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## Age moderates the association between social integration and diurnal cortisol measures



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#### ABSTRACT

Social integration is defined as the degree to which an individual participates in a broad range of social relationships. Although measures of social integration vary across studies, it is often assessed as the number of social roles (e.g., parent, friend, student, volunteer) that an individual reports actively participating in. More socially integrated individuals tend to be healthier than those less socially integrated, but the biological mechanisms through which this occurs remain unclear. One possibility is that social integration might alter the function of the hypothalamic-pituitary-adrenal axis, of which cortisol is a key product, and in turn influence a broad range of health outcomes. This study examined the association between social integration and two indices of cortisol in a community sample of 680 healthy men and women aged 18-55. Because the social roles held by younger individuals may be more numerous yet superficial than those held by older individuals, this study also tested the hypothesis that these associations could be moderated by age such that lower levels of integration would be associated with cortisol dysregulation for older but not younger individuals in our sample. Participants provided salivary cortisol samples during waking hours on three days that were used to calculate diurnal cortisol levels and slopes. Increased social integration was associated with lower cortisol AUC among older (ages 35-55) but not younger (ages 18-34) individuals in our sample. Moreover, while increased social integration was associated with steeper diurnal cortisol slopes regardless of age, this association was strongest among older individuals. Differences in health behaviors, affect, and psychological stress did not mediate these associations. The results of this study support cortisol as a candidate biological mechanism through which increased social integration is associated with better physical health among older individuals.

#### 1. Introduction

Social integration is the degree to which an individual is included in or connected to a broad range of social relationships (Brissette et al., 2000). Although measures of social integration vary across studies, it is often assessed as the number of social roles (e.g., parent, friend, student, volunteer) that an individual reports actively participating in (e.g., Chang et al., 2017; Cohen et al., 1997). Numerous studies demonstrate an association between social integration and lower rates of morbidity (e.g., Barefoot et al., 2005; Seeman, 1996; Kroenke et al., 2012) and all-cause mortality (reviews by Holt-Lunstad et al., 2010; Shor and Roelfs, 2015). Importantly, social integration appears to be theoretically and empirically distinct from related social interaction measures that assess social contact frequency (Brissette et al., 2000) and has been shown to be more reliably associated with health outcomes (Barefoot et al., 2005; Chang et al., 2017; Cheng et al., 2014; Cohen et al., 1997; Holt-Lunstad et al., 2010; Shor and Roelfs, 2015) than measures of contact frequency.

Despite this compelling evidence, there are few studies of plausible biological mechanisms through which greater social integration may be associated with better long-term health. Previous work has demonstrated that more socially integrated individuals have lower allostatic loads assessed by an undifferentiated aggregation of biomarkers reflecting cardiovascular activity, metabolism and adipose tissue deposition, glucose metabolism, hypothalamic-pituitary-adrenal axis (HPA), and sympathetic nervous system (SNS) activity (Seeman et al., 2002), as well as lower levels of systemic inflammation (Shankar et al., 2011). An alternative possibility is that social integration might influence health outcomes primarily through its impact on the HPA axis, of which cortisol is a key product. Cortisol is a glucocorticoid hormone thought to regulate immunological and metabolic processes relevant to health (Sapolsky et al., 2000). Cortisol follows a diurnal pattern, rising rapidly immediately after waking and then declining steadily throughout the waking day. Flatter diurnal cortisol slopes have been associated with negative physical and mental health outcomes (review by Adam et al., 2017). Heightened total cortisol AUC has similarly been

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associated with negative outcomes including metabolic syndrome (Anagnostis et al., 2009; Brunner et al., 2002) and coronary atherosclerosis (Dekker et al., 2008). Flatter diurnal cortisol slopes and heightened total cortisol AUC may therefore represent distinct plausible biological pathways through which low levels of social integration are associated with poorer physical health.

There are several potential psychological and behavioral pathways through which social integration may alter the HPA response. For example, those low in social integration (socially isolated) may experience psychological stress which in turn induces HPA axis dysregulation (Berkman et al., 2000; Cohen et al., 1995; Grant et al., 2009). Alternatively, greater social integration may promote positive affect, decrease negative affect, or act as a source of social pressure and motivation to engage in better health practices (Berkman and Breslow, 1983; Berkman and Glass, 2000; Cohen, 1988; Cohen, 2004; Cohen and Lemay, 2007; Umberson, 1987). All of these have been found to aid in the regulation of the HPA response (e.g., Badrick et al., 2008; Badrick et al., 2007).

Finally, the majority of social integration and health research has focused on older adults (ages 55 and above) due to their higher risk for morbidity and mortality. One way to study this association in younger individuals is to focus on how social integration relates to biological markers with implications for long-term health. However, few studies thus far have pursued this strategy in younger participants. One notable exception is work by Yang et al. (2016), which found that lower levels of social integration were associated with greater inflammation and increased hypertensive risk among older adults (two samples ages 50-98 and 57-91), but not among younger adults (ages 24-32) or adolescents (ages 12-18). The social motivations and social roles held by younger individuals are likely to be quite different than those of older individuals (Carstensen, 1992). Younger individuals may possess more numerous yet more superficial connections, while older individuals may possess fewer but more meaningful connections. Moreover, the more superficial connections among younger individuals may not be sufficient to drive affective response or produce the social pressures and motivation to alter health practices. Consistent with previous research (Yang et al., 2016), we hypothesized that lower levels of social integration would be associated with greater average cortisol AUC and flatter diurnal slopes for individuals in their mid- to late-30 s and older, but that social integration would not be associated with cortisol dysregulation for individuals in their early-30 s and younger.

In the current study, we collected measures of social integration, social contact frequency, and salivary cortisol from 680 healthy volunteers between the ages of 18-55. Social integration was assessed as the number of social roles an individual participates in; and social contact frequency as the average number of people one interacts with daily. We expected social integration to be a more potent predictor of diurnal cortisol AUC and slopes than related measures of social contact frequency (Cohen et al., 1997; Shor and Roelfs, 2015). Salivary cortisol was collected across the waking period of three separate days. We hypothesized an association of greater social integration with lower cortisol AUC and steeper diurnal slopes in older but not younger individuals in our sample. Moreover, we expected that social integration would be associated with more positive affect, less negative affect, less psychological stress, and better health practices among older individuals, which would in turn mediate the association between social integration and diurnal cortisol (e.g., Cohen, 2004). Consistent with earlier research suggesting that social integration is a more potent predictor of morbidity and mortality than measures of social contact frequency, we expected social integration to account for more variance than contact frequency, and predict cortisol outcomes independently of frequency.

#### 2. Methods

#### 2.1. Participants

We examined aggregated archival data from three viral-challenge studies conducted by our laboratory between 1997 and 2011: Pittsburgh Cold Study 2 (PCS2), Pittsburgh Cold Study 3 (PCS3), and Pittsburgh Mind-Body Center Study (PMBC). Complete procedures and data from each study can be found at www.commoncoldproject.com. Prior to the beginning of all three studies, participants completed health screenings on the telephone, as well as an in-person medical examination administered by a study physician to determine that they were in good health and did not meet any study exclusion criteria: history of chronic illness, previous nasal/otologic surgery, regular use of prohibited medication, recent psychiatric diagnosis or hospitalization, HIV seropositivity, abnormal clinical profiles as determined by urinalysis, complete blood count, and analysis of blood chemistry, currently pregnant, lactating, or planning to become pregnant, recently participated in another psychology study, having cold or flu-like symptoms within the previous 30 days, previous hospitalization due to flu-like illness, use of steroids or immunosuppressants within previous 3 months, or allergies to egg or egg-products.

In total, 740 participants completed the three studies. We excluded participants from analyses if they did not provide information about their social interactions during the interview period (n=1), or were missing either relevant covariates (n=1) or primary outcome data (n=58). The final sample consisted of 680 healthy adults between the ages of 18 and 55 years (M=31.39, SD=10.8) recruited from the Pittsburgh, PA area. The sample was 49.7% female, 65.7% white, 30.0% African-American, and 4.3% other ethnicities. Participants provided informed consent prior to study enrollment and received financial compensation following their participation. The institutional review boards of both Carnegie Mellon University and the University of Pittsburgh School of Medicine approved each study.

#### 2.2. Procedures

As part of the parent studies, participants were then exposed to a virus known to cause the common cold, then followed in quarantine and monitored for the development of infection. All data reported here were collected during the baseline period of the parent studies prior to viral-exposure. Eligible participants completed baseline assessments at home, during in-person laboratory visits, and during an initial day of quarantine prior to viral-exposure.

#### 2.3. Measures

#### 2.3.1. Salivary cortisol

Salivary cortisol samples were collected across the waking period of three separate non-consecutive days (see suggestions by Kraemer et al., 2006; Saxbe, 2008). Participants were provided with rolls of cotton inside of a plastic collection tube used to collect each sample (Salivettes°; Sarstedt AG & Co, Nümbrecht, Germany), as well as detailed written instructions and either a pre-programmed wristwatch (PCS2) or handheld computer (PCS3, PMBC) that signaled participants at each collection time. For each collection, participants were instructed to place the cotton in their mouth, allow it to become saturated with saliva, spit it back into the tube, and then reseal the tube. At each collection time, the signaling device provided a unique alphanumeric code. Participants were instructed to write this code as well as the time and date of collection on each tube. Finally, participants stored completed samples in their refrigerator and then brought the tubes with them to their baseline study session where they were collected by staff and frozen for storage.

Two of the three sets of cortisol samples were collected on separate non-consecutive days in the participant's natural environment 1–6

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