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# Reciprocal relationship between acute stress and acute fatigue in everyday life in a sample of university students



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#### ABSTRACT

We investigated whether stress may influence fatigue, or vice versa, as well as factors mediating this relationship. Fifty healthy participants (31 females,  $23.6 \pm 3.2$  years) completed up to 5 momentary assessments of stress and fatigue during 5 days of preparation for their final examinations (exam condition) and 5 days of a regular semester week (control condition). Sleep quality was measured by self-report at awakening. A sub-group of participants (n = 25) also collected saliva samples. Fatigue was associated with concurrent stress, stress reported at the previous measurement point, and previous-day stress. However, momentary stress was also predicted by concurrent fatigue, fatigue at the previous time point, and previous-day fatigue. Sleep quality mediated the association between stress and next-day fatigue. Cortisol and alpha-amylase did not mediate the stress–fatigue relationship. In conclusion, there is a reciprocal stress–fatigue relationship. Both prevention and intervention programs should comprehensively cover how stress and fatigue might influence one another.

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#### 1. Introduction

Stress is associated with numerous bodily complaints, such as fatigue—a very common symptom in the general population (Nijrolder, van der Horst, & van der Windt, 2008; Pawlikowska et al., 1994) that can be defined as a subjective state of exhaustion, tiredness, weakness, and lack of energy that impairs daily activities (Riley et al., 2010; Schwarz, Krauss, & Hinz, 2003). Both clinical evidence and individual experiences indicate that it may be assumed that high stress puts people at risk of developing fatigue. Yet, most available data on the interaction between stress and fatigue come from cross-sectional studies with only one point of assessment (e.g., Brown & Thorsteinsson, 2009; Kocalevent, Hinz, Brahler, & Klapp, 2011). There are only very few longitudinal studies showing that stress may temporally precede fatigue (e.g., Kato, Sullivan, Evengard, & Pedersen, 2006). Nevertheless, the mechanisms of how

stress may ultimately translate into fatigue are not well understood. While experimental studies have the advantage of being able to control for a variety of potentially confounding variables, they are also limited in terms of the generalization of the findings to real life, i.e., they result in reduced ecological validity. There is a relative scarcity of studies examining the relationship between stress and fatigue as individuals engage in their daily life routines in their own environments. One notable exception is a study by Dittner, Rimes, and Thorpe (2011), in which the authors showed that fatigue levels in first-year college students were significantly higher following a period of academic stress than at the beginning of the academic year. However, in this study, perceived stress was only measured at the second time point. In a recent study by Akerstedt, Axelsson, Lekander, Orsini, and Kecklund (2014), fatigue at bedtime was found to be associated with average stress during the day. The results do not take into account influences on short-term changes in fatigue within individual days.

Besides evidence that stress may precede fatigue, it might also be considered that fatigue precedes stress (e.g., because fatigue limits coping abilities which might help the individual not to feel stressed by challenging situations). To the best of the authors' knowledge, there has been no study investigating this direction of causality.

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Apart from choosing an appropriate design to tackle the question of directionality, it is also important to consider mediating factors that might explain the predicted association between stress and fatigue. One of these factors is subjective sleep quality: a negative relationship between stress and sleep quality was found in several cross-sectional studies (e.g., Akerstedt, Fredlund, Gillberg, & Jansson, 2002; Knudsen, Ducharme, & Roman, 2007). This effect was also shown in an everyday life study using an end-of-day measurement of stress (Akerstedt et al., 2012). Furthermore, subjective sleep quality has also been found to be a predictor of fatigue (Akerstedt et al., 2014; Lavidor, Weller, & Babkoff, 2003). Interestingly, one (cross-sectional) study indicated that sleep quality mediated the relationship between stress and fatigue (Thorsteinsson & Brown, 2009). It thus seems reasonable to predict that subjective sleep quality may be an important mediating factor that needs to be considered in studies examining the relationship between stress and fatigue.

The effects of stress on fatigue are also likely to be impacted by the body's stress systems, i.e., the hypothalamic pituitary adrenal (HPA) axis and the autonomic nervous system (ANS). Powell, Liossi, Moss-Morris, and Schlotz (2013) point out the relevance of measures of cortisol (the main effector of the HPA axis) variability, which indicate general "responsiveness" of the HPA axis, especially cortisol concentrations in the morning (e.g., morning values, cortisol awakening response, CAR), and measures assessing the decrease in cortisol throughout the day (slope). Previous studies have shown higher morning values in chronically stressed individuals compared to non-stressed controls (e.g., Schulz, Kirschbaum, Pruessner, & Hellhammer, 998). In an intra-individual comparison, Dahlgren, Kecklund, and Ackerstedt (2005) reported no abnormalities in the morning, but an overall flattened diurnal cortisol slope during a period of higher stress. Other studies indicate that fatigue is associated with a reduction of cortisol variability across the day (e.g., Dahlgren, Kecklund, Theorell, & Akerstedt, 2009). On the other hand, Eek, Karlson, Garde, Hansen, and Orbaek (2012) found positive associations between cortisol increases in the morning and several aspects of fatigue (lack of energy, lack of motivation, physical exertion). Furthermore, Adam, Hawkley, Kudielka, and Cacioppo (2006) found an association between low morning cortisol values and high fatigue levels throughout the day in a sample of older adults. Thus, research illustrates the importance of considering measures of cortisol variability when analyzing associations between stress and fatigue.

As fatigue is a prominent feature in autonomic dysregulation, it can be assumed that it is related not only to changes in HPA axis activity, but also to changes in ANS (Nater, Heim, & Raison, 2012). Some studies indeed point to ANS alterations in fatigued individuals: Boneva et al. (2007), for instance, report higher heart rates as well as lower heart rate variability in persons with chronic fatigue syndrome. De Vente, Olff, Van Amsterdam, Kamphuis, and Emmelkamp (2003) found higher resting heart rate in fatigued persons compared to healthy controls. In a recent study using a sample of persons with chronic fatigue syndrome, we found a lower response of epinephrine to a physical stress test compared to healthy controls, indicating altered ANS dynamics in the affected persons (Strahler, Fischer, Nater, Ehlert, & Gaab, 2013). Overall, previous findings point to signs of ANS dysregulation in fatigued persons, but the results are far from unequivocal. Furthermore, we are not aware of any studies examining associations between ANS activity and fatigue in everyday life.

In summary, research has established a positive relationship between stress and fatigue, but few studies have examined this relationship across multiple time points. The question of directionality, i.e., whether stress temporally precedes fatigue or vice versa, has, to our knowledge, never been addressed. To investigate this, temporal associations (carry-over effects within individual days from one time point to the next and/or between days) need to be considered. Furthermore, an analysis of possible mediators is crucial when examining the association between stress and fatigue. We expect sleep quality as well as changes in the biological stress systems, i.e., the HPA axis and the ANS, to be of particular importance in this regard. Concerning the question of how the organism changes and adapts to higher stress levels, a within-subjects design clearly allows for stronger conclusions than a between-subjects design. An adequate paradigm to test such associations is to examine students during a period of exam preparation and during a more relaxed phase of the term (for an overview see Biondi & Picardi, 1999).

In the current study, we, thus, examined whether and how stress translates into fatigue in everyday life. We also wanted to be open to the alternative hypothesis that fatigue may influence stress experiences. To maximize ecological validity, we used an ambulatory assessment design. Rather than exploring differences between groups, we assessed students in two different everyday life conditions: on five days during the beginning of the semester (control condition) and on five days during the preparation for final exams (exam condition).

#### 2. Methods

#### 2.1. Participants

Data collection took place during the summer term (May through August) of 2012 at the Philipps-Universität Marburg, Germany. Participants were recruited via university student mailing lists or notices on campus. Inclusion criteria were being a university student, speaking German fluently, age 18-35 years, no obesity (body mass index of 29 or less), no psychiatric or medical illness known to affect endocrine or autonomic functioning, smoking less than 5 cigarettes per week, no drug use, and for women not being pregnant, no breast feeding and having regular menstruation. The initial sample consisted of 55 participants (35 women,  $23.3 \pm 3.11$  years), of whom three declined to participate further after completing the first assessment period. A fourth person had to be excluded due to device failures. After completion of data collection, a fifth person was removed from statistical analysis due to incomplete data (more than 50% missing data in exam condition). Thus, data from 50 participants were included in the final statistical analyses. Participants received 50 Euro (about 64 USD) or course credit. The study was approved by the local ethics committee of the Faculty of Psychology at the Philipps-Universität Marburg, Germany. All participants provided written informed consent.

#### 2.2. Materials and procedure

We used an ambulatory assessment approach. Participants were assessed for 5 days during the first weeks of the semester (control condition) and for 5 days during the preparation for final examinations within the last weeks of the semester (exam condition). Following the initial contact, participants were invited to the laboratory of the department of Clinical Biopsychology, Philipps-Universität Marburg, Germany, for an assessment to rule out exclusion criteria. Furthermore, they were instructed in the use of a pre-programmed (iDialogPad, G. Mutz, Cologne, Germany) iPod touch® as well as, in a sub-sample, ambulatory saliva sampling with the SaliCap® system (IBL, Hamburg, Germany). Finally, participants were instructed to complete questionnaires online at home. During both assessment conditions, the iDialogPad program was activated by the participants every morning upon awakening. There was a pre-programmed alarm 30 min after initial activation (i.e., after awakening), at 10 am, 2 pm, 6 pm, and 9 pm.

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