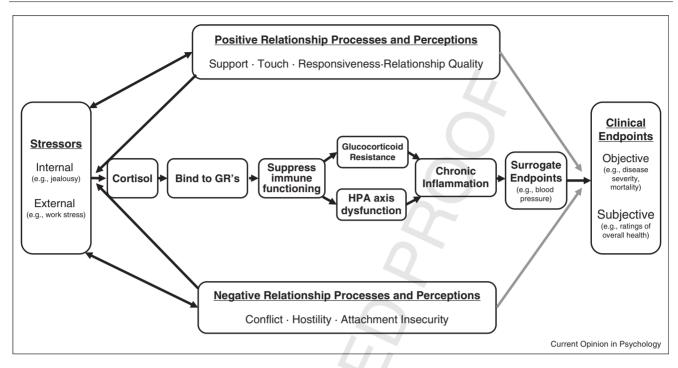
When individuals encounter frequent or chronic stress, however, the body resists hyperactivation induced by cortisol. This has two major consequences. First, following prolonged activation, cortisol drops below baseline levels. This can lead to dysregulation of the HPA-axis and flat cortisol levels throughout the day, instead of normal declines over the day [3]. Second, glucocorticoid receptor resistance (GCR) can develop. Immune cells with GCR have GRs that are desensitized to cortisol, requiring larger concentrations to begin transcription [4]. With the antiinflammatory effects of cortisol reduced, GCR produces inflammatory factors and chronic inflammation, which is associated with myriad health risks and diseases [5]. Health outcomes fall into two categories [6^{••}]. Clinical outcomes include disease presence (e.g., cardiovascular disease [CVD]), disease severity (e.g., hospitalization frequency), mortality, and subjective health ratings. Surrogate outcomes include biological markers of disease and mortality, such as high blood pressure and high blood sugar.

Relationship processes affecting health

The effects of positive and negative relationship perceptions and processes have been documented throughout the biological experience of stress leading to physical health outcomes. Negative relationship perceptions/processes generally intensify stress responses leading to worse health outcomes (see the bottom of Figure 1). For example, being insecurely attached or having a relationship with an insecure partner are associated with several health risks [7^{••}]. Attachment insecurity, which involves having negative expectations for relationships which lead to unconstructive reactions under stress, predicts perceiving relationship situations as more stressful [8], having higher cortisol levels, and experiencing slower return to cortisol baselines [9]. Insecurely attached individuals also have flatter diurnal cortisol patterns [10], fewer and less effective immune cells [10], and higher inflammation [11]. The toll of insecure attachment is also seen in endpoint measures, such as more inflammationrelated symptoms [12] and higher incidence of strokes, heart attacks, and ulcers [13].

Hostility is another major negative relationship process. Individuals who express more hostility to their partners

2 Relationships and stress



This model outlines the biological experience of stress, both acutely and over time, and its effects on health. Well-documented relationship processes and perceptions known to affect stress responses and health are listed in the upper (positive) and lower (negative) portions of the model. Relationship processes are known to directly affect the perception and impact of stressors, as signified by the black diagonal arrows on the left side of the model; they are also likely to impact the extent to which surrogate endpoints lead to clinical endpoints, but this requires further study (as signified by the gray arrows on the right side of the model).

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(or are the targets of greater hostility) show greater cortisol reactivity during conflict discussions [14] and worse immune functioning following conflict [15]. Negative marital interactions are also associated with delayed wound healing, an effect mediated by overproduction of pro-106 inflammatory factors [16]. Greater anger and hostility have also been tied to more arterial calcification [17]. 108 Conflicts do not have to be overtly hostile to generate adverse health outcomes, however. The frequency of 110 conflict and marital distress also predict worse immune functioning [18], higher infection rates after virus expo-112 sure [19], flatter diurnal cortisol patterns [20], higher 114 blood pressure [21], and worse asthma [22]. Moreover, frequent conflict and marital distress forecast greater risk for developing CVD [24] and experiencing recurrent 116 cardiac problems [25^{••}].

118 In addition, positive relationship perceptions/processes are 119 systematically related to smaller stress responses and better 120 overall health outcomes (see the upper portion in Figure 1). 121 Higher quality relationship partners buffer us from stress 122 123 [25^{••}]. For example, individuals experiencing external stressors who self-disclose more to their partners [26] or 124 125 whose partners touch them [27] display less cortisol reactivity. Children at risk for poor health due to low SES [28] or 126 high life stress [29] are buffered by warm/sensitive parental

care and experience relatively better health outcomes in adulthood. Higher quality relationships characterized by greater intimacy and responsiveness predict steeper (healthier) diurnal cortisol slopes [30,31[•]]. These individuals also have lower blood pressure and healthier overnight dips in blood pressure [32], and are less likely to be rehospitalized [33] or die from CVD [34].

However, the effects of relationships on health are not always straightforward. Sometimes positive relationship processes are tied to greater health risks. The passionate, early stages of love, for instance, are associated with higher cortisol levels [35], suggesting that intensely positive relationship experiences are short-term stressors. Moreover, even though providing and receiving support typically are good for health, individuals with chronic health problems and their partner-caretakers often experience greater stress and poor health outcomes [36]. Positive and negative relationship experiences are also not mutually exclusive; individuals may behave in a hostile manner in some situations, but be responsive in others, so the relative impact of positive and negative relationship processes can be mixed. Some studies indicate that such 'ambivalent' relationships are risky [37], whereas others find positive elements protect individuals from health risks [38].

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The current literature indicates that the effects of posi-155 tive and negative relationship perceptions/processes oc-156 cur at every stage of the biological experience of stress 157 and physical health model. Researchers have demonstrat-158 ed *what* effects relationships have on stress; research now 159 needs to determine how these effects occur, when these 160 effects occur (developmentally and longitudinally), and 161 162 for *whom* relationships are more versus less impactful on stress and health. 163

164 First, we need to identify how relationship functioning 165 'gets under the skin' to affect stress and health. When, for 166 example, do relationships directly influence the biological 167 experience of stress and health, and when are their effects 168 mediated through previous stages? To be more specific, 169 we would not expect relationship functioning to interfere 170 with the ability of GRs to start transcription after binding 171 172 with cortisol. Instead, relationships are likely to affect this process at the beginning and end of the stress-health 173 174 pathway (see the diagonal arrows in Figure 1). Much is 175 already known about how relationships affect the frequency and perception of stressors and coping styles. 176 Relationships can affect the occurrence of potential 177 stressors, particularly those internal to relationships. Ad-178 ditionally, relationship functioning can affect the extent 179 to which a stressor generates stress. Positive relationship 180 processes reduce stress responses through support and 181 other forms of buffering. In contrast, individuals in poorly 182 183 functioning relationships may be predisposed to find 184 these situations more stressful (e.g., due to attachment 185 insecurity), or they may become more stressed by their 186 inability to successfully seek support. Relationships may 187 also have direct effects on the degree to which surrogate endpoints influence clinical endpoints via health-relevant 188 behaviors. The effects of relationships on health-relevant 189 behaviors have not been studied as much as their biologi-190 cal effects, but relationship partners do shape the likeli-191 hood of engaging in preventative behaviors [39], 192 screenings for health problems [40], and adherence to 193 194 treatment regiments [41]. Few studies have examined the 195 possible mediating effects of relationships across multiple stages (e.g., hostility \rightarrow inflammation \rightarrow CVD), so it 196 197 remains unclear where specific effects are occurring (for an exception, see [16]). 198

By understanding these mechanisms, we can predict how 200 the effects of relationships are maintained over time or 201 might be reversed. Although early family experiences can 202 have lasting effects on health into adulthood [28,29,42], we 203 do not know how these effects are internalized. Recent 204 205 findings suggest that mental representations of early 206 experiences mediate effects for some health outcomes (e.g., weight), but not others [43]. Other potential path-207 208 ways, such as biological embedding through epigenetic processes [44], should also be tested. We also know very 209 little about when the impact of relationships may change or be reversed. This information is critical for informing relationship-based health interventions, which can be effective [45[•]].

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Understanding when and how relationships affect stress and health over time will require developmental models. For example, when during the life-course are different types of close relationships more versus less impactful? As other health-risk factors encountered early in life (e.g., low SES, high stress) have enduring health effects [42,44], the quality of the early parent-child relationship might exert the strongest impact on long-term health. Recent work, however, has also documented the longitudinal impact of stress occurring in adolescence and concurrently on adult health [29,46[•]], so the quality of close relationships at these stages may be similarly impactful. Since the most meaningful relationships often change over development, this fact must also be considered when predicting health outcomes. For example, maternal support is effective at reducing stress responses of children but not adolescents, who may rely more on peer support [47[•]].

232 Finally, key individual differences may affect for whom 233 relationships are more versus less impactful. Early studies 234 found stronger relationship effects on health for women 235 than men [48], but a recent meta-analysis found evidence 236 for gender effects only on surrogate endpoints [6]. Most 237 prior studies have focused on married couples, but studies 238 investigating dating couples have found similar patterns 239 of cortisol reactivity in response to stressors [49]. Deter-240 mining how long (or how close) relationships must be to 241 have 'marital-like' effects would demonstrate how gen-242 eralizable these effects are. Furthermore, work on differ-243 ential susceptibility shows the impact of conflict and high 244 quality parenting on outcomes like behavioral problems 245 and social skills differ across individuals based on their 246 sensitivity to environmental influences. There may be 247 similar effects of these relationship processes on health 248 [50]. By understanding not just what effects relationships 249 have on stress and health, but also how, when, and for 250 whom, we can better utilize relationship science for 251 improving health across the lifespan. 252

Conflict of interest Nothing declared.		253 254
Uncited reference [23].	Q2	255 256
References and recommended reading		257 258
Papers of particular interest, published within the period of review, have been highlighted as:		259 260
of special interest		261
of outstanding interest		262 263
1 Understanding the links between social support		

1. Uchino BN: Understanding the links between social support and physical health. Perspect Psychol Sci 2009, 4:236-255.

www.sciencedirect.com

Current Opinion in Psychology 2016, 13:1-5

Please cite this article in press as: Farrell AK, Simpson JA: Effects of relationship functioning on the biological experience of stress and physical health, Curr Opin Psychol (2016), http://dx.doi.org/10.1016/j.copsyc.2016.04.014

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322 323

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325 326

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329 330

331

- 4 Relationships and stress
- Melmed M, Polonsky KS, Larsen PR, Kronenberg HM: Williams Textbook of Endocrinology. edn 13th. Elsevier; 2015.
- 3. Gunnar MR, Vazquez DM: Low cortisol and a flattening of expected daytime rhythm: potential indices of risk in human development. *Dev Psychopathol* 2001, **13**:515-538.
- Miller GE, Cohen S, Ritchey K: Chronic psychological stress and the regulation of pro-inflammatory cytokines: a glucocorticoidresistance model. *Health Psychol* 2002, 21:531-541.
- Brennan FM, Maini RN, Feldmann M: Cytokine expression in chronic inflammatory disease. Br Med Bull 1995, 51:368-384.
- Robles TF, Slatcher RB, Trombello JM, McGinn MM: Marital
 quality and health: a meta-analytic review. Psychol Bull 2014, 140:140-187.

This comprehensive meta-analysis on the effects of relationship quality on health finds that relationships influence a variety of outcomes, with effect sizes of similar magnitude to those for health behaviors like dietary choices.

7. Pietromonaco PR, Uchino B, Dunkel Schetter C: Close

 relationship processes and health: implications of attachment theory for health and disease. Heal Psychol 2013, 32:499-513.
 This review explains how attachment orientations are relevant for a variety of health processes, including physiology, affective states, health behavior, and health outcomes. The authors propose a theoretical model linking attachment and health.

- Mikulincer M, Shaver PR: Attachment in Adulthood: Structure, Dynamics and Change. Guilford Press; 2010.
- Pietromonaco PR, DeBuse CJ, Powers SI: Does attachment get under the skin?. adult romantic attachment and cortisol responses to stress. Curr Dir Psychol Sci 2013, 22:63-68.
- Jaremka LM, Glaser R, Loving TJ, Malarkey WB, Stowell JR, Kiecolt-Glaser JK: Attachment anxiety is linked to alterations in cortisol production and cellular immunity. *Psychol Sci* 2013, 24:272-279.
- 11. Gouin JP, Glaser R, Loving TJ, Malarkey WB, Stowell J, Houts C et al.: Attachment avoidance predicts inflammatory responses to marital conflict. Brain Behav Immun 2009, **23**:898-904.
- Puig J, Englund MM, Simpson JA, Collins WA: Predicting adult physical illness from infant attachment: a prospective longitudinal study. *Heal Psychol* 2013, 32:409-417.
- McWilliams LA, Bailey SJ: Associations between adult attachment ratings and health conditions: evidence from the National Comorbidity Survey Replication. Am Psychol Assoc 2010, 29:446-453.
- Miller GE, Dopp JM, Myers HF, Fancy JL, Stevens SY: psychosocial predictors of natural killer cell mobilization during marital conflict. *Heal Psychol* 1999, 18:262-271.
- 15. Kiecolt-Glaser JK, Malarkey WB, Chee M: Negative behavior during marital conflict is associated with immunological. *Psychosom Med* 1993, **55**:395-409.
- Kiecolt-Glaser JK, Loving TJ, Stowell JR, Malarkey WB, Lemeshow S, Dickinson SL et al.: Hostile marital interactions, proinflammatory cytokine production, and wound healing, arch. Gen Psychiatry 2005, 62:1377-1384.
- Smith TW, Uchino BN, Berg CA, Florsheim P, Pearce G, Hawkins M et al.: Hostile personality traits and coronary artery calcification in middle-aged and older married couples: different effects for self-reports versus spouse ratings. *Psychosom Med* 2007, 69:441-448.
- Jaremka LM, Glaser R, Malarkey WB, Kiecolt-Glaser JK: Marital distress prospectively predicts poorer cellular immune function. *Psychoneuroendocrinology* 2013, 38:2713-2719.
- Cohen S, Janicki-Deverts D, Turner RB, Doyle WJ: Does hugging provide stress-buffering social support? A study of susceptibility to upper respiratory infection and illness. *Psychol Sci* 2016, 26:135-147.
- Slatcher RB, Robles TF: Preschoolers everyday conflict at home and diurnal cortisol patterns. *Heal Psychol* 2012, 31:834-838.

21. Holt-Lunstad J, Smith TB, Layton JB: **Social relationships and mortality risk: a meta-analytic review**. *PLoS Med* 2010, **7**. 332

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379 380

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382 383

384

385

386 387

388

389

390 391

392

393 394

395

396

397

399

400

04

- Tobin ET, Kane HS, Saleh DJ, Naar-king S, Poowuttikul P, Pierantoni W et al.: Health psychology naturalistically observed conflict and youth asthma symptoms naturalistically observed conflict and youth asthma symptoms. *Heal Psychol* 2015, 34:622-631.
- De Vogli R, Chandola T, Marmot MG: Negative aspects of close relationships and heart disease. Arch Intern Med 2007, 167:1951-1957.
- 24. Orth-Gomer K, Horsten M, Schneiderman N: Marital stress worsens prognosis in women with coronary heart disease. *JAMA* 2000, **284**:3008-3014.
- 25. Hostinar CE, Sullivan RM, Gunnar MR: Psychobiological
- mechanisms underlying the social buffering of the hypothalamic-pituitary-adrenocortical axis: a review of animal models and human studies across development. Psychol Bull 2014, 140:256-282.

This comprehensive review integrates animal models and human studies to illuminate how social relationships result in a dampened response to stressors, and also discusses neurological mediators and developmental perspectives.

- 26. Slatcher RB, Robles TF, Repetti RL, Fellows MD: Momentary work worries, marital disclosure, and salivary cortisol among parents of young children. *Psychosom Med* 2010, **72**:887-896.
- 27. Ditzen B, Neumann ID, Bodenmann G: Effects of different kinds of couple interaction on cortisol and heart rate responses to stress in women. *Psychoneuroendocrinology* 2007, **32**:565-574.
- Miller GE, Lachman ME, Chen E, Gruenewald TL, Karlamangla AS, Seeman TE: Pathways to resilience: maternal nurturance as a buffer against the effects of childhood poverty on metabolic syndrome at midlife. *Psychol Sci* 2011, 22:1591-1599.
- 29. Farrell AK, Simpson JA, Carlson EA, Englund MM, Sung S: Timing and buffering effects of life stress on adult physical health: a prospective longitudinal study. *Heal Psychol.* (in press).
- Saxbe DE, Repetti RL, Nishina A: Marital satisfaction, recovery from work, and diurnal cortisol among men and women. *Heal Psychol* 2008, 27:15-25.
- 31. Slatcher RB, Selcuk E, Ong AD: Perceived partner
 responsiveness predicts diurnal cortisol profiles 10 years later. *Psychol Sci* 2015, 26:972-982.

One of the few prospective longtudinal studies of relationship quality and health, this paper shows that reports of greater partner responsiveness predict healthier diurnal cortisol slopes 10 years later.

- 32. Holt-Lunstad J, Jones BQ, Birmingham W: **The influence of close relationships on nocturnal blood pressure dipping**. *Int J Psychophysiol* 2008.
- Helgeson VS: The effects of masculinity and social support on recovery from myocardial infarction. *Psychosom Med* 1991, 53:621-633.
- Coyne JC, Rohrbaugh MJ, Shoham V, Sonnega JS, Nicklas JM, Cranford JA: Prognostic importance of marital quality for survival of congestive heart failure. *Am J Cardiol* 2001, 88: 526-529.
- 35. Loving TJ, Crockett EE, Paxson AA: **Passionate love and** relationship thinkers: experimental evidence for acute cortisol elevations in women. *Psychoneuroendocrinology* 2009, **34**: 939-946.
- Bennett JM, Fagundes CP, Kiecolt-Glaser JK: The chronic stress of caregiving accelerates the natural aging of the immune system. *Immunosenescence* 2013:35-46.
- 37. Uchino BN, Smith TW, Berg CA: **Spousal relationship quality and** cardiovascular risk: dyadic perceptions of relationship ambivalence are associated with coronary-artery calcification. *Psychol Sci* 2014, **25**:1037-1042.
- Guyll M, Cutrona C, Russell D, Hostility: Relationship quality, and health among African American couples. J Consult Clin Psychol 2010, 78:646-654.

Current Opinion in Psychology 2016, 13:1-5

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409

410

414

415

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420

Relationship functioning, stress, and physical health Farrell and Simpson 5

- Howland M, Farrell AK, Simpson JA, Rothman AJ, Burns RJ, Fillo J et al.: Health psychology relational effects on physical activity: a dyadic approach to the theory of planned behavior. Heal Psychol 2016.
 - Stimpson JP, Wilson FA: Cholesterol screening by marital status and sex in the United States. Prev Chronic Dis 2009, 6:1-9.
- Delamater AM, Jacobson AM, Anderson B, Cox D, Fisher L, Lustman P et al.: Psychosocial therapies in diabetes report of the psychosocial therapies working group. Diabetes Care 2001, 24:1286-1292.
 - Fagundes CP, Way B: Early-life stress and adult inflammation. Psychol Sci 2014, 23:277-285.
- Q5 43. Farrell AK, Simpson JA, Young ES, Roisman GI: Early maternal sensitivity and physical health: The mediating role of adult attachment (in press).
 - 44. Miller GE, Chen E: **The biological residue of childhood poverty**. *Child Dev Perspect* 2013, **7**:67-73.
 - 45. Miller GE, Brody GH, Yu T, Chen E: A family-oriented
 - psychosocial intervention reduces inflammation in low-SES African American youth. Proc Natl Acad Sci U S A 2014, 111:11287-11292.
- In a rare intervention study, Miller and colleagues find that an intervention designed to improve parenting and family relationships in poor rural African Americans leads to reduced inflammation levels at age 19.

425 426 46. Ehrlich KB, Miller GE, Rohleder N, Adam EK: Trajectories of relationship stress and inflammatory processes in adolescence. Dev Psychopathol 2016, **28**:127-138. . 428 This paper examines stress over time in two types of relationships (family and peer) on several biological mediators and tests for a key individual 429 430 difference - race. The authors find that stress trajectories predict GCR and inflammation for White individuals, but not Asians. 431 432 Hostinar CE, Johnson AE, Gunnar MR: Parent support is less 47. 433 effective in buffering cortisol stress reactivity for adolescents compared to children. Dev Sci 2014:1-17.

424

440 441

442

This paper emphasizes the importance of considering developmental stage when studying the effects of relationships on stress and health by showing that maternal support buffers the physiological effects of stress on children, but not adolescents. 48 Kiecolt-Glaser IK Newton TL: Marriage and health; his and 439

- Kiecolt-Glaser JK, Newton TL: Marriage and health: his and hers. Psychol Bull 2001, 127:472-503.
- Laurent HK, Powers SI: Social-cognitive predictors of hypothalamic-pituitary-adrenal reactivity to interpersonal conflict in emerging adult couples. J Soc Pers Relat 2006, 23:703-720.
- 50. Belsky J, Pluess M: Beyond diathesis stress: differential susceptibility to environmental influences beyond diathesis stress: differential susceptibility to environmental influences. *Psychol Bull* 2009, 135:885-908.
 444
 445
 446
 447
 448

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