Cancer-related fatigue in a couples’ context
Müller, Fabiola

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Associations of daily partner responses with fatigue interference and relationship satisfaction in colorectal cancer patients

Fabiola Müller, Marrit A. Tuinman, Ellen Stephenson, Ans Smink, Anita DeLongis, Mariët Hagedoorn

Health Psychology, in press
Chapter 5

Abstract

Objective: Investigating the associations of daily partner responses towards patient’s fatigue- and well-behavior with patient’s fatigue interference and relationship satisfaction. The moderating effect of fatigue severity was also examined.

Methods: In an intensive longitudinal design, patients treated for colorectal cancer and their partners (n = 101 dyads) completed diaries for 14 days. Patients and partners reported on partner responses towards patient’s fatigue-behavior (e.g., resting), partner responses towards patient’s well-behavior (e.g., being active) and fatigue severity. Patients also indicated their fatigue interference and relationship satisfaction. Multilevel modeling was applied to assess within-person main- and interaction-effects.

Results: Patient-reported solicitous responses towards fatigue-behavior and negative responses towards well-behavior were associated with increases in fatigue interference, while facilitative responses towards well-behavior were associated with a decrease in fatigue interference. The latter two associations were intensified on days patients reported relatively high fatigue. Solicitous responses towards fatigue-behavior and facilitative responses towards well-behavior were also associated with increases in relationship satisfaction. Punishing responses towards fatigue-behavior were associated with a decrease in relationship satisfaction, especially on days patients reported higher fatigue. Models using partner reports largely confirmed the main-effects of partner responses on fatigue interference and relationship satisfaction but failed to reproduce the moderating effect of fatigue.

Conclusions: Daily partner responses appear to impact patients’ fatigue adjustment, especially on days patients experience high fatigue levels. Only facilitative responses towards well-behavior seem to benefit both patients’ fatigue interference and relationship satisfaction. Couple-interventions should guide partners to encourage patients’ well-behavior and aid them to correctly estimate patients’ current fatigue severity.

Keywords: partner responses, symptom severity, daily diary method, fatigue, cancer
Partner responses and fatigue severity

Introduction

Often, patients encounter severe and persistent symptoms within the context of their intimate relationship. Research based on the operant model (Fordyce, 1976) demonstrated that the patient’s intimate partner can both relieve or worsen the patient’s symptom and its interfering effects (e.g., Newton-John, 2002). However, so far, operant research has mainly focused on the conditioning effects of partner responses towards the patient’s illness-behavior and has not considered that partner responses might also impact the couple’s relationship (Cano & Williams, 2010). Further, the effect of partner responses might vary as a function of symptom severity, as severe symptoms may indicate high stress and need for support. To foster our understanding of dyadic interactions in couples confronted with persistent and interfering symptoms, this diary study investigated the associations of partner responses towards cancer patient’s fatigue- and well-behavior with fatigue interference and relationship satisfaction, and it tested the dependency of these associations upon current fatigue levels.

The operant model in the field of pain (Fordyce, 1976) acknowledges that symptoms are experienced within a social context which contributes to patients’ symptom development. The model states that partner responses towards patients’ illness-behavior (e.g., resting, complaining about the symptom) can either function as reinforcement or punishment of that behavior. As such, partner responses can either increase or reduce the frequency of illness-behavior and hence impact other symptom outcomes, including symptom interferences, i.e., the degree to which patients’ symptoms interfere with their daily life activities (e.g., work, social activities). Ample evidence supports the notion that solicitous responses towards illness-behavior (e.g., taking over household chores, encouraging the patient to rest) act as reinforcement and hence increase symptom severity and its interfering effects (Newton-John, 2002; Pence, Thorn, Jensen, & Romano, 2008; Schmaling, Smith, & Buchwald, 2000). Only mixed evidence is available for the assumption that punishing partner responses towards illness-behavior (e.g., getting irritated, expressing frustration) reduce illness-behavior and thus decrease symptoms and its interfering effects (Flor, Kerns, & Turk, 1987; Newton-John, 2002; Pence et al., 2008; Prenevost & Reme, 2017). Most studies so far focused on the effect of partner responses towards patient’s illness-behavior only. However, there is some evidence that symptom interferences are also influenced by partner responses towards the
patient’s well-behavior (e.g., maintaining activity, performing exercises). That is, facilitative responses towards well-behavior (e.g., encouraging activity, supporting well-behavior) have been found to be related to less, and negative responses towards well-behavior (e.g., expressing concern, telling the patient to ‘slow down’) to more symptoms and its interfering effects (Raichle, Romano, & Jensen, 2011; Rosen, Bergeron, Glowacka, Delisle, & Baxter, 2012; Schwartz, Jensen, & Romano, 2005). Even though most research so far has been limited to patients with pain and had a cross-sectional design, it demonstrates the need to study responses towards both patient’s illness- and patient’s well-behavior in order to fully grasp the impact partner responses can have on patient’s symptom interference.

The operant model guided ample research indicating that partner responses can alter symptom interferences but has fallen short in acknowledging the impact the same partner responses might have on the couple’s relationship. The intimacy model (Reis & Shaver, 1988) allows conceptualizing partner responses as an interpersonal process that can communicate understanding, validation and caring to the patient, which is assumed to foster intimacy and thereby enhance relationship satisfaction. In contrast, partner responses that fail to convey responsiveness can create distance between partners and thus decrease relationship satisfaction. Accordingly, solicitous and facilitative responses might be interpreted as responsiveness by patients and hence increase their relationship satisfaction, while punishing and negative responses might have the opposite effect. In line with the predictions derived from the intimacy model, solicitous responses towards illness-behavior and facilitative responses towards well-behavior have been found to be related to better, and punishing responses towards illness-behavior to worse relationship outcomes (Flor et al., 1987; McWilliams, Kowal, Verrier, & Dick, 2017; Pence et al., 2008; Raichle et al., 2011). Hence, the limited evidence so far suggests that behavior-specific partner responses can also be conceptualized as intimacy processes and as such can improve or impair the couple’s relationship. Considering that a healthy relationship is an important coping resource for patients’ adjustment to cancer (Manne & Badr, 2008; Yang & Schuler, 2009), research needs to investigate the effect of partner responses on both the patient’s symptom interference and relationship satisfaction.

The impact of partner responses might vary as a function of current symptom severity. The severity of symptoms such as fatigue differ between patients
Partner responses and fatigue severity

along the disease trajectory (Müller et al., 2017) and, importantly, also fluctuate within patients on a daily level (Timmerman, Dekker-van Weering, Tönis, Hermens, & Vollenbroek-Hutten, 2015). The majority of studies, however, only control for symptom severity (e.g., McWilliams et al., 2017; Raichle et al., 2011) which precludes examining whether severe symptoms make patients more amenable to their partners’ responses. Conceptualizing symptom severity as a stressor within the stress-buffering model (Cohen & Wills, 1985) suggests that partner responses might have a stronger effect on symptom interference on days that patients experience more severe symptoms. Similarly, symptom severity might intensify the effect of partner responses on the patient’s relationship satisfaction. That is, patients currently experiencing severe symptoms might feel an increased need for support from their partner. Receiving support that matches someone’s needs is known to be positively related to relationship satisfaction (Dehle, Larsen, & Landers, 2001), possibly because the recipients perceive their partners as responsive towards their needs (Bar-Kalifa, Bar-Kalifa, Rafaeli, George-Levi, & Vilchinsky, 2016; Cutrona, Shaffer, Wesner, & Gardner, 2007; Maisel & Gable, 2009). In short, the beneficial and detrimental effects of partner responses on symptom interference and relationship satisfaction may be intensified with increasing levels of patients’ symptom severity. Research applying an intensive longitudinal design (Bolger & Laurenceau, 2013) can capture fluctuations in symptom severity and allows to investigate whether its relative within-person changes moderate the effect of partner responses on symptom interference and relationship satisfaction. Additionally, the diary method allows an investigation of partner interactions as they naturally occur in daily life. From a theoretical perspective, assessing the moderating effect of current symptom severity will broaden our understanding of contextual factors influencing the effects of dyadic interactions in couples coping with persistent symptoms. From a clinical perspective, identifying which and when partner responses are most beneficial or detrimental for patient’s symptom interference and relationship satisfaction can inform intervention development targeting adaptive dyadic coping with persistent symptoms.

In sum, this diary study investigated the associations of partner responses with the outcomes fatigue interference and relationship satisfaction, as well as the moderating effect of fatigue severity. Fatigue experienced after completion of the cancer treatment is well suited to study these associations as it is a prevalent and
persistent symptom that substantially interferes with patients’ daily life (e.g., Jones et al., 2016) and, similar to chronic pain, seems amenable to social interactions (e.g., Goedendorp, Gielissen, Verhagen, & Bleijenberg, 2013). We expected solicitous responses towards fatigue-behavior (H1a) and negative responses towards well-behavior (H2a) to be associated with *increases* in fatigue interference. In contrast, punishing responses towards fatigue-behavior (H3a) and facilitative responses towards well-behavior (H4a) were expected to be associated with *decreases* in fatigue interference. Further, solicitous responses towards fatigue-behavior (H1b) and facilitative responses towards well-behavior (H2b) were expected to be associated with *increases* in relationship satisfaction. In contrast, punishing responses towards fatigue-behavior (H3b) and negative responses towards well-behavior (H4b) were expected to be associated with *decreases* in relationship satisfaction. These associations were expected to be intensified on days patients experience high levels of fatigue (H5a/b – H8a/b). See Figure 1 for a model of the expected associations. As patient’s and partner’s reporting of symptom severity and support provision do not necessarily correspond (Badr & Milbury, 2011; Lehman et al., 2011), analyses were also conducted with the partner responses and patient’s fatigue severity as reported by the partner.
Figure 1. Model depicting the hypotheses for the outcome (a) fatigue interference and (b) relationship satisfaction.

Note. H, Hypothesis. Solid lines represent expected positive associations and dashed lines represent expected negative associations. Hypotheses printed in bold were confirmed (patient-model), see Results for details.
Methods

Participants
Diary data used were from a larger study investigating dyadic coping with cancer (Müller et al., 2018). Patients treated for colorectal cancer were recruited via four Dutch hospitals. A nurse invited patients and their partners to participate in the study during the patients’ follow-up visit or patients were mailed a letter inviting them and their partners to participate. Eligibility criteria were that patients (1) completed cancer treatment at least 6 months previously, (2) were not terminally ill, (3) were married or cohabiting with a partner for at least 1 year, and (4) scored at least a 1 on average fatigue during the previous week on a scale from 0 (‘no fatigue’) to 10 (‘as fatigued as I could be’). Couples were excluded if one or both partners were (1) younger than 18 years, (2) not able to understand Dutch, (3) cognitively impaired, or (4) diagnosed with chronic fatigue syndrome or fibromyalgia.

Of the 519 eligible couples, 185 agreed to participate and were mailed the baseline questionnaire. Scores on the baseline questionnaire were used to select couples to participate in the diary component of the study. Couples were eligible if the patient reported relevant levels of fatigue as indicated by scoring above the cut-off score (1) on the Checklist Individual Strength (Knoop, Bleijenberg, Gielissen, van Der Meer, & White, 2007; Vercoulen et al., 1994) or (2) the Fatigue Symptom Inventory (Donovan, Jacobsen, Small, Munster, & Andrykowski, 2008; Hann et al., 1998), or by reporting (3) at least 2 days of fatigue during the previous week. Thirty-six of the invited couples (n = 137) did not agree to participate in the diary component, mainly due to lack of interest (39%), resulting in a final sample of 101 cancer patients and their partners. According to the Dutch law for medical research involving human subjects (WMO), the Medical Ethical Committee of the Medical University of Groningen provided a waiver for ethical assessment (METc 2013/158). The study was conducted according to the declaration of Helsinki. Participants signed an informed consent form prior to participation.

Procedure
Diary data were collected between September 2014 and July 2016. The research assistant visited the couples at home to provide instructions for the diary procedure. Diary assessments were delivered through an app on tablets 3 times daily for 14 consecutive days to each partner of the couple. Participants received a reminder-
Partner responses and fatigue severity

signal on the tablet to fill in each assessment. The assessment schedule was adapted to match their daily routines, that is, participants received the reminder signal within approximately 1 hour after waking (morning assessment), 1 hour after lunch (noon assessment) and 1 hour prior to going to bed (evening assessment). Couples were instructed to respond to the assessments separately. An overview of the diary items relevant to this study can be found in the supplementary material.

None of the participants dropped out during the diary period and adherence to the protocol was excellent. Of the total number of 1414 diary days (101 couples x 14 days), 10/12 morning-, 15/23 noon- and 16/15 evening assessments of the patients and partners respectively were missing. The focal predictor variables as well as the two outcome measures were reported at the evening assessments. Of the data collected in partners, only evening assessments were used in the current study. Fourteen valid evening assessments were available for 81% of the patients and 76% of the partners.

Measures

Demographic and clinical variables. Gender, age, relationship duration, occupational status, and clinical variables were assessed by self-report in the baseline questionnaire. The cancer site was dichotomized into a carcinoma located in (1) the colon and (2) the rectum, or anus. Cancer stage was dichotomized into (1) good prognosis (stage I, stage II) and (2) poor prognosis (stage III, stage IV). Treatment was dichotomized into (1) surgery only and (2) surgery and additional treatment (chemo- and/or radiotherapy). Patients with a permanent or temporary stoma were categorized as having a stoma.

Partner responses. Items were developed based on the Spouse Response Inventory (Schwartz et al., 2005), the West Haven-Yale Multidimensional Pain Inventory (Kerns, Turk, & Rudy, 1985) and its significant-other version (Kerns & Rosenberg, 1995). Items were chosen and adapted to be applicable to the daily context (e.g., referring to ‘today’) and fatigue instead of pain. Every evening, both partners of the couple reported on the degree to which they received (‘How did your partner respond to you today?’, patient) or provided (‘How did you respond to your partner today?’, partner) responses towards the patient’s fatigue- and well-behavior during the day. Solicitous responses towards fatigue-behavior (e.g., ‘My partner took over my chore (e.g., in the household, cooking)’, patient) and pun-
ishing responses towards fatigue-behavior (e.g., ‘I expressed my frustration at my partner’, partner) were each assessed with 3 items. Also, facilitative responses towards well-behavior (e.g., ‘My partner encouraged me to do something’, patient) and negative responses towards well-behavior (e.g., ‘I told my partner to slow down’, partner) were each assessed with 3 items. Responses ranged from 0 (‘not at all’) to 4 (‘very much’). Higher mean scores indicate more frequent responses of any type.

**Fatigue severity.** Three times daily, patients reported on their momentary level of fatigue with 1 item (‘How fatigued do you feel right now?’). These reports were aggregated to represent patient’s average level of fatigue across the day. Once daily, at each evening assessment, partners reported with 1 item on the fatigue they believed the patients were experiencing during the day (‘How fatigued did your partner feel today, according to you?’). Responses ranged from 0 (‘not at all’) to 10 (‘as fatigued as I (he/she) could be’).

**Fatigue interference.** Every evening, patients responded to 6 items regarding how much their fatigue interfered with their daily activities (i.e., physical, social and mental activities, plans and appointments) and their enjoyment of the day (e.g., ‘Today, my fatigue interfered with my physical activities (e.g., biking, vacuum cleaning, lifting objects, sports, hiking)’; ‘Today, I have moved an appointment or revised a plan because I was feeling fatigued.’). Responses ranged from 0 (‘not at all/strongly disagree’) to 4 (‘extremely/strongly agree’). Higher mean scores indicate higher daily fatigue interference.

**Relationship satisfaction.** In the morning- and evening assessment, patients reported on their momentary relationship satisfaction with 1 item (‘How satisfied are you with your relationship right now?’). Responses ranged from 0 (‘not at all satisfied’) to 10 (‘extremely satisfied’).

**Statistical analysis**

Multilevel modeling was used to account for the nesting of diary assessments within patients (Bolger & Laurenceau, 2013). Models were run in R using the lme4 package (Bates, Mächler, Bolker, & Walker, 2015). To examine the within-person associations between partner responses and the outcome variables, the diary measures (level 1 predictors) were person-mean centered (i.e., each participant’s mean score was subtracted from his/her raw score at each assessment point). For the
Partner responses and fatigue severity

Patient-model, fatigue severity was aggregated across the day prior to the centering. The predictor variables were also included as grand-mean centered variables (level 2) to facilitate model estimation and the interpretation of the intercepts. Random intercepts and slopes of the predictors were included in all models unless otherwise specified.

To test the moderating effect of daily fatigue severity, lower-level interaction-terms (i.e., the product of the person-mean centered predictor variables) were entered as fixed terms. Non-significant interactions were removed from the models. To interpret significant interactions, we plotted the conditional effect of the focal predictor on the outcome at mean values of fatigue severity and 1 SD above and below its mean. As fatigue severity was entered as person-mean centered variable, its mean (0) represents each patient’s level of fatigue that was typical for him/her across the entire diary period. Second, we estimated the region of significance for significant interactions using the Johnson-Neyman technique (Johnson & Neyman, 1936), which provides the value of the moderator (i.e., fatigue severity) at which the focal predictor (i.e., partner responses) reaches significance in predicting the outcome (i.e., fatigue interference, relationship satisfaction; Preacher, Curran, & Bauer, 2006). For these two steps, the online tool provided by Preacher et al. (2006) was used.

Demographics, clinical and relationship characteristics, daily sleep and diary day were tested as possible confounders in the patient-models. We retained those that significantly contributed to the final models, which was diary day. In order to predict changes in the outcome variables, we controlled for the outcome measures as assessed at the previous assessment. The previous assessment of fatigue interference was conducted at the prior evening (t-1) and previous relationship satisfaction was assessed in the morning at the same day as the outcome was assessed (t). The primary analyses were conducted with patient reports only. Lastly, final models were also run with partner responses and fatigue severity as reported by the partner to examine the robustness of the findings.

Results

Demographics and descriptive results
The sample consisted of 101 post-treatment colorectal cancer patients and their partners (see Table 1). Participating patients (n = 101) did not differ significantly
from patients who did not agree to participate in the diary component (n = 36) on any of the study-relevant variables, i.e., baseline fatigue and the demographic and clinical characteristics as reported in Table 1. Descriptive statistics of the within-person variables can be found in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Sample characteristics and descriptives of daily diary measures</th>
<th>Patients, n = 101</th>
<th>Partners, n = 101</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD) n (%)</td>
<td>Mean (SD) n (%)</td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>64.3 (10.2) 67 (66.3%)</td>
<td>63.2 (11.2) 34 (33.7%)</td>
</tr>
<tr>
<td>Gender, male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relationship duration, years</td>
<td>37.7 (13.4) 26 (25.7%)</td>
<td>37.7 (13.4) 29 (28.7%)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed (full- or part-time)</td>
<td>26 (25.7%) 44 (43.6%)</td>
<td>29 (28.7%) 40 (39.6%)</td>
</tr>
<tr>
<td>Retired</td>
<td>44 (43.6%) 15 (14.9%)</td>
<td>40 (39.6%) 22 (21.8%)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>15 (14.9%) 11 (10.9%)</td>
<td>22 (21.8%) 2 (2.0%)</td>
</tr>
<tr>
<td>Unable to work</td>
<td>11 (10.9%) 3 (3%)</td>
<td>2 (2%) 6 (5.9%)</td>
</tr>
<tr>
<td>Unpaid work</td>
<td>3 (3%) 2 (2%)</td>
<td>6 (5.9%) 2 (2%)</td>
</tr>
<tr>
<td>Other, unknown</td>
<td>2 (2%) 2 (2%)</td>
<td>2 (2%) 2 (2%)</td>
</tr>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer site, colon</td>
<td>63 (62.4%) .</td>
<td></td>
</tr>
<tr>
<td>Prognosis, good</td>
<td>78 (77.2%) .</td>
<td></td>
</tr>
<tr>
<td>Treatment, surgery only</td>
<td>45 (44.6%) .</td>
<td></td>
</tr>
<tr>
<td>Stoma, yes</td>
<td>50 (49.5%) .</td>
<td></td>
</tr>
<tr>
<td>Time since diagnosis, months</td>
<td>17 (9) .</td>
<td></td>
</tr>
<tr>
<td>Time since treatment, months</td>
<td>13 (8) .</td>
<td></td>
</tr>
</tbody>
</table>
Partner responses and fatigue severity

Table 1 (continued)

<table>
<thead>
<tr>
<th></th>
<th>Patients, n = 101</th>
<th>Partners, n = 101</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>ICC</td>
</tr>
<tr>
<td>Daily diary predictors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solicitous Fatigue-Behavior</td>
<td>1.41 (0.55)</td>
<td>0.60</td>
</tr>
<tr>
<td>Punishing Fatigue-Behavior</td>
<td>0.24 (0.36)</td>
<td>0.49</td>
</tr>
<tr>
<td>Facilitative Well-Behavior</td>
<td>1.59 (0.57)</td>
<td>0.52</td>
</tr>
<tr>
<td>Negative Well-Behavior</td>
<td>0.74 (0.56)</td>
<td>0.63</td>
</tr>
<tr>
<td>Fatigue Severity^a</td>
<td>3.54 (1.22)</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily diary outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue Interference</td>
<td>0.65 (0.42)</td>
<td>0.65</td>
</tr>
<tr>
<td>Relationship Satisfaction, eveng</td>
<td>8.87 (0.72)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Note. SD, within-person standard deviation; ICC, intraclass correlation; eveng, evening.
^a Aggregated across the day (patient). ^b The within-person reliability coefficient R_C was calculated as proposed by Shrout and Lane (2012) and reflects whether there are reliable within-person differences in change over time.

Associations of partner responses with fatigue interference

Results are shown in Table 2. As expected, solicitous responses towards patient’s fatigue-behavior (H1a, b = 0.05, p = .044) and negative responses towards well-behavior (H2a, b = 0.14, p < .001) were positively associated with fatigue interference. In other words, an increase of 1 unit on the person-mean centered scale for solicitous responses towards fatigue-behavior (e.g., from 0 to 1) would translate into a 0.05 unit increase on the fatigue interference scale that ranges from 0 (‘no interference’) to 4 (‘extreme interference’), while controlling for fatigue interference as assessed at the previous day (t-1). We failed to find the expected association between punishing responses towards fatigue-behavior and fatigue interference (H3a, b = 0.06, p = .067) but, as expected, facilitative responses towards well-behavior were associated with a decrease in fatigue interference (H4a, b = -0.05, p = .018).
### Table 2

**Associations of partner responses with fatigue interference and relationship satisfaction and the moderating effect of fatigue severity**

<table>
<thead>
<tr>
<th></th>
<th>Fatigue Interference</th>
<th>Relationship Satisfaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>95% CI</td>
</tr>
<tr>
<td><strong>Level 1: Within-person effects</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>0.66</td>
<td>0.57 – 0.74</td>
</tr>
<tr>
<td>Diary day (1-14)^b</td>
<td>-0.004</td>
<td>-0.01 – 0.002</td>
</tr>
<tr>
<td>Solicitous Fatigue-Behavior</td>
<td>0.05</td>
<td>0.003 – 0.10</td>
</tr>
<tr>
<td>Punishing Fatigue-Behavior</td>
<td>0.06</td>
<td>-0.004 – 0.13</td>
</tr>
<tr>
<td>Facilitative Well-Behavior</td>
<td>-0.05</td>
<td>-0.09 – -0.01</td>
</tr>
<tr>
<td>Negative Well-Behavior</td>
<td>0.14</td>
<td>0.08 – 0.20</td>
</tr>
<tr>
<td>Fatigue Severity</td>
<td>0.08</td>
<td>0.05 – 0.10</td>
</tr>
<tr>
<td>Punishing Fatigue-Behavior x Fatigue</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Facilitative Well-Behavior x Fatigue</td>
<td>-0.05</td>
<td>-0.09 – -0.02</td>
</tr>
<tr>
<td>Negative Well-Behavior x Fatigue</td>
<td>0.09</td>
<td>0.06 – 0.13</td>
</tr>
<tr>
<td>Fatigue Interference (t-1)</td>
<td>-0.05</td>
<td>-0.10 – 0.01</td>
</tr>
<tr>
<td>Relationship Satisfaction (t), mrng</td>
<td>.</td>
<td>.</td>
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</tbody>
</table>
**Table 2 (continued)**

<table>
<thead>
<tr>
<th></th>
<th>Fatigue Interference</th>
<th></th>
<th>Relationship Satisfaction</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>95% CI</td>
<td>p</td>
<td>SD&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Level 2: Between-person effects</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solicitous Fatigue-Behavior</td>
<td>0.08</td>
<td>-0.09 – 0.25</td>
<td>.367</td>
<td>.</td>
</tr>
<tr>
<td>Punishing Fatigue-Behavior</td>
<td>0.08</td>
<td>-0.15 – 0.31</td>
<td>.481</td>
<td>.</td>
</tr>
<tr>
<td>Facilitative Well-Behavior</td>
<td>-0.16</td>
<td>-0.31 – -0.004</td>
<td>.048</td>
<td>.</td>
</tr>
<tr>
<td>Negative Well-Behavior</td>
<td>0.27</td>
<td>0.10 – 0.44</td>
<td>.003</td>
<td>.</td>
</tr>
<tr>
<td>Fatigue Severity</td>
<td>0.12</td>
<td>0.08 – 0.17</td>
<td>&lt;.001</td>
<td>.</td>
</tr>
</tbody>
</table>

n patients/n diary assessments  
101/1201<sup>c</sup>  
101/1297

*Note.* Constructs as reported by the patient. mrng, morning; CI, confidence interval. *Standard deviation for random effects.* Following the recommendation of Bolger and Laurenceau (2013), we rescaled the ‘diary day’ variable in a way that 0 represents the middle of the 14-day diary period. *Given that the model controls for Fatigue Interference as assessed on the previous evening (t-1), the first assessment-day was excluded resulting in a smaller number of diary assessments available for this analysis.*
**Associations of partner responses with relationship satisfaction**

In line with hypothesis H1b and H2b, solicitous responses towards fatigue-behavior \( b = 0.08, p = .032 \) and facilitative responses towards well-behavior \( b = 0.08, p = .033 \) were related to an increase in relationship satisfaction throughout the day. Punishing responses towards fatigue-behavior \( (H3b, b = -0.34, p = .001) \) were related to a decrease in relationship satisfaction, but negative responses towards well-behavior were unrelated to relationship satisfaction \( (H4b, b = 0.01, p = .866) \).

**Moderating effect of fatigue severity**

We found partial support for the moderating effect of fatigue severity between partner responses and the outcomes fatigue interference and relationship satisfaction. Fatigue severity significantly interacted with negative responses towards well-behavior in predicting fatigue interference \( (H6a, \text{see Figure } 2a) \). The region of significance indicates that only when patients experienced levels of fatigue that were near typical or higher than typical for them \( (> -0.8) \), fatigue severity significantly interacted with negative responses towards well-behavior in predicting fatigue interference. The positive interaction-term \( (b = 0.09, p < .001) \) indicates that at levels of fatigue higher than -0.8, negative responses towards well-behavior predicted an increase in fatigue interference. Second, fatigue severity significantly interacted with facilitative responses towards well-behavior in predicting fatigue interference \( (H8a, \text{see Figure } 2b) \). The negative interaction-term \( (b = -0.05, p = .006) \) and the region of significance indicate that at levels of fatigue higher than -0.2, facilitative responses towards well-behavior predicted a decrease in fatigue interference.

Third, fatigue severity significantly interacted with punishing responses towards fatigue-behavior in predicting relationship satisfaction \( (H7b, \text{see Figure } 2c) \). The negative interaction-term \( (b = -0.13, p = .011) \) and the region of significance indicate that at levels of fatigue higher than -0.9, punishing responses towards fatigue-behavior predicted a decrease in relationship satisfaction. Figure S1 in the supplementary material depicts the region of significance for the three significant interaction-effects. The remaining interaction-effects predicting fatigue interference and relationship satisfaction were not significant.
**Partner responses and fatigue severity**

**Figure 2.** Lower-level interaction-effects between partner responses and fatigue severity, depicted at mean levels of fatigue severity and 1 SD above/below the mean. (a) Interaction-effect between negative responses towards well-behavior and fatigue severity predicting fatigue interference. (b) Interaction-effect between facilitative responses towards well-behavior and fatigue severity predicting fatigue interference. (c) Interaction-effect between punishing responses towards fatigue-behavior and fatigue severity predicting relationship satisfaction.

**Note.** The significance levels of the slopes representing low, average and high levels of fatigue were calculated with the online tool of Preacher et al. (2006).
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Associations based on the partner report
Results of the model using the partner responses and fatigue severity as reported by the partner largely supported the main-effects (see Table S1). The association of solicitous responses towards fatigue-behavior with patient’s fatigue interference pointed into the same direction, but was non-significant (H1a, $b = 0.05, p = .069$). As in the patient-model, negative responses towards well-behavior were associated with an increase in fatigue interference (H2a, $b = 0.07, p = .011$) and punishing responses towards fatigue-behavior were unrelated to fatigue interference (H3a, $b = 0.03, p = .307$). Also in line with the patient-model, facilitative responses towards well-behavior were associated with an increase in relationship satisfaction (H2b, $b = 0.07, p = .023$), while punishing responses towards fatigue-behavior were associated with a decrease in relationship satisfaction (H3b, $b = -0.14, p = .001$). Negative responses towards well-behavior were also unrelated to relationship satisfaction (H4b, $b = -0.01, p = .818$). In general, the effects were smaller in size than those of the patient-model and the three interaction-effects failed to reach significance.

Discussion
This diary study of patients treated for cancer showed that partner responses towards patient’s fatigue- and well-behavior are associated with how much fatigue interferes with patient’s daily activities and how satisfied they are with their relationship. Some partner responses were found to have a stronger impact on patient outcomes on days patients were more fatigued than usual.

As expected based on the operant model, solicitous responses towards fatigue-behavior were associated with an increase in fatigue interference. This finding underlines the reinforcing function of solicitous responses and their maladaptive effect for patients’ functioning. We extended research in the field of pain and show that this reinforcing effect also operates in couples coping with cancer-related fatigue. Importantly, by applying the diary method with repeated assessments within individuals, we demonstrated that this maladaptive effect also applies to daily within-person processes. When patients receive more reinforcing responses towards their illness-behavior than usual for them, their symptom interference worsens, even in the short-term. In line with the intimacy model, solicitous responses were also associated with an increase in patient’s relationship satisfaction. This implies that solicitous responses have divergent effects for patients’ adjust-
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ment, as they hamper their daily functioning but benefit their relationship. This is an important finding as it suggests that partner responses that are maladaptive for patients’ fatigue interference might be sustained, as they benefit the couples’ relationship.

We failed to find the expected negative association between punishing responses towards fatigue-behavior and fatigue interference. However, the evidence on the putative adaptiveness of punishing responses for patient’s functioning has generally been mixed in the literature (e.g., Newton-John, 2002; Prenevost & Reme, 2017). However, the size of the standard deviation around the non-significant fixed effect (see Table 2) suggests that for some patients, there is a negative association between punishing responses and fatigue interference while for others, there is a positive association. Future studies may investigate which between-person moderators explain this heterogeneity. In line with the intimacy model, punishing responses predicted decreases in relationship satisfaction. This negative effect was intensified when patients reported feeling fatigued. Jointly, these findings suggest that punishing responses do not benefit patients’ functioning and are detrimental for the couple’s relationship, especially when patients experience increased symptom levels. Of note, the frequency of punishing responses was low in our sample. However, even though infrequent, negative partner interactions might have a stronger impact on well-being than positive ones (Manne, Taylor, Dougherty, & Kemeny, 1997; Westdahl et al., 2007). Indeed, our results suggest that the negative impact of punishing responses on relationship satisfaction is larger than the positive impact of solicitous responses.

In line with the operant model, facilitative responses towards well-behavior were related to decreased and negative responses towards well-behavior were related to increased fatigue interference. Fatigue severity intensified these associations. These moderation-effects suggest that, especially on days patients experience high fatigue, encouraging patients’ activity might be a helpful strategy to foster their functioning, whereas discouraging well-behavior might be especially detrimental. In support of the intimacy model, facilitative responses were beneficial for the couple’s relationship. This effect, similar to the positive association between solicitous responses and relationship satisfaction, was independent of fatigue. This indicates that responsive partner interactions are beneficial for the relationship irrespective of fluctuations in symptoms and possibly related support needs. We did not find
the expected association between negative responses towards well-behavior and decreases in relationship satisfaction. This lack of association might be due to the items selected for our diary assessments, which reflected the partners’ concern and worry that the patients exhaust themselves. In order to shorten the original 6-item subscale of Schwartz et al. (2005) for the diary assessment, the only item with a clear negative connotation (i.e., criticizing the patient for being active), was not used in this study. However, two cross-sectional studies among patients with pain (Pence et al., 2008; Raichle et al., 2011) that did use the full 6-item subscale, also failed to find a correlation between negative responses towards well-behavior and relationship satisfaction. This suggests that discouraging well-behavior might be interpreted as less negatively by patients than punishing responses towards illness-behavior.

The strengths of this study include its intensive longitudinal design allowing to analyze daily within-person processes, and its dyadic design allowing to validate the patient-perspective with reports provided by the partner. Further, we extended earlier research based on the operant model by studying the effects of partner responses on both symptom interferences and the relationship. Lastly, we investigated the moderating effect of fatigue severity, which informs theory and practice on the importance of within-person changes in symptom severity for couples’ coping.

The results should be interpreted in light of some limitations. First, items measuring partner responses were based on established measures in the field of pain but were adapted to be applicable to daily life. To capture as many relevant partner responses as possible on a daily level, items were formulated less specifically and did not explicitly refer to fatigue- and well-behavior. Hence, we cannot be certain about which patient behaviors partners were responding. Second, partner responses and fatigue interference were assessed simultaneously and retrospectively for the whole day at every evening assessment, which makes it difficult to disentangle the temporal order of effects. However, we controlled for the outcome variables as assessed at the previous assessment, which indicates that partner responses towards fatigue- and well-behavior predict changes in fatigue interference and relationship satisfaction. Relatedly, as the focal predictor variables were only measured once daily, fatigue severity (measured three times daily from the patient perspective) was aggregated across the day. This approach masks within-
day variability of fatigue but estimates the effects of average fatigue experienced across the day.

The response rate of the larger study (36%) was lower than the rate reported in other psycho-oncological research (Wakefield et al., 2017), which is possibly due to the dyadic (Dagan & Hagedoorn, 2014) and intensive longitudinal design of this study. The demographic and clinical characteristics of the patients in our study are, however, comparable to those of a large population-based study among post-treatment colorectal cancer patients in the Netherlands (van Putten et al., 2016). Our sample consisted of post-treatment colorectal cancer patients, most of whom had early stage disease and were highly satisfied with their relationship. As a result, our findings may not be generalizable to populations with other clinical characteristics or to couples that are less satisfied with their relationship as those included in the current study.

The effects found were statistically significant, but relatively small in size. For example, for fatigue interference of the average patient to be predicted to decrease by 1 unit (e.g., from 4 to 3 on a scale from 0 ‘no interference’ to 4 ‘extreme interference’), partners’ facilitative responses towards well-behavior and patients’ fatigue severity would both need to be much higher than usual (e.g., an increase by 4 and 7 units respectively). Note that the interaction-effects were entered as fixed terms, which assumes that the terms do not vary across patients.

Despite the relatively small size of the found effects, we believe they are of theoretical and clinical relevance. From a theoretical perspective, our results confirm that symptom interferences are amenable to partner responses and indicate that the same partner responses also have an impact on the couple’s relationship. Given the persistent and interfering nature of symptoms such as fatigue as well as the importance of a healthy relationship for patient’s well-being, a more comprehensive understanding of dyadic coping processes can be achieved by considering the dual effects of partner responses on individual and relationship outcomes. Beyond that, the finding that symptom severity intensifies some of these associations suggests that both outcomes are most socially contingent on days patients encounter a stressor and experience a high need for support.

From a clinical perspective, cancer-related fatigue is a highly common and persistent symptom that is challenging to treat. Current treatments are directed at patients primarily and target mainly intrapersonal factors perpetuating fatigue
(e.g., patient catastrophizing; Bruggeman Everts, van der Lee, & de Jager Meezenbroek, 2015; Gielissen, Verhagen, Witjes, & Bleijenberg, 2006). However, our results indicate that the treatment focus should include interpersonal factors and shift to involve the couple. Targeting partner responses alongside intrapersonal perpetuating factors could provide an additional treatment effect for relieving cancer-related fatigue. Our results further indicate that targeting partner responses is not only promising to foster patients’ better adjustment to fatigue, but also to strengthen the couples’ relationship. To be specific, our findings indicate that patients experiencing persistent and interfering symptoms benefit most from facilitative responses towards their well-behavior, both in terms of their symptom burden and relationship satisfaction. Importantly, encouraging well-behavior is most beneficial for patients’ functioning on days they feel more fatigued. Given that partners tend to misjudge patients’ symptom severity (Lehman et al., 2011; Poort et al., 2016), couples might need training to communicate about the patients’ current symptom severity. This might enable partners to properly respond to the patients’ current need for support. Contrary to clinical recommendations based on the operant model, punishing partner responses should be discouraged, as they seem not to decrease patients’ symptom interference, but harm the couples’ relationship.

In short, clinicians should be aware that the dyadic context contributes to patients’ fatigue development and that couples’ coping with fatigue also impacts their relationship. Hence, treatment of cancer-related fatigue should extend to the couple. Dyadic interventions should educate couples on the dual effects of partner responses on patients’ functioning and their relationship. Supporting couples’ effective communication about patients’ current symptom severity and encouraging partners to facilitate patients’ activity, particularly on high fatigue days, can foster the adjustment of patients suffering from cancer-related fatigue.

Footnote: The HLMdiag package was used to test the assumptions inherent in multilevel linear modeling. Following recommended diagnostic procedures (Loy, 2013; Loy & Hofmann, 2014), no evidence for major violations of the distributional assumptions for the residuals of both outcome variables in the linear models were found. Using the glmmPQL function, it was also examined whether a non-linear model was a better approximation of the distribution of fatigue interference and relationship satisfaction scores and whether this yielded different conclusions than
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the linear model. The results of these sensitivity analyses showed that the linear and non-linear models resulted in the same conclusions for the effects of partner responses, thus the linear model was retained.

Supporting information
Table S1
Associations of partner responses with fatigue interference and relationship satisfaction and the moderating effect of fatigue severity, partner perspective

Figure S1. Plots depicting slopes with their confidence bands (red [curved] lines) and regions of significance (blue [dotted] lines) for the three significant interaction-effects.

S3. Item list, translated from Dutch to English

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Conflict of interest
The authors declare that they have no conflict of interest.
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References


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