Associations between post-traumatic stress symptoms and sleep/circadian parameters: exploring the effect of chronotype as a moderator variable

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Abstract

The present study aimed at evaluating how post-traumatic stress symptoms (PTSS) are associated with rest-activity circadian and sleep-related parameters, assessed both subjectively (via questionnaires) and objectively (via actigraphy). Specifically, we explored whether chronotype could moderate the association between sleep/circadian parameters and PTSS. Participants (n = 120 adults; mean age 35.6 ± 14; 48 male) were assessed through the Trauma and Loss Spectrum Self Report (TALS-SR) for lifetime PTSS, the reduced version of the Morningness-Eveningness Questionnaire (rMEQ) for chronotype, the Pittsburgh Sleep Quality Index (PSQI) for self-reported sleep quality, and wrist actigraphy for sleep and circadian parameters. Eveningness, poor self-reported sleep quality, lower sleep efficiency (SE), lower interdaily stability (IS), and higher intradaily variability (IV) were correlated with higher TALS-SR scores. Regression analyses showed that IV, SE, and PSQI remained associated with TALS symptomatic domains after adjusting for potentially confounding factors (age and gender). Moderation analysis showed that only the PSQI remained significantly associated with TALS symptomatic domains; however, the interaction with chronotype was not significant. Targeting self-reported sleep disturbances and rest-activity rhythms fragmentation could mitigate PTSS. Although the effect of chronotype as a moderator of the associations between sleep/circadian parameters and PTSS was not significant, eveningness was associated with higher TALS scores, thus confirming the vulnerability of evening types to worse stress reactions.

Keywords: chronotype; post-traumatic stress symptoms; sleep quality; actigraphy; rest-activity rhythms; intradaily variability; interdaily stability

1 Introduction

Lifetime exposure to loss and potentially traumatic events may increase the vulnerability to develop Post-Traumatic Stress Disorder (PTSD), a frequently chronic and invalidating disorder that negatively impacts physical and mental health (Carmassi et al., 2020; Eisenbarth et al., 2019). Increasing evidence highlights how lifetime exposure to potentially traumatic events may also trigger the onset of partial or subthreshold forms of PTSD that may be significantly invalidating, leading to a need for care (Dell'Osso et al., 2011; Mclaughlin et al., 2015). In light of this evidence, dimensional approaches to PTSD have been developed, such as the Trauma and Loss Spectrum (TALS, Dell'Osso et al., 2009). This approach addresses the occurrence not only of criterion symptoms (according to DSM-5 diagnosis) but also of non-criterion ones, such as atypical symptoms and subthreshold manifestations, that may occur as early-onset precursors, prodromal features, or persistent residual symptoms of a full-blown DSM disorder and that may be detected in the general population (Carmassi et al., 2020; Stratta et al., 2016).

Sleep disturbances have been associated with both subthreshold post-traumatic stress symptoms (PTSS) and full-blown PTSD. Indeed, nightmares, anxiety dreams, difficulties falling asleep, frequent awakenings, and difficulties falling back to sleep represent core symptoms of PTSD (Babson & Feldner, 2010; Germain et al., 2005; Maher et al., 2006; Pillar et al., 2000; Schäfer & Bader, 2013; Spoormaker & Montgomery, 2008). A meta-analysis of polysomnographic studies in PTSD patients documented a frequent appearance of increased stage 1 sleep, decreased slow-wave sleep (SWS), and increased density of rapid eye movements (REMs) (Kobayashi et al., 2007). Interestingly, subjective and objective sleep disruption occurring early after the trauma may predict PTSD development (Koren et al., 2002; Mellman et al., 2002), by which sleep disruption has been suggested as a specific mechanism involved in the pathophysiology of chronic PTSD, and as a predictor of poor clinical outcomes in this

disease (Germain et al., 2008). Likewise, exposure to traumatic events has been related to sleep disturbances. Subjects exposed to major traumatic events, such as holocaust survivors, war veterans, and sea disaster survivors, have shown long-term disruptions in sleep, even after several years from the trauma exposure, also in the absence of a specific diagnosis of PTSD (Hefez et al., 1987; Kaminer & Lavie, 1991; Rosen et al., 1991).

Besides sleep disturbances, circadian variables such as the preferred timing of sleep and activity (also named chronotype or circadian typology) and the robustness and/or regularity of rest-activity rhythms may also play a relevant role in PTSD. Regarding the circadian typology, the study of Hasler et al., 2013, performed in combat-exposed military veterans with varying degrees of posttraumatic stress symptomatology, showed that eveningness was associated with greater lifetime PTSD symptoms, more disturbed sleep, and more frequent and intense nightmares (Hasler et al., 2013). Likewise, studies performed in healthy adults exposed to stressful work have reported that eveningness was correlated with more severe symptoms of PTSD in a group of service members (Harrison et al., 2021) and that in a group of firefighters, subjects classified as evening chronotype showed higher scores than morning chronotypes in a stress response scale, thus suggesting worse stress reactions in this group (Yun et al., 2015). Recently, some of us explored the role of chronotype in response to a prolonged stressful condition such as the Covid-19 pandemic, showing that evening chronotypes reported worse resilience levels compared to morning chronotypes, as revealed by lower scores in the *Connor–Davidson Resilience Scale* and that, in line with the literature, resilience levels were negatively correlated to the severity of post-traumatic stress reactions, as measured through the *Impact of Event Scale*. Moreover, the association between chronotype and resilience was found to be mediated by self-reported sleep quality (Bazzani et al., 2021). These results suggest that both circadian typology and sleep-related parameters are associated with the response to stressful events; however, because of the exceptional circumstances due to the pandemic, we could not

account for objectively assessed sleep and circadian parameters in that study. Since self-reported sleep quality may not precisely reflect objective sleep patterns (Buysse et al., 2008), and this discrepancy may be influenced by psychosocial characteristics, such as depressive symptoms and perceived stress and social support (Jackowska et al., 2011), it is highly relevant to include both subjective and objective measurements to explore the associations between sleep-related parameters and post-traumatic stress response.

Regarding robustness and/or regularity of rest-activity rhythms, recent studies have demonstrated that PTSD patients exhibited greater intradaily variability (IV), a measurement of rest-activity rhythm fragmentation, compared with controls (Tsanas et al., 2020). Likewise, it was reported that both patients with a diagnosis of PTSD and patients diagnosed with insomnia showed lower interdaily stability (IS), a measure of constancy of the 24-h rest-activity pattern over days, relative amplitude (RA), a non-parametric measure of rhythm robustness, and sleep regularity than healthy controls, confirming that diurnal rhythms may be compromised in PTSD (Mascaro et al., 2021). A recent article reported that healthy subjects classified as E-types show less robust rhythmicity, as reflected by lower amplitude and IS (Martinez-Nicolas et al., 2019). Therefore, considering that both eveningness and rest-activity rhythm disruption may be associated with a worse stress response, it could be expected that both eveningness and disturbances in robustness/stability of rest-activity rhythms may be synergistically associated with more severe PTSS.

The aim of the present study was to evaluate how PTSS, as measured through a specific assessment instrument to detect post-traumatic stress spectrum symptoms such as the TALS-SR lifetime version, are associated with rest-activity circadian and sleep-related parameters, assessed both subjectively (via questionnaires) and objectively (via actigraphy) in a sample of healthy adults. More specifically, we explored whether chronotype could moderate the association between sleep-related and rest-activity circadian parameters and PTSS. We hypothesized

that (1) subjects classified as evening chronotypes could show higher scores in the TALS-SR domains; (2) eveningness, poor self-reported sleep quality, and disturbed sleep-related and circadian parameters could be correlated to higher scores in the TALS-SR symptomatic domains; and (3) the possible association between TALS-SR symptomatic domains and sleep-related (subjective and objectively measured) and circadian (objectively measured) parameters could be moderated by chronotype.

2 Materials and methods

2.1 Participants

All participants were enrolled among students and their relatives as well as among the personnel of the Department of Clinical and Experimental Medicine of the University of Pisa and of the Azienda Ospedaliero-Universitaria Pisana (AOUP). Inclusion criteria included a negative history of psychiatric or neurologic disorders. All eligible subjects were asked to provide written informed consent after receiving a complete description of the study and having the opportunity to ask questions before joining the study. The study was conducted in accordance with the Helsinki Declaration and received the approval of the Ethics Committee of AOUP, Area Vasta Toscana Nord Ovest (code 14785/2019).

2.2 Instruments

Socio-demographic data and lifestyle

Socio-demographic information included age, sex, height, weight, occupation, and years of education. Health-related lifestyle variables included alcohol and tobacco consumption. Alcohol intake was quantified as alcohol units per week (one alcohol unit corresponds to a half-pint of beer, a glass of wine, or a measure of spirit). Tobacco intake was quantified as the number of cigarettes smoked in a week.

The Trauma and Loss Spectrum (TALS-SR)

Includes 116 items exploring the lifetime experience of a range of loss and/or traumatic events and lifetime symptoms, behaviors, and personal characteristics that might represent manifestations and/or risk factors for the development of a stress response syndrome (Dell'Osso et al., 2009). The instrument is organized into nine domains:

- *Domain I Loss events:* evaluates the lifetime exposure to a range of loss events from mild to extreme, such as the death of a loved one, the end of a meaningful relationship, the loss of reference figures in childhood or adolescence, among others.
- *Domain II Grief reactions:* analyzes symptoms related to the possible occurrence of persistent grief in response to loss.
- *Domain III Potentially traumatic events (PTE):* evaluates the lifetime exposure to a wide and heterogeneous spectrum of low- and high-magnitude life events, such as a threat to physical integrity, unwanted changes in economic or social status, among others.
- *Domain IV Reaction to losses and PTE:* includes a range of emotional, physical, and cognitive responses to loss and/or traumatic events identified in *Domains* I and III.
- *Domain V Re-experiencing:* includes a range of criterion and non-criterion symptoms related to re-experiencing, e.g., bad dreams or nightmares about the loss, bad feelings, acting or feeling as if the events were happening again, having distressing thoughts or feelings about the loss, having physical sensations and intense emotions thinking about the event, feeling guilty or ashamed for what happened.
- *Domain VI Avoidance and numbing:* includes a range of criterion and non-criterion symptoms related to avoidance and numbing such as avoiding thinking or talking about the event, avoiding places, people, situations activities that could remind to the loss or event. Finding activities meaningless or insignificant, difficulty in trusting people, dulled emotions.

- *Domain VII Maladaptive coping:* maladaptive coping responses for both loss and trauma: using alcohol or drugs, decreased self-care, self-destructing thoughts and risk-taking behaviors such as driving fast or promiscuous sex.
- *Domain VIII Arousal:* includes a range of criterion and non-criterion related to arousal symptoms: having trouble in concentrating, feeling more irritable, having difficulty in falling asleep.
- *Domain IX Personal characteristics:* includes a list of personality traits that are not included in the analyses: being extremely sensitive to stress, being provocative, taking pleasure in being the center of attention, finding exciting what others would find frightening, engaging in dangerous activities.

In addition, we calculated the *TALS-SR symptomatic domain*, which corresponds to the sum of the TALS-SR domains that account for the clinical symptoms of the post-traumatic spectrum (Domains: IV, V, VI, VII, VIII).

The Reduced Morningness-Eveningness Questionnaire (rMEQ)

Is the reduced version of the Horne-Ostberg Morningness-Eveningness Questionnaire (Adan & Almirall, 1991). It provides the individual preference for daily rhythms and activities, as well as the timing of the individual sleep/wake patterns, allowing to identify three main circadian typologies based on the total score: Morning Type (M-type) = 19-25, Neither Type (N-type) = 11-18, Evening Type (E-type) = 4-10. The cut-point was established following the recommendations derived from the validation of the rMEQ for the Italian population (Natale et al., 2006).

The Pittsburgh Sleep Quality Index (PSQI)

Is a self-report questionnaire that assesses sleep quality and disturbances over a one-month time interval, providing indexes for subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction (Buysse et al., 1989). We use the PSQI version translated and adapted into Italian (Curcio et al., 2013). The sum of scores for these seven components yields one global score, which is interpreted as follows: Minimum Score = 0 (better); Maximum Score = 21 (worse); Score > 5: poor sleep quality.

Actigraphic Data

To objectively measure sleep, we used a waterproof wrist actigraph Fitbit Flex2 (FF2). Data were sampled in one-minute epochs and digitally stored for subsequent analysis. Quantitative sleep parameters derived from the FF2 were estimated through an artificial neural network (ANN)-based, certified algorithm: Dormi by sleepActa s.r.l. The Dormi software is a medical, risk class I device. As such, it is registered within the Italian Ministry of Health Data Bank of Medical Devices (CND: 217 Z12030682). The algorithm was validated in a sample including both healthy subjects and patients undergoing a diagnostic exam for sleep disturbances (Banfi et al., 2021), and was used to estimate the following parameters:

- Total Sleep Time (TST): defined as the total sleep duration (hours and minutes).
- Waking After Sleep Onset (WASO): defined as the time spent awake after sleep onset and before sleep offset (in minutes).
- Sleep Efficiency (SE): defined as the percentage of time spent asleep between sleep onset and offset.

In addition, we estimated the sleep regularity index and the mid-sleep point as follows:

- Sleep Regularity Index: it measures the likelihood of the same sleep-wake state occurring in epochs that are 24h apart, thereby measuring the similarity of sleep-wake patterns between consecutive days (Phillips et al., 2017).
- Mid-sleep point: the middle of the sleep period between the sleep onset and final awakening, measured by actigraphy. It was calculated by adding to the average sleep onset half of the average total sleep time (average sleep onset + average TST/2).

To estimate rest-activity circadian rhythm parameters, we used a parametric approach using the cosinor method to characterize diurnal rhythms by fitting a sine wave to the actigraphy data and computing the Midline Estimating Statistic of Rhythm (MESOR), amplitude, and acrophase (Cornelissen, 2014). To perform the cosinor analysis we used the R package *Extract Circadian Rhythms Metrics from Actigraphy Data 'ActCR'* (Junrui Di and Vadim Zipunnikov, 2021). Non-parametric measurements of rest-activity rhythms, such as interdaily stability, intradaily variability, and relative amplitude (Van Someren et al., 1999) were calculated using the R package *Non-Parametric Measures of Actigraphy Data 'nparACT'* (Blume et al., 2016; Blume Christine, Santhi Nayantara, 2017). Variables are defined as follows:

- Mesor: is a rhythm-adjusted mean. It represents the mean activity level;
- Amplitude: is the peak-to-nadir difference, a measure of half the extent of predictable variation within a cycle. More robust rhythms have a higher amplitude;
- Acrophase: timing of peak activity or the point in the cycle at which activity is highest;
- Interdaily stability (IS): estimates the variability in rest-activity patterns across all days. It is a measure of rest-activity rhythms regularity. In this study, it is expressed as values ranging from 0 to 1. Higher values indicate greater stability between days;

- Intradaily variability (IV): quantifies the fragmentation and magnitude of rest-activity transitions within each day. In this study, it is expressed as values ranging from 0 to approximately 2. Higher values indicate frequent transitions between rest and activity (i.e., frequent naps, increased night-time awakenings);
- Relative amplitude: measures the robustness of the 24-h rest-activity rhythm by calculating the normalized mean difference in activity between the most active 10 hours and the least active 5 hours, ranging from 0 to 1. Higher values indicate lower activity during the night and high activity during the day, i.e., increased robustness of rest-activity rhythm.

2.3 Procedures

After signing the informed consent, participants were asked to respond to the questionnaires about socio-demographic data and lifestyle, the PSQI, the rMEQ, and the TALS-SR. Then, the experimenter provided each participant with a wrist actigraph. Participants were asked to wear it continuously on their non-dominant wrist for seven days without interruption. After that period, participants returned the actigraph to the sleep laboratory, concluding the study. Participants did not receive any compensation for their participation in the study.

2.4 Statistical Analyses

To test our first hypothesis, stating that subjects classified as evening chronotypes could show higher scores in the TALS-SR domains, the sample was classified into three different circadian typologies based on the rMEQ score, i.e., Evening type (E-type), Neither type (N-type), and Morning type (M-type). Circadian typologies were compared regarding demographic variables, TALS-SR domains, sleep-related and circadian parameters, using the Kruskal-Wallis and post-hoc pairwise Mann-Whitney-Wilcoxon rank-sum test for continuous variables and the Fisher exact test for categorical variables. To test our second hypothesis, stating that eveningness, poor self-reported sleep quality, and disturbed sleep-related and circadian

parameters objectively measured could be correlated to higher scores in the TALS-SR *symptomatic domains*, the Spearman's correlation test was performed. Finally, to test our third hypothesis, stating that the possible association between TALS-SR *symptomatic domains* and sleep-related (subjective and objectively measured) and circadian (objectively measured) parameters could be moderated by chronotype, linear regression models were estimated to explore the association between the TALS-SR *symptomatic domains* and sleep/circadian parameters that were found to be significantly correlated to the TALS-SR domains, adjusting for potential confounding factors (e.g., age and gender). Then, regression analyses were performed positioning chronotype as a moderator of the associations between sleep/circadian and TALS *symptomatic domains*. For Chronotype, the reference value was evening chronotype, such that the regression model included two binary indicators (i.e. Morning and Neither Chronotypes). Regression coefficients ß are reported to characterize the effects of the independent variables. All variables with p-value ≤ 0.05 were considered significant. All statistical analyses were conducted using R Studio.

3 Results

3.1 Sample description

Socio-demographic characteristics of the sample (n = 120, age: 35.6 ± 14, males 48, 40%) are presented in Table 1. Descriptive information on the types of traumatic and loss events participants experienced is described below.

Overall, in our sample each subject has experienced around 2,54± 2,08 potentially traumatic events, while twenty-seven (22.5%) subjects reported not having experienced a potentially traumatic event. Among the potentially traumatic events reported, the event more frequently reported was repeated severe arguments in family (n = 57, 47.50%), followed by repeated failures in school or at work (n = 44, 33.33%), receiving unwanted sexual advances (n = 34, 28.33%), being repeatedly teased or harassed (n = 31, 25.83%), having a serious medical

illness, surgery, or other distressing medical procedure (n = 31, 25.83%). Furthermore, some participants reported have being a victim of a crime, for example, being robbed, assaulted, etc. (n = 23, 19.17%), having experienced an event that seriously threatened the well-being, employment, professional status, social standing or financial security (n = 22, 18.83%), experiencing a serious accident or injury (n=21, 17.50 %). being beaten up or physically threatened (n = 20, 16.67%,), physical or sexual abuse (n = 11, 9.17%), being the object of a lawsuit or disciplinary action (n = 8, 6.67%), being threatened by criminals or terrorists (n = 2, 1,67%) experienced a natural disaster (n = 2, 1.67%), being in a war zone (n = 2, 1.67%) and being imprisoned, kidnapped, tortured, or held hostage (n = 1, 0.83%).

Regarding the domain of *Loss events*, overall, in our sample, each subject has experienced around 4,00 ± 1.64 loss events, while only two subjects (1.66%) reported not having experienced a loss event. The loss event more frequently reported was the death of a relative or loved friends (n = 100, 85.33%), followed by a painful break-up (n = 98, 81.67%), separation from a close friend romantic partner, or family member because of relocation, hospitalization, military service, or because of an argument or disagreement (n = 72, 60,0%), the loss or death of a cherished pet (n = 71, 59.17%) a change in home, caregivers, schools, jobs, etc. (n = 49, 40.83%), being neglected or abandoned (n = 43, 35.83%), a miscarriage, stillbirth, or abortion (n = 23, 19.17%), divorce in family (n = 22, 18.63 %), other important losses (n = 2, 1.67%), and loss of sight, hearing, or have a serious disability (n = 1, 0.83%).

3.2 Distribution of Chronotype and comparisons between groups.

The sample was divided into three circadian typologies as measured through the rMEQ: evening type (E-type, n = 23 (19%)), neither type (N-type, n = 72 (60%)) and morning type (M-type, n = 25 (21%)). We observed that alcohol and tobacco intake was significantly different between groups. Post-hoc analyses showed that E-types reported significantly higher

alcohol and tobacco consumption than M-types. Also, N-types reported higher alcohol and tobacco consumption than M-types. Regarding the TALS-SR domains, significant differences emerged between groups in the *Maladaptive coping* domain, in which the E-type group showed higher scores than the N-type and the M-type groups. Regarding actigraphic metrics, differences between groups emerged in acrophase, mid sleep point, and IS. Post-hoc analyses revealed that acrophase was delayed in E-types as compared to N-types and M-types, and in N-types compared with M-Types. Likewise, Mid sleep-point occurred later in E-types than in N-types and M-types, and in N-types compared to M-types. Finally, IS was higher in M-types than in N-types and E-types.

INSERT TABLE 1 ABOUT HERE

3.3 Correlations between TALS-SR domains and circadian and sleep-related parameters

Significant negative correlations emerged between rMEQ total score and the TALS-SR *Reaction to losses and potentially traumatic events*, *Re-experiencing*, *Avoidance and numbing*, *Maladaptive coping* domains, as well as the TALS-SR symptomatic domains, suggesting that eveningness is correlated with a tendency to more severe post-traumatic stress reactions. IS was negatively correlated with the TALS-SR *Reaction to losses and potentially traumatic events* domain and with the TALS-SR *symptomatic domains*, so that more unstable rest-activity rhythms were correlated with more severe stress reactions. IV was positively correlated with the TALS-SR *Re-experiencing and Avoidance and numbing* domains as well as with the TALS-SR *symptomatic domains*, further suggesting that more fragmented rest-activity rhythms are correlated with more severe stress reactions. Finally, the mid-sleep point was correlated with the TALS-SR *Maladaptive coping* domain, in which a later mid-sleep point was correlated with higher scores in this domain (See Table 2).

INSERT TABLE 2 ABOUT HERE

Correlations analyses between TALS-SR domains and sleep measurements (objective and subjective) showed that the PSQI total score was positively correlated with the TALS-SR *Grief reactions, Potentially traumatic events, Reaction to losses and potentially traumatic events, Re-experiencing, Avoidance and numbing, Maladaptive coping, Arousal* domains, as well as the TALS-SR *symptomatic domains*. Higher scores in the PSQI - suggestive of poor sleep quality - correlated with greater lifetime trauma exposure and more severe stress reactions. Likewise, sleep efficiency (SE) was negatively correlated with the *Potentially traumatic events, Re-experiencing, and the Maladaptive coping domains* (See Table 3).

INSERT TABLE 3 ABOUT HERE

3.4 Associations between sleep/circadian parameters and TALS-SR symptomatic domains adjusting for potentially confounding factors and chronotype.

Linear regression analyses were conducted to investigate whether the association between sleep/circadian parameters and TALS-SR *symptomatic domains* could be influenced by chronotype. Previously we have found that among circadian variables, IV and IS were significantly correlated with TALS-SR domains; likewise, among the sleep-related variables, the PSQI and the SE were significantly correlated with TALS-SR domains. Therefore, we estimated four linear regression models (Table 4.1) using the TALS-SR *symptomatic domains* as the dependent variable and introducing in separate models each circadian/sleep parameter of interest (IV, IS, SE, PSQI) as the independent variables adjusting for potentially confounding factors (age and gender). These regression analyses showed that only the IS, SE and PSQI remained associated with TALS *symptomatic domains* (Table 4.1). Then the chronotype was added to the models to evaluate its potential effect as a moderator of the associations between sleep/circadian and TALS *symptomatic domains* (Table 4.2). We found that the IV was no longer significantly associated with TALS *symptomatic domains*, while the global p-value of chronotype was significant suggesting that the chronotype has an effect on TALS *symptomatic domains*; however, no significant interaction effect between IV and chronotype was observed (Model 5). The association between SE and TALS *symptomatic domains* was no longer significant and no interaction effect with chronotype was found (Model 6). The PSQI remained significantly associated with TALS *symptomatic domains*, where higher scores in the PSQI (suggestive of

poorer seep quality) were associated with higher scores in the TALS *symptomatic domains*; however, no interaction effect with chronotype was found (Model 7).

INSERT TABLE 4.1 AND 4.2 ABOUT HERE

4 Discussion

To the best of our knowledge, this is the first study exploring the possible role of rest-activity circadian rhythms and sleep-related parameters, assessed both subjectively (via questionnaires) and objectively (via actigraphy), on post-traumatic spectrum symptoms (PTSS). Consistently with our first hypothesis, results showed that E-types report higher scores in all the TALS-SR *symptomatologic domains* as compared to the other two circadian typologies (N-types and M-types), with a statistically significant difference in the TALS-SR *Maladaptive-coping* domain. Correlation analyses showed that eveningness, poor self-reported sleep quality, lower actigraphic sleep efficiency (SE), lower interdaily stability (IS), and higher intradaily variability (IV) were correlated with higher TALS-SR scores. Regression analyses adjusted for age and gender showed that IV, SE and PSQI were associated with TALS *symptomatic domains*. Models exploring the effect of chronotype as a moderator of these associations showed that only the PSQI remained significantly associated with TALS *symptomatic domains*; however, no interaction effect between chronotype and PSQI was found.

4.1 Evening chronotype and PTSS

Some evidence in the literature suggests that the chronotype may be related to PTSS in adults exposed to stressful situations. For example, morningness was negatively correlated with PTSD symptoms in a sample of US sailors (Harrison et al., 2021), and E-types reported more depression, alcohol use, PTSD, stress response, and sleep disturbances compared to other chronotypes in a sample of Korean firefighters (Yun et al., 2015). Likewise, in combat-exposed

veterans with varying degrees of PTSS, eveningness was associated with higher levels of PTSD symptoms, which in turn were associated with greater affective and sleep disturbances such as nightmares, insomnia, and poor sleep quality (Hasler et al., 2013). Our study suggests that chronotype could be associated with PTSS in the general adult population, with no selection bias towards subjects exposed to particularly stressful situations. In particular, we found significant correlations between eveningness and higher scores in TALS-SR symptomatic domains, including *Re-experiencing*, *Avoidance and numbing*, and *Maladaptive coping.*

Within the sphere of symptomatic domains, a key role in re-experiencing symptoms is played by nightmares that are highly frequent after trauma exposure and are part of the re-experiencing cluster (Creamer et al., 2018; Schultz et al., 2021). Previous studies proved that E-types have a greater proportion of REM sleep than M-types (Carrier et al., 1997) and that E-types are more prone to experience nightmares (Nielsen, 2010; Selvi et al., 2012). The higher REM propensity has been associated with more intense dream experiences and this has been suggested as a possible mechanism underlying an increased propensity to experience nightmares in E-types (Nielsen, 2010). Moreover, some authors propose that the circadian misalignment experienced by E-types could contribute to dysregulation in the circadian modulation of REM sleep. This might lead to impairments in memory consolidation and mood regulation processes, possibly contributing to the propensity to nightmares in E-types exposed to traumatic events (Hasler et al., 2013). Other aspects of re-experiencing are trauma-related intrusive thoughts. Several reports in the literature have highlighted that E-types may show increased tendency to ruminative thinking (Antypa et al., 2017) and failures in cognitive functions belonging to executive domains, such as self-regulation, behavioral and emotional control, as well as cognitive flexibility (Cohen-Zion & Shiloh, 2018). Regarding maladaptive behaviors, we found that E-types showed significantly higher scores in the TALS-SR

Maladaptive coping domain and reported greater use of alcohol compared to N-types and M-types. This is consistent with previous research showing how E-types consume more substances (drugs and alcohol) than other chronotypes and have a greater propensity for risk behaviors (Adan, 1994; Killgore, 2007), particularly in the health and safety domains (Gowen et al., 2019). Moreover, maladaptive coping symptoms have been strongly correlated with avoidance symptoms in subjects exposed to traumatic events (Dell'Osso et al., 2013). Since avoidance can be considered as a maladaptive coping strategy (Sica et al., 2021), this could explain the significant correlation between eveningness and avoidance symptoms found in our sample. Social jetlag theory, proposed by Wittman et al., explains how, in most social environments, E-types must work against their internal clock, which may lead to circadian misalignment and may affect sleep quality and psychological wellbeing (Wittmann et al., 2006). Circadian disruptions may also be associated to maladaptive behaviors, such as substance abuse, via alterations in the reward system modulation (Hasler et al., 2012). These lines of evidence could explain how circadian disruptions and sleep disturbances experienced by E-types could predispose to maladaptive behaviors in response to stressful situations.

4.2 The role of chronotype on the association between sleep-related parameters and PTSS

Several studies have reported that sleep disturbances are a core feature of PTSS and that sleep disturbances may be associated with a worse response to stressful situations (Pace-Schott et al., 2015). Likewise, E-types frequently experience sleep disturbances (Barclay et al., 2010; Merikanto et al., 2012; Taylor & Hasler, 2018), mainly during the weekdays (Vitale et al., 2015), as well as more irregular sleep times (Gau et al., 2007; Pieters et al., 2010; Wittmann et al., 2006). Therefore, it could be expected that the association between sleep disturbances and PTSS could be moderated by chronotype, for example, E-Types could suffer more severe sleep

disturbances after experiencing a traumatic event, when compared with other chronotypes. Previously, some of us have demonstrated that although M-types may show higher levels of resilience than E-types, that association was mediated by sleep quality, thus suggesting that sleep disturbances and the resilient response are strongly associated, and that this association could explain the link between chronotype and stress responses (Bazzani et al., 2021). Likewise, in other studies conducted by some of us, we have also found that being an E-type and experiencing poor sleep implies a higher likelihood of changing food-related health habits (Bazzani et al., 2022) and that poor subjective sleep quality predicted unhealthy lifestyles adoption during the COVID-19 pandemic (Bruno et al., 2022), thus highlighting the role of sleep disturbances as a trigger for maladaptive behaviors in response to stressful conditions. In the present study, we report that self-reported sleep quality was strongly associated to PTSS and that chronotype did not significantly moderate that association, thus suggesting that it is not evening tendency, but poor sleep quality the main predictor of PTSS.

We also found that objective SE was associated with PTSS, however that association was no longer significant after adjusting for chronotype, even when no interaction effects between SE and chronotype were found. This result could suggest a less robust predictability of PTSS based on SE. In our sample, the self-reported sleep quality and actigraphic sleep efficiency were significantly correlated (Spearman rho= -0.20, p-value =0.03), suggesting a certain degree of consistency between different measurements of sleep quality, however subjective sleep quality was a stronger predictor of PTSS than objective sleep efficiency. This result demonstrates the close relationship between perceived sleep quality and mental health outcomes, further highlighting the importance of considering complaints about sleep disturbances as a relevant target of intervention.

As an additional result, we found that higher lifetime exposure to potentially traumatic events (PTE), including a wide and heterogeneous range of events such as medical illness,

natural disasters, critical incidents, among others, as evaluated through the TALS-SR *Potentially traumatic events* domain, was significantly correlated with poor perceived sleep quality and reduced actigraphic sleep efficiency. Literature shows that exposure to events such as serious medical illnesses (Fortmann et al., 2021), natural disasters (Wu et al., 2015), critical incidents (Neylan et al., 2002), war (Gibson et al., 2019), and pandemics (Liu et al., 2020), even in the absence of a full-blown diagnosis of PTSD, are associated with poor sleep quality as measured through the PSQI. Likewise, increased childhood trauma exposure has been related to objective sleep disturbances measured through actigraphy (Brindle et al., 2018; Schäfer & Bader, 2013). Before us, only one study investigated the association between the cumulative lifetime exposition to PTE and sleep disturbances (Berg et al., 2020). In that study, self-reported sleep disturbances were identified as a mediator between lifetime exposure to trauma and the development of suicidal ideation and pathological distress in college undergraduate students (Berg et al., 2020). As a novelty, our results indicate that the cumulative lifetime exposure to PTE may be associated with subjective and objective sleep disturbances. Accordingly, some neurobiological models recognize the exposition to traumatic events as a possible cause of sleep disorders (Germain et al., 2008). From this perspective, our results suggest that the cumulative exposure to PTE may represent a risk factor for the development of sleep disturbances, even in subjects without a full-blown diagnosis of PTSD.

4.3 The role of chronotype in the association between rest-activity rhythms and PTSS

We have found that IV and IS were correlated with more severe PTSS, and that IV remained significantly associated with PTSS in regression models adjusted for potentially confounding factors (age and gender). This result may be interpreted in several ways.

On the one hand, subjects with lifetime exposure to potentially traumatic events may suffer from sleep disturbances that may lead to more fragmented rest-activity rhythms charac-

terized by awakenings during the night, less restorative sleep, and increasing rest periods during the day. A previous study reporting greater IV in PTSD patients has interpreted these results as an indicator of more fragmented sleep during the night, as confirmed by greater WASO and more frequent awakenings compared to healthy volunteers (Tsanas et al., 2020). Likewise, rest-activity rhythm disruption in PTSD has been associated with nightmares awakenings, which are characterized by significant hyperarousal, and may interfere with the time to fall back asleep, contributing to greater levels of activity during the night (Mascaro et al., 2021).

On the other hand, these results could be interpreted in light of the interaction between the circadian and stress systems (Agorastos & Olff, 2020; Nader et al., 2010). It is well known that in response to sub-acute and time-restricted stressful stimuli, the stress system activation can phase-shift peripheral circadian rhythms leading to a temporary uncoupling of the central and peripheral clocks (Balsalobre et al., 2000; Yamamoto et al., 2005) and that the peripheral circadian rhythms eventually return to the regular rhythm after the termination of the stress system activation thanks to the intrinsically maintained rhythmicity of the central pacemaker, the suprachiasmatic nucleus (SCN) (Nader et al., 2010; Tahara et al., 2017). However, in response to extensive acute or chronic stress exposure, circadian genes expression may be disturbed in a sustained way at the peripheral level, as well as in central nervous tissues such as the hippocampus, amygdala, prefrontal cortex, and even in the SCN (Logan et al., 2015; Razzoli et al., 2014; Tahara et al., 2015; Weber et al., 2014), thus leading to long-term changes in the circadian system (Helfrich-Förster, 2017). Therefore, traumatic stress exposure may be significantly associated with circadian rhythm disruption (Agorastos & Olff, 2020). This could explain the alterations in stability and robustness of rest-activity rhythms observed in patients diagnosed with PTSD (Mascaro et al., 2021; Tsanas et al., 2020) and the correlations between higher IV and lower IS with more severe PTSS observed in the present study. From this perspective, it could be possible that subjects expressing higher PTSS may experience rest-activity

rhythm disturbances as a long-term effect of the stress system activation on the circadian system. Our results suggest that the association between PTSS and rest-activity rhythm disturbances may be independent of chronotype, since no interaction effects with chronotype were found. However, it is relevant to highlight that the chronotype independently showed an association with TALS *symptomatic domains*. This result suggests that both evening circadian typology and rest-activity rhythm disturbances may be independently associated with PTSS and may represent relevant targets of intervention.

4.4 Limitations and future perspectives

This study has some limitations. First, we explored a heterogeneous exposure to different types of trauma with different levels of magnitude, which could result in different severity of stress reactions depending on the trauma. Furthermore, our approach is cross-sectional, and causality between trauma exposure and sleep/circadian disturbances cannot be established. Likewise, we did not collect information about the time elapsed between the trauma exposure and the moment of the evaluation. In fact, time can attenuate PTSS, including those related to disturbances in sleep and circadian processes. A large number of statistical comparisons may have led to type I errors; however, the use of multiparametric statistical models may mitigate this concern. We have observed a consistent effect of gender in all regression models, indicating that trauma reactions may be worse in females than in males, consistently with previous studies (Carmassi et al., 2015; Dell'Osso et al., 2013); nevertheless, sleep and circadian variables have reached significant effects on PTSS independently of gender. Despite these limitations, our study remains the first to explore the association between PTSS and circadian and sleep-related parameters, using both subjective and objective measures, in adults belonging to the general population.

Identifying modifiable risk factors is essential to protect subjects exposed to stress from developing trauma and stress-related disorders. Among these factors, sleep and circadian

disturbances could represent a therapeutic target. The evidence in the literature indicates that subjective and objective sleep disruption occurring early after trauma may predict PTSD development (Koren et al., 2002; Mellman et al., 2002). Trauma exposure may lead to disturbances in sleep-related and circadian mechanisms, but simultaneously sleep and circadian disturbances may be associated with a worse prognosis in subjects with a full-blown PTSD (Germain et al., 2008)(Agorastos & Olff, 2020), thus highlighting the complexity of the pathways involved. Our results have shown that, although chronotype alone was correlated with trauma reactions, its effect as a moderator of the association between sleep/circadian parameters and PTSS was not significant, suggesting that fragmented sleep-wake patterns, sleep efficiency and self-reported poor sleep quality are associated to PTSS independently from chronotype, being the self-reported sleep quality is the main predictor of trauma reactions. Further investigations are required to explore the role of interventions focused on sleep disturbances and rest-activity rhythm in mitigating trauma symptoms. Furthermore, particular attention should be directed to subjects classified as evening chronotypes, as they seem to be more vulnerable to sleep and circadian disturbances and more vulnerable to maladaptive trauma reactions.

Acknowledgments

The authors thank the participants and their relatives for their generous contribution in this research.

Funding

This work has been partially supported by Italian Ministry of Health under grant-RC 1.21 "Monitoraggio e tele-monitoraggio del sonno in età evolutiva e in pazienti adulti" and the 5 x 1000 voluntary contributions; Fondazione Arpa Onlus, a non-profit organization (https://fondazionearpa.it).

Declaration of interest statement

U.F. is co-founder and president of sleepActa S.r.l, a spin-off company of the University of Pisa operating in the field of sleep medicine. All other authors have no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data availability statement

Supporting data is not available, according to the informed consent approved by the Ethics Committee of AOUP, Area Vasta Toscana Nord Ovest (code 14785/2019).

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Table 1. Distribution of Chronotype and comparisons between groups.

	Evening type N= 23		Neither type N= 72		Morning type N= 25		p-value
	Mean (SD)	Median [IQR]	Mean (SD)	median [IQR]	Mean (SD)	Median [IQR]	
Demographic data							
Age, years	29.30 (7.38)	27.00 [25.00, 31.50]	34.76 (14.00)	28.50 [24.00, 47.00]	43.76 (17.41)	52.00 [26.00, 60.00]	0.064
Sex, male %	47.8		44.4		20.00		0.069
Educative level, years	16.78 (2.91)	17.00 [13.00, 19.00]	16.07 (3.26)	17.00 [13.00, 19.00]	16.44 (3.75)	17.00 [13.00, 19.00]	0.798
Alcohol intake, u/w[b, c]	3.04 (3.28)	2.00 [0.00, 5.00]	2.12 (2.41)	1.00 [0.00, 3.00]	0.92 (2.08)	0.00 [0.00, 1.00]	**0.003**
Tobacco intake, u/w[b, c]	11.83 (20.71)	0.00 [0.00, 23.50]	7.25 (15.86)	0.00 [0.00, 10.00]	1.80 (8.02)	0.00 [0.00, 0.00]	**0.050**
BMI, kg/m^2	23.31 (4.91)	21.83 [19.96, 25.27]	22.13 (3.36)	21.62 [19.95, 23.98]	23.80 (3.77)	22.86 [21.16, 26.72]	0.152
TALS-SR Domains							
Loss events	3.61 (1.41)	4.00 [3.00, 4.00]	4.12 (1.57)	4.00 [3.00, 5.00]	3.92 (2.10)	4.00 [2.00, 5.00]	0.335
Grief reactions	11.22 (7.16)	11.00 [5.50, 17.50]	9.19 (4.83)	9.00 [6.00, 13.00]	9.28 (4.87)	10.00 [7.00, 12.00]	0.505
Potentially traumatic events	3.91 (2.70)	3.00 [2.00, 5.00]	3.53 (2.87)	3.00 [1.00, 5.00]	3.52 (3.06)	2.00 [2.00, 5.00]	0.728
Reaction to losses	7.22 (4.69)	7.00 [3.50, 10.50]	5.75 (4.22)	5.00 [2.75, 8.25]	5.08 (4.37)	5.00 [0.00, 9.00]	0.291
Re-experiencing	3.65 (2.89)	3.0 0 [1.00, 6.50]	2.96 (2.61)	2.50 [0.00, 5.00]	2.28 (2.41)	1.00 [0.00, 5.00]	0.199
Avoidance and numbing	3.35 (2.72)	3.00 [1.00, 4.50]	2.76 (2.79)	2.00 [0.00, 4.00]	2.04 (2.37)	1.00 [0.00, 3.00]	0.180
Maladaptive coping [a, b]	1.26 (1.29)	1.00 [0.00, 2.00]	0.60 (1.18)	0.00 [0.00, 1.00]	0.36 (0.86)	0.00 [0.00, 0.00]	**0.005**
Arousal	1.96 (1.85)	2.00 [0.00, 4.00]	1.31 (1.52)	1.00 [0.00, 2.25]	1.52 (1.53)	1.00 [0.00, 3.00]	0.320
Personal characteristics	1.96 (1.26)	2.00 [1.00, 3.00]	2.03 (1.60)	2.00 [1.00, 3.00]	1.56 (1.36)	1.00 [1.00, 2.00]	0.405
symptomatic domains	17.43 (12.09)	16.00 [7.50, 25.50]	13.38 (10.58)	13.00 [4.75, 19.25]	11.28 (10.08)	10.00 [0.00, 20.00]	0.165
Circadian parameters							
Acrophase [a, b, c]	17:21 (1:15)	17:23 [16:42, 18:18]	16:16 (1:22)	16:27 [15:24, 16:51]	15:24 (1:03)	15:06 [14:49,16:13]	**<0.001**
Amplitude	0.38 (0.05)	0.38 [0.36, 0.41]	0.39 (0.05)	0.39 [0.36, 0.42]	0.38 (0.05)	0.38 [0.34, 0.42]	0.561
Mesor	0.57 (0.05)	0.58 [0.53, 0.61]	0.59 (0.07)	0.59 [0.55, 0.62]	0.61 (0.08)	0.58 [0.55, 0.66]	0.366
Mid sleep point [a, b, c]	05:16 (01:15)	05:26 [04:47, 05:59]	04:28 (01:33)	04:14 [03:28, 04:52]	03:26 (01:37)	03:18 [02:42, 03: 47]	**<0.001**
Interdaily stability (IS)[b, c]	0.77 (0.09)	0.77 [0.74, 0.83]	0.80 (0.12)	0.81 [0.76, 0.88]	0.85 (0.07)	0.88 [0.82, 0.90]	**0.019**
Intradaily variability (IV)	0.31 (0.05)	0.30 [0.27, 0.34]	0.34 (0.07)	0.32 [0.30, 0.38]	0.35 (0.09)	0.32 [0.29, 0.40]	0.182

Relative amplitude (RA)	0.78 (0.09)	0.79 [0.71, 0.83]	0.78 (0.12)	0.83 [0.72, 0.86]	0.78 (0.12)	0.80 [0.73, 0.88]	0.799
Sleep-related parameters							
PSQI total score	6.13 (2.90)	6.00 [4.00, 8.00]	5.04 (2.20)	4.00 [3.00, 7.00]	5.76 (3.32)	5.00 [3.00, 8.00]	0.278
Actigraphic SE	83.27 (9.90)	82.05 [76.40, 92.47]	88.32 (9.26)	91.30 [84.50, 95.00]	87.61 (9.29)	90.50 [87.15, 92.67]	0.087
Actigraphic WASO	59.86 (43.67)	49.50 [28.25, 77.75]	40.81 (32.55)	32.00 [20.00, 51.00]	46.21 (29.10)	41.00 [28.00, 53.50]	0.060
Actigraphic TST	7.90 (1.30)	7.90 [6.88, 9.07]	7.35 (1.05)	7.40 [6.60, 8.10]	6.97 (1.35)	7.00 [5.97, 8.05]	0.086
Sleep Regularity Index (SRI)	62.97 (15.66)	62.85 [53.98, 73.05]	69.01 (15.43)	71.70 [57.70, 79.40]	70.78 (15.78)	77.20 [61.45, 82.05]	0.130

Abbreviations: BMI: Body Mass Index; Alcohol intake u/w: Alcohol units per week; Tobacco intake u/w: Tobacco (cigarettes) units per week; TALS-SR: Trauma and Loss Spectrum–Lifetime version; PSQI: Pittsburgh Sleep Quality Index total score; SE: sleep efficiency, WASO: Wake After Sleep Onset; TST: total sleep time. Results are presented in mean (SD: Standard deviation) and median [IQR: Interquartile range]). Acrophase and mid sleep point are reported as hours. Comparisons between groups were performed through the Kruskal-Wallis for continuous variables and the Fisher test for categorical variables. Significance values were considered at p-value ≤ 0.05. Post-hoc pairwise Mann-Whitney-Wilcoxon rank-sum test results are reported as follows:

[a] Significant difference between Evening type and Neither type groups.

[b] Significant difference between Evening type and Morning type groups.

[c] Significant difference between Neither type and Morning type groups.

Table 2. Correlation values between TALS-SR domains and subjective and objective circadian parameters.

TALS-SR domains	rMEQ rho (p-value)	Mesor rho (p-value)	Amplitude rho (p-value)	Acrophase rho (p-value)	IS rho (p-value)	IV rho (p-value)	RA rho (p-value)	Mid sleep point rho (p-value)
Loss events	0.04	0.03	0.04	-0.12	0.06	0.07	-0.02	-0.10
	(0.655)	(0.718)	(0.637)	(0.184)	(0.496)	(0.453)	(0.820)	(0.310)
Grief reactions	-0.09	-0.06	-0.04	0.00	-0.05	0.05	-0.01	0.01
	(0.328)	(0.507)	(0.706)	(0.999)	(0.568)	(0.600)	(0.944)	(0.932)
PTE	-0.08	0.04	-0.09	-0.09	-0.07	0.07	-0.15	-0.04
	(0.389)	(0.681)	(0.316)	(0.316)	(0.480)	(0.473)	(0.119)	(0.698)
Reaction to losses/PTE	-0.19	-0.09	-0.12	0.08	-0.19	0.17	-0.05	0.06
	(0.041)	(0.286)	(0.194)	(0.365)	(**0.040**)	(0.064)	(0.622)	(0.545)
Re-experiencing	-0.19	-0.14	-0.12	0.08	-0.17	0.23	-0.04	0.09
	(**0.044**)	(0.125)	(0.186)	(0.397)	(0.076)	(**0.015**)	(0.701)	(0.304)
Avoidance & numbing	-0.20	-0.17	-0.06	0.13	-0.11	0.20	-0.03	0.10
	(**0.029**)	(0.065)	(0.492)	(0.163)	(0.238)	(**0.030**)	(0.788)	(0.277)
Maladaptive coping	-0.29	-0.04	-0.13	0.17	-0.18	0.06	-0.10	0.20
	(**0.001**)	(0.651)	(0.162)	(0.068)	(0.053)	(0.539)	(0.297)	(**0.030**)
Arousal	-0.11	-0.08	-0.06	0.07	-0.13	0.11	-0.02	0.07
	(0.224)	(0.386)	(0.526)	(0.450)	(0.152)	(0.232)	(0.832)	(0.439)
Symptomatic domains	-0.21	-0.12	-0.12	0.11	-0.18	0.21	-0.06	0.11
	(**0.022**)	(0.192)	(0.194)	(0.245)	(**0.049**)	(**0.026**)	(0.521)	(0.255)

Abbreviations: TALS-SR: Trauma and Loss Spectrum–Lifetime version; rMEQ: Morningness-Eveningness Questionnaire reduced version; PTE: potentially traumatic events. Results are presented as Spearman's rank correlation coefficient (rho) and p-values. Significant correlations were considered at p-value ≤0.05.

Table 3. Correlation values between TALS-SR Domains and subjective and objective sleep-related parameters

TALS-SR domains	PSQI rho (p-value)	WASO rho (p-value)	TST rho (p-value)	SE rho (p-value)	SRI rho (p-value)
Loss events	0.12	0.09	-0.03	-0.10	0.05
	(0.244)	(0.363)	(0.746)	(0.311)	(0.588)
Grief reactions	0.29	0.13	0.04	-0.13	-0.09
	(**<0.001**)	(0.180)	(0.688)	(0.182)	(0.329)
PTE	0.34	0.12	-0.15	-0.20	-0.08
	(**<0.001**)	(0.193)	(0.112)	(**0.033**)	(0.408)
Reaction to losses/PTE	0.32	0.07	-0.03	-0.17	-0.09
	(**<0.001**)	(0.461)	(0.781)	(0.063)	(0.328)
Re-experiencing	0.34	0.11	0.01	-0.21	-0.05
	(**<0.001**)	(0.236)	(0.978)	(**0.024**)	(0.565)
Avoidance & numbing	0.29	0.03	0.05	-0.10	-0.05
	(**0.001**)	(0.742)	(0.574)	(0.298)	(0.584)
Maladaptive coping	0.31	0.12	-0.05	-0.21	-0.17
	(**<0.001**)	(0.215)	(0.622)	(**0.026**)	(0.065)
Arousal	0.34	0.03	0.01	-0.10	-0.08
	(**<0.001**)	(0.768)	(0.900)	(0.298)	(0.412)
Symptomatic domains	0.35	0.08	-0.01	-0.18	-0.09
	(**<0.001**)	(0.405)	(0.898)	(0.056)	(0.357)

Abbreviations: TALS-SR: Trauma and Loss Spectrum–Lifetime version; PTE: potentially traumatic events; PSQI: Pittsburgh Sleep Quality Index; SE: sleep efficiency, WASO: Wake After Sleep Onset; TST: total sleep time, SRI: Sleep Regularity Index. Results are presented as Spearman's rank correlation coefficient (rho) and p-value. Significant correlations were considered at p-value ≤0.05.

Table 4.1. Regression analyses estimating the associations between sleep/circadian parameters and TALS-SR *symptomatic domains*

	Model 1			Model 2			Model 3			Model 4		
	β	p-value	95% CI	β	p-value	95% CI	β	p-value	95% CI	β	p-value	95% CI
Age	-0.17	**0.013**	-0.30 -0.03	-0.14	**0.059**	-0.29 0.05	-0.13	**0.049**	-0.27 0.02	-0.24	**<0.001**	-0.37 -0.11
Gender (male)	-5.10	**0.012**	-9.07 -1.12	-5.54	**0.007**	-9.61 -1.47	-6.09	**0.004**	-10.19 1.98	-3.96	**0.033**	-7.62 -0.30
IV	29.03	**0.037**	1.64 56.42	-	-	-	-	-	-	-	-	-
IS				-13.40	0.210	-34.49 7.67	-	-	-	-	-	-
SE							-0.23	**0.032**	-0.44 0.019	-	-	-
PSQI							-	-		1.61	**<0.001**	0.96 2.26
R^2	0.10			0.08			0.08			0.21		

All models used the TALS-SR symptomatic domains as outcome. The *TALS-SR symptomatic domain* corresponds to the sum of the TALS-SR domains that account for the clinical symptoms of the post-traumatic spectrum: Domain IV *Reaction to losses and potentially traumatic events*, Domain V *Re-experiencing*, Domain VI *Avoidance and numbing*, Domain VII *Maladaptive coping*, and Domain VIII *Arousal*.
All models were adjusted for age and gender. Significance values were considered at p-value ≤0.05.
Model 1 = IV (intradaily variability) as independent variable
Model 2 = IS (interdaily stability) as independent variable
Model 3 = SE (sleep efficiency) as independent variable
Model 4 = PSQI (Pittsburgh Sleep Quality Index) as independent variable

Table 4.2 Regression analyses estimating the associations between sleep/circadian parameters and TALS-SR *symptomatic domains* evaluating the potential effect of chronotype as a moderator

	Model 5 (Predictor: IV)			Model 6 (Predictor: SE)			Model 7 (Predictor: PSQI)		
	β	p-value	95% CI	β	p-value	95% CI	β	p-value	95% CI
Age	-0.12	0.087	-0.26 -0.17	-0.10	0.149	-0.25 0.04	-0.22	**0.001**	**-0.35 -0.08**
Gender (male)	-5.50	**0.006**	-9.45 -1.55	-6.74	**0.001**	-10.95 -2.53	-4.40	**0.022**	**-8.17 -0.63**
Predictor (IV; SE; PSQI)	83.82	0.064	-4.99 172.64	-0.36	0.113	-0.82 0.09	1.94	**0.007**	0.52 3.67
Chronotype (E-type vs N-type)	-6.30	0.029	-11.97 -6.62	-0.91	0.739	-6.31 4.49	-1.30	0.589	-6.10 3.48
Chronotype (E-type vs M-Type)	-9.46	0.007	-16.33 -2.58	-4.10	0.225	-10.77 2.56	-3.34	0.272	-9.34 2.66
global p-value of chronotype		**0.050**			0.368			0.48	
Predictor * Chronotype (E-Type vs N-Type)	-61.71	0.203	-157.43 34.00	0.10	0.697	-0.42 0.63	-0.59	0.495	-2.30 1.12
Predictor * Chronotype (E-Type vs M-Type)	-34.71	0.495	-135.40 65.93	0.38	0.249	-0.27 1.03	-0.28	0.759	-2.15 1.57
global p-value of interaction		0.366			0.478			0.780	
R^2		0.13			0.08			0.21	

All models used the TALS-SR symptomatic domains as outcome. The *TALS-SR symptomatic domain* corresponds to the sum of the TALS-SR domains that account for the clinical symptoms of the post-traumatic spectrum: Domain IV *Reaction to losses and potentially traumatic events*, Domain V *Re-experiencing*, Domain VI *Avoidance and numbing*, Domain VII *Maladaptive coping*, and Domain VIII *Arousal*.
All models were adjusted for age and gender. Significance values were considered at p-value ≤0.05.
Model 5 = Interaction between Intradaily variability (mean centered) and Chronotype as independent variable
Model 6 = Interaction between Sleep Efficiency (mean centered) and Chronotype as independent variable
Model 7 = Interaction between PSQI (mean centered) and Chronotype as independent variable
Note: IS was not included in moderation models because IS was no longer associated with TALS symptomatic domains in regression models adjusting for age and gender.