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Trajectories of posttraumatic stress symptoms after whiplash:

A prospective cohort study

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Significance statement

Distinct recovery patterns after whiplash were identified with a significant subgroup reporting elevated and slightly increasing PTSD symptoms over time, highlighting both recovery variability and the presence of PTSD symptoms in a significant subgroup of individuals with whiplash. This subgroup also displayed enhanced pain-related disability over time compared to the recovering and resilient subgroups, thereby linking PTSD symptoms to functional pain outcomes over time. These findings suggest that clinicians should be attentive of potential PTSD symptoms in whiplash patients.

Abstract

Background: Posttraumatic stress disorder (PTSD) symptoms are highly prevalent after whiplash and associated with pain-related symptoms. While mutual maintenance between pain and PTSD has been suggested, knowledge on individual differences in the course of these symptoms is needed. The present study aimed to identify trajectories of PTSD symptoms following whiplash and test predictors and functional outcomes of such trajectories.

Methods: In a prospective cohort design with assessments at baseline (<4 weeks), 3 months, and 6 months post-injury (n=229, whiplash-grade I-III), we identified PTSD-trajectories using Latent Growth Mixture Modeling. Predictors (pain, fear-avoidance-beliefs, pain-catastrophizing, depression, age, and gender) were tested using multinomial logistic regression, and group mean differences in physical and psychosocial pain-related disability at 6 months after controlling for baseline levels were tested as outcomes.

Results: Three trajectories were identified: “Resilient” (75.1%) with little or no PTSD symptoms over time, “Recovering” (10.0%) with high initial PTSD symptom levels, then decreasing substantially, and “Chronic” (14.9%) with high initial PTSD symptom levels and a small increase over time. Initial higher pain and depression levels predicted the recovering and chronic trajectories, while the latter had more pain-related disability at 6 months compared to both other trajectories.

Conclusions: Three trajectories were identified, with the chronic trajectory suggesting that a significant subset of people does not recover from PTSD symptoms. This class also reported more pain-related disability. Pain and depression predicted membership, but did, however, not succeed in differentiating between the two high-starting trajectories, suggesting that targeting PTSD symptoms may be important to ensure recovery.

Keywords: PTSD, posttraumatic stress symptoms, whiplash, pain, pain-related disability, trajectories, prospective study

Introduction

Persistent symptoms such as pain and disability, collectively known as whiplash associated disorder (WAD; Spitzer et al., 1995), are common after whiplash with up to 50% not fully recovering (Carroll et al., 2008). WAD is a complex, biopsychosocial condition characterized by great heterogeneity (Sterling, 2011; Sterling and Kenardy, 2008). Unlike many other musculoskeletal pain conditions, WAD is a posttraumatic condition by definition, making comorbid symptoms of posttraumatic stress disorder (PTSD) a potential risk. Indeed, PTSD symptoms have gained growing attention within the field and have been found to be a meaningful way to subgroup individuals with WAD (Pedler and Sterling, 2013).

PTSD is a maladaptive reaction to a trauma defined by the DSM-IV-TR as symptoms of intrusion, avoidance, and hyperarousal (APA, 2000) with the DSM-5 adding alterations in cognitions and mood (APA, 2013). 15-25% with chronic WAD report clinical PTSD symptom levels (Andersen et al., 2013; Buitenhuis et al., 2006; Mayou and Bryant, 2002; Sterling et al., 2010), and these patients report more pain and disability compared to those without (Pedler and Sterling, 2013). Further, initial PTSD symptom levels predict WAD severity after a year (Buitenhuis et al., 2006; Kongsted et al., 2008), highlighting the

potential importance of PTSD symptoms in WAD. Theoretically, mutual maintenance between pain and PTSD has been proposed (Liedl and Knaevelsrud, 2008; Sharp and Harvey, 2001); a view supported in recent non-systematic reviews (Beck and Clapp, 2011; Brennstuhl et al., 2015). In a recent empirical testing of cross-lagged associations between pain and PTSD symptoms after whiplash, we found evidence of a main effect of PTSD symptoms on pain and not vice versa, suggesting only unidirectional and not bidirectional maintenance (Ravn et al., 2018). Hence, PTSD symptoms may contribute to poorer recovery in these patients. Generally, however, understanding recovery patterns after whiplash remains a challenge (Ritchie and Sterling, 2016), and such pathways for PTSD symptoms remain largely unclear.

To our knowledge, only one study has investigated longitudinal trajectories of PTSD symptoms after whiplash. Here, Sterling and colleagues (2010) identified three PTSD symptom trajectories: A resilient one with mild symptoms (40%), a recovering one with elevated symptoms initially, then declining to mild levels (43%), and a chronic one reporting clinical PTSD levels initially, then declining to moderate levels (17%). Within PTSD-research, four trajectories are commonly found, labeled chronic, delayed, recovering, and resilient (Bonanno and Mancini, 2012), which have also been found in injury patients (deRoos-Cassini et al., 2010). Adding longer follow-up among injury patients, however, a study found a fifth trajectory of delayed-onset-then-recovering (Bryant et al., 2015). Summing this, a large resilient subgroup is consistently found, as well as smaller chronic and recovering subgroups, while some inconsistency exists on the distribution of individuals between these and on additional trajectories.

Regarding predictors, Sterling and colleagues (2011) reported that hyperalgesia, pain, and age predicted the chronic moderate-to-severe trajectory. Also, they found a good correspondence of the trajectories of PTSD symptoms and disability, indicating a higher level

of disability in the chronic subgroup (Sterling et al., 2011). However, this is yet to be replicated in a study also including more process-related variables as potential predictors, as such more latent cognitive and emotional mechanisms and factors related to pain (e.g., pain-catastrophizing) may underpin the course of PTSD symptoms in samples experiencing pain (e.g., Andersen et al., 2016). Identification of such modifiable and latent variables potentially underlying recovery trajectories is important for early clinical intervention.

The current study aimed to identify PTSD-trajectories after whiplash and test predictors and functional outcomes of such trajectories. Identification of trajectories was undertaken in a data-driven manner, while it was hypothesized that gender, age, pain, pain-catastrophizing, fear-avoidance-beliefs, and depressive symptoms would be predictive of class membership and that poorer functional outcome would be associated with membership of trajectories displaying more severe PTSD symptoms.

Methods

Participants and procedure

The present study represents secondary analysis of data collected for a prospective cohort study published in 2016 (Andersen et al., 2016). Potential participants were consecutively contacted after visiting a large emergency department in Denmark in the period from July 2009 to July 2011. The emergency department physician conducted routine assessment and CT scans. Only patients with whiplash grade I-III using the Quebec Task Force classification (Spitzer et al., 1995) were recruited for this study. Grades I-III are characterized by neck pain, increased stiffness or tenderness, musculoskeletal symptoms including decreased neck mobility, and for grade III also neurological signs (Spitzer et al., 1995). People with whiplash grade IV (fracture or dislocation) were excluded. Further, patients presenting with head injuries and/or severe comorbidities leading to hospitalization

were excluded. All patients above the age of 18 years and conforming to the above eligibility criteria were invited to participate (n=578).

The study was designed with three assessments (<4 weeks post-injury, 3 months post-injury, and 6 months post-injury). At each assessment, the participants were given a set of questionnaires distributed by post. The Danish Data Protection Agency approved the data collection, and the conduct of this study complied with the Declaration of Helsinki. As it was not an intervention study, this study did not need ethics approval as according to Danish law (National Committee on Health Research Ethics).

Outcome measures

For the purpose of the present study, PTSD symptoms, pain intensity, pain-related disability (physical and psychosocial), depressive symptoms, pain-catastrophizing, and fear-avoidance-beliefs were measured using self-report questionnaires. PTSD symptoms were used at all three time points, while pain intensity, depressive symptoms, pain-catastrophizing, and fear-avoidance-beliefs were only used at baseline serving as potential predictors, and physical and psychosocial pain-related disability were only used at T3 as functional outcomes related to the trajectories with control for baseline levels.

PTSD symptoms were measured with the Harvard Trauma Questionnaire (HTQ) part IV (Mollica et al., 1992). The first 16 items of the scale correspond to the core symptoms of the PTSD diagnosis as proposed by the DSM-IV-TR (APA, 2000) with four items measuring intrusion symptoms, seven items measuring avoidance symptoms, and five items measuring hyperarousal symptoms (Mollica et al., 1992). Hence, these 16 items were used for the purpose of this study. The items are answered on a 4-point Likert scale ranging from 1 (not at all) to 4 (very often) with a higher score indicating higher severity. For the purpose of the present study, the participants were asked to answer the HTQ based on the

incident causing their whiplash. The original study found the scale to be reliable and valid (Mollica et al., 1992). The Danish version has been used extensively across trauma populations and is recommended for use in Denmark by The National Board of Social Services (Socialstyrelsen, 2013), but has, to our knowledge, only been subject to minor validation work as part of other studies (e.g., Bach, 2006). In the present study, the internal consistency measured by Cronbach's alpha was excellent at all three time points (T1-T3; $\alpha = 0.93, 0.93, 0.93$).

Pain intensity was measured as the mean of four numeric rating scales (NRS). The NRS has long been used to measure pain intensity in different forms and is a recommended measurement tool with good psychometric properties (Downie et al., 1978; Ferraz et al., 1990; Hjermstad et al., 2011; Jensen et al., 1986; McCaffery et al., 1989; Williamson & Hogart, 2005). Danish versions of NRS are extensively used in Denmark for the assessment of pain in both clinical work and research, but are to the knowledge of the authors not formally validated. A recent review paper did, however, recommend the use of NRS across languages due to minimal translation difficulties (Hawker et al., 2011). In the current study, the four scales measured present pain, highest level of pain, lowest level of pain, and average level of pain over the past week on 11-point Likert scales ranging from 0 (no pain) to 10 (worst imaginable pain). Internal consistency at baseline was excellent ($\alpha = 0.94$).

Pain-related disability was measured with the Pain Disability Questionnaire (PDQ) (Anagnostis et al., 2004). The scale is designed to measure pain-related dysfunction among people with chronic musculoskeletal conditions. The scale has 15 items, and each item is rated from 0 (no disability) to 10 (worst imaginable disability) on a numeric scale. The scale consists of two subscales measuring physical (nine items) and psychosocial (six items) pain-related disability, which were used for the present study. The scale has good

psychometric properties among chronic musculoskeletal pain patients (Anagnostis et al., 2004) and is a recommended tool for assessing pain-related disability (Gatchel et al., 2006).

The Danish version used for the present study was translated (forwards and backwards) for the purpose of the present data collection. This work was carried out by the last author of the present paper before being approved by Professor Gatchel, who was a part of the original development (Anagnostis et al., 2004). In the present study, excellent internal reliability was found for both the psychosocial subscale ($\alpha = 0.94$) and the physical subscale ($\alpha = 0.97$) at T3.

The Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) was used to assess symptoms of depression. The subscale measuring depressive symptoms consists of seven items each ranging from 0 (no symptoms) to 3 (maximum impairment) with a higher score indicating a higher symptom level and a score above 11 indicating presence of depression (Zigmond and Snaith, 1983). The original study found the scale to perform well (Zigmond and Snaith, 1983), and a large literature review of 747 papers concluded that the scale is well-validated and has good psychometric properties across lingual versions (Bjelland et al., 2002). The scale is also extensively used in Denmark, but is, to the knowledge of the authors, not formally validated. Internal consistency in the present study at T1 was very good ($\alpha = 0.87$).

The Pain Catastrophizing Scale (PCS) (Sullivan et al., 1995) was used to measure pain-catastrophizing. Reflecting on past painful experiences, participants are asked to indicate the degree to which they experienced different thoughts or emotions in relation to their pain. 13 items reflecting three subscales (rumination, magnification, and helplessness) are presented and answered on a five-point Likert scale ranging from 0 (not at all) to 4 (all the time). Scores are summed (0-52) with a higher score indicating higher levels of pain-

related catastrophizing. The Danish version of the scale has recently been validated (Kjørgx et al., 2014). In the present study, internal consistency was excellent at T1 ($\alpha = 0.94$).

The three fear-avoidance items on the Örebro Musculoskeletal Pain Screening Questionnaire (Örebro) (Linton and Boersma, 2003) were used to assess fear-avoidance-beliefs. The items are answered on an 11-point Likert scale ranging from 0 (completely disagree) to 10 (completely agree). Earlier studies have found Örebro to be a reliable and valid instrument (Linton and Boersma, 2003; Schmidt et al., 2016; Westmann et al., 2008). The three items were translated from Swedish to Danish, which are very similar languages, by the last author for the purpose of the present data collection. Here, internal consistency was very good at T1 ($\alpha = 0.86$).

Statistical analyses

First, total symptom severity scales were computed. Only cases responding to the HTQ at two or three time points were included in the data analyses ($n=229$; 70.0% of baseline sample). Participant characteristics were then presented and compared to characteristics of participants that dropped out (i.e., people with only one completed PTSD questionnaire). Means and standard deviations (SD) were presented for each outcome variable at each time point along with their inter-correlations at the time points they were used in the study. Then, the data set was transferred into Mplus. Of note, we assumed that data were missing at random (MAR) for this purpose based on the attrition analyses, as this cannot be explicitly tested (Potthoff et al., 2006).

To identify trajectories of PTSD symptoms, we conducted Latent Growth Mixture Modeling (LGMM). This approach relaxes the assumption of one distribution accounting for all the variance in a sample and instead assumes that multiple subpopulations with unique distributions exist within the sample. However, no assumptions about the

number of such distributions are made. In a data driven manner, models estimating unique growth parameters (intercept and slope) for 1 to n classes are fitted to the data, and the model providing the best fit of the data is selected. Model fit is determined based on a range of fit indices: The Akaike Information Criteria (AIC) (Akaike, 1987), the Bayesian Information Criteria (BIC), and the sample size adjusted BIC (Adj BIC). In addition, fit of nested models can be evaluated by estimation of the Lo-Mendel-Rubin (LMR) Likelihood test and the Bootstrapped LMR. Significant outcomes of these tests suggest that a model with n classes fits the data better than the model with n-1 classes. While fit indices provide solid scaffolding for model selection, parameters such as parsimony and theoretical meaningfulness should also be taken into account. As such, the best model provides adequate fit of the data while remaining parsimonious and theoretically meaningful (Nylund et al., 2007). After selection of the final model, we inspect entropy, which indicates classification accuracy (with 1 being perfect classification and $>.80$ indicating acceptable accuracy) (Clark & Muthén, N.d.). The LGMM analysis was performed in Mplus (Muthén & Muthén, 1998-2017). The model was estimated using Full Information Maximum Likelihood to account for missing data.

Predictors (age, gender, pain intensity, pain-catastrophizing, fear-avoidance-beliefs, and symptoms of depression) of trajectory membership were, after inspection of entropy to ensure sufficient classification accuracy, done in a post hoc fashion with class membership treated as the dependent variable in a multinomial regression analysis. Before entering all predictor variables simultaneously into the multinomial logistic regression model, we tested for interactions between predictor variables and found that no interactions added significantly to the model. Therefore, we did not include interactions in the multinomial logistic regression.

In a subsequent post-hoc step, we tested differences in outcomes (physical and psychosocial pain-related disability) of the estimated trajectories by comparing the estimated means on these outcome measures of each class in an one-way ANCOVA controlling for baseline levels of physical and psychosocial pain-related disability, respectively.

All descriptive analyses as well as all post hoc analyses were conducted in SPSS using a non-imputed data set, leaving between 188 and 229 cases for the descriptive analyses, 208 cases for the multi-nominal prediction analysis, and 195 cases for the outcome analyses.

Results

Sample characteristics

Of the 578 potential participants, the first questionnaire was returned by 327 participants, while 229 participants (30% attrition from baseline) fulfilled study criteria by filling out the HTQ at two or three time points. At baseline, the mean age was 36.9 years (SD = 13.62), and 62.9% was women. 77.7% were injured in traffic-related crashes, and the mean time for participants to answer the baseline questionnaire was 19.27 days (SD = 8.96) after the accident. There were no statistical differences between responders and dropouts (i.e., people who did only respond to one questionnaire) in gender, $\chi^2(1)=0.080$, $p=0.777$, the number of people injured in traffic, $\chi^2(1)=0.099$, $p=0.753$, age, $t(324)=0.938$, $p=0.349$, mean pain intensity at baseline, $t(315)=-1.756$, $p=0.080$, nor mean PTSD symptoms at baseline, $t(317)=-0.524$, $p=0.600$. All used variables were significantly and positively correlated ($p<0.001$) with the exception of age that did not correlate significantly with any of the other variables (Table 1). Further, mean scores of all variables decreased from time point to time point (Table 2).

Table 1 and 2.

Trajectories

Fit indices of models with 1-5 classes can be seen in Table 3. For all models, variance of the slope was fixed to zero to handle non-convergence. For the 1-3 class models, fit indices suggested that addition of every new class improved fit of the model (lower AIC, lower BIC, lower Adj BIC, and significant Bootstrapped LRT). Both LRTs were non-significant with the addition of the second class, but significant with the addition of the third class. With the addition of the fourth class, AIC, BIC, and adjusted BIC decreased only marginally and the LRTs became insignificant once again. While one could still argue in favor of a 4-class model, this solution included a class with only eight individuals, or less than 3.5 percent of the sample. Hence, this solution might not represent the most parsimonious solution. Upon inspection of the three-class model (Figure 1), we found that this model was parsimonious and theoretically meaningful. Entropy of the three-class model was 0.89. Hence, we settled on the three-class model as the best representation of the data.

An estimated 75.1% of the sample belonged to a trajectory of little or no PTSD symptoms (“resilient”) that remained low albeit with a small, significant decrease across assessments ($i=22.65$, $s=-0.61$, $p=0.002$). A trajectory with high initial symptom levels ($i=44.19$) decreasing to a substantially lower level ($s=-9.00$, $p<0.001$) constituted 10.0% of the sample (“recovering”). Finally, one trajectory (“chronic”) showed a pattern of high initial symptom levels ($i=39.64$) with a small, but significant increase over time ($s=1.36$, $p=0.038$). This trajectory represented 14.9% of the sample.

Table 3 and Figure 1.

Predictors of trajectories

We tested our six hypothesized predictors of trajectory membership in a multinomial logistic regression model with the resilient class as reference. We found no predictive effect of age, gender, fear-avoidance-beliefs, or pain-catastrophizing, but higher pain intensity and higher depression score were predictive of membership of the recovering (pain: OR=1.86 (CI= 1.26-2.76), $p=0.002$; depression: (OR=1.31 (CI= 1.15-1.50), $p<0.001$)) and chronic trajectories (pain: OR=1.86 (CI= 1.27-2.73), $p=0.001$; depression: OR=1.23 (CI= 1.07-1.41), $p=0.004$) (Table 4).

Table 4.

Functional outcomes of trajectories

First, a one-way ANCOVA showed an overall difference for both outcomes between classes (physical pain-related disability: $F(2,191)=5.25$, $p=0.006$, $\eta^2=0.021$; psychosocial pain-related disability: $F(2, 191)=9.52$, $p<0.001$, $\eta^2=0.031$) (Table 5) when controlling for baseline level of the respective outcomes. The observed power was 0.829 and 0.979 for physical and psychosocial pain-related disability, respectively.

For physical disability, post-hoc-tests with Bonferroni correction showed significant differences between the chronic and recovering classes ($p=0.009$) and between the chronic and resilient classes ($p=0.003$). No significant difference in physical disability was found when comparing the recovering to the resilient class.

For psychosocial pain-related disability, post-hoc-tests with Bonferroni correction also revealed a significant difference in psychosocial pain-related disability between the chronic and the recovering classes ($p<0.001$) as well as between the chronic and the resilient classes ($p=0.005$), while no significant difference was found between the resilient and the recovering classes.

Table 5.

Discussion

The present study aimed to identify trajectories of PTSD symptoms following whiplash and test predictors and functional outcomes of such trajectories. Three distinct trajectories were identified: A resilient trajectory (75.1%) with little or no PTSD symptoms over time, a recovering trajectory (10.0%) with high initial levels, then decreasing to substantially lower levels, and a chronic trajectory (14.9%) with high initial PTSD symptoms and a small, but significant increase over time. Initial pain and depressive symptoms predicted the recovering and chronic trajectories, and the chronic trajectory was associated with significantly more physical and psychosocial pain-related disability at 6 months compared to both other trajectories after controlling for baseline disability.

The present study supports the findings of Sterling and colleagues (2010) who also identified three trajectories of PTSD symptom levels (resilient, recovering, and chronic) after whiplash. In the present study, the symptom levels stayed quite similar across time points, with the exception of the recovering subgroup that diminished substantially. This is, on the other hand, not similar to Sterling and colleagues (2010) who found that all trajectories declined markedly the first three months. Such a three-month recovery window in WAD patients has been reported across studies (Kamper et al., 2008), but we did not see indication

of this in the present study. Sterling and colleagues (2010) found that 17% would take the chronic PTSD trajectory, which in the current study were 14.9%, highlighting that a significant proportion of individuals with WAD displays significant PTSD symptom levels over time. This is also in agreement with studies reporting 15-25% of clinical PTSD symptom levels in chronic WAD (Andersen et al., 2013; Buitenhuis et al., 2006; Mayou and Bryant, 2002; Pedler and Sterling, 2013; Sterling et al., 2010). For the two other trajectories, Sterling and colleagues (2010) found that 43% had elevated symptoms initially, then declining to mild symptoms, while 40% followed the resilient trajectory with mild symptoms from the beginning and forth. In the present study, 75.1% followed the resilient trajectory and only 10.0% followed the recovering trajectory. Hence, even though the classes are alike, the specific distribution between them is different. Looking at the endpoints, however, 85.1% ended up recovered from their PTSD symptoms in the present study compared to 83% found by Sterling and colleagues (2010), making the studies quite similar. The present study did only partially support trajectory studies in other injury samples (Bryant et al., 2015; deRoon-Cassini et al., 2010). Bryant and colleagues (2015) and deRoon-Cassini and colleagues (2010) also found evidence of a large resilient subgroup and a significant, but smaller chronic subgroup. However, neither the present study nor Sterling and colleagues (2010) found evidence of trajectories of delayed distress (Bryant et al., 2015; deRoon-Cassini et al., 2010) or recovery from delayed onset (Bryant et al., 2015). This could be because individuals with WAD compose a fundamentally different patient group and therefore present different recovery patterns. It may also be that both samples had more severe injuries and also had a significant proportion having injuries after inter-personal traumas (Bryant et al., 2015; deRoon-Cassini et al., 2010), making the samples differ in potentially important ways. It could also be that the present study did not follow the participants long enough to detect delayed symptoms. Likewise, a larger sample would have allowed identifying more

trajectories. With regards to a trajectory of delayed-onset-then-recovery, we may not detect this due to statistical issues, as we only had three assessments, which only allow us to estimate linear, and not quadratic, growth. However, Sterling and colleagues (2010) did have four assessments, thereby also enabling them to test for non-linear fluctuations without finding evidence of this.

Looking into predictors of group-membership, we found no predictive effects of fear-avoidance-beliefs nor pain-catastrophizing as would be expected based on earlier findings that these variables are important in the relationship between PTSD symptoms and pain (e.g., Andersen et al., 2016; Carty et al., 2011). Similarly, age and gender were not predictive of group-membership. This is only partially in agreement with Sterling and colleagues (2011), who found age to be a significant predictor. Instead, initial pain and depression were predictive of the recovering and chronic trajectories, indicating that higher levels of pain and depressive symptoms after whiplash enhance the likelihood of following one of the high starting PTSD symptoms trajectories. This is partially in accordance with Sterling and colleagues (2011), who also found initial pain to be predictive of the high PTSD symptoms group, while they did not test the predictive value of depressive symptoms. However, the predictors in the present study did not permit us to differentiate between the two high-trajectories. Hence, using these predictors, it was not possible to predict who would decrease and who would stay high in PTSD symptoms. This is, however, not to say that these factors are not of potential importance in the interplay between pain, disability, and PTSD symptoms post-injury.

When testing pain-related disability across trajectories, we found that the chronic trajectory had significantly higher disability levels compared to the two others when controlling for baseline disability, while no difference was found between the remaining. This indicates that membership of the chronic class with ongoing PTSD symptoms heightens

the likelihood of a greater loss of function over time despite initial disability levels, suggesting that early interventions directly targeting PTSD symptoms may be required to prevent both PTSD symptoms and pain-related disability in the chronic post-injury phase. Sterling and colleagues (2011) did not test functional outcomes of the trajectories per se, but did find indications of more disability in the chronic PTSD symptom group. Our findings support this. This is also in agreement with many other studies reporting that chronic pain patients with PTSD symptoms report more pain and disability when compared to patients without, both in WAD (Pedler and Sterling, 2013) and in other pain conditions (Aakerblom et al., 2017; Andersen et al., 2014; Ruiz-Parraga and Lopez-Martinez, 2014). This is also in accordance with longitudinal studies finding initial PTSD levels predictive of WAD severity one year post-injury (Buitenhuis et al., 2006; Kongsted et al., 2008). Further, these findings are indirectly partly supportive of the mutual maintenance proposal (Sharp and Harvey, 2001), suggesting that PTSD symptoms may contribute to a poorer recovery by negatively influencing and maintaining WAD symptoms. This is also in line with our recent study on the cross-lagged relationship between pain and PTSD symptoms after whiplash, where we found evidence of a main effect of PTSD symptoms on pain and not vice versa, suggesting that PTSD symptoms negatively affect and thereby maintain pain over time at certain time points post-injury (Ravn et al., 2018). In relation to the opposite scenario, i.e. pain as a predictor of PTSD symptoms over time, the findings of Ravn et al. (2018) did not support this. In the present study, pain was a significant predictor of group membership, but failed to distinguish between trajectories of decreased or slightly increased PTSD symptoms over time. Hence, pain may not be predictive of PTSD symptoms over time, but may be related to more acute stress symptoms early post-trauma. Returning to the discussion of functional outcomes across classes, it is important to take the low effect sizes (i.e., $\eta^2=0.031$ and $\eta^2=0.021$ for psychosocial and physical pain-related disability, respectively) into consideration, as these

point to class membership (and hence patterns of PTSD symptoms) not being of great importance in explaining functional outcomes at 6 months. For comparison purposes, η^2 for the covariate (i.e., baseline levels of the outcomes) was 0.169 for psychosocial pain-related disability and 0.223 for physical pain-related disability.

Clinically, the present study demonstrates the importance of PTSD symptoms by highlighting that a significant proportion of people with whiplash are likely to follow a trajectory of high PTSD symptom levels, which is also associated with more pain-related disability. Hence, it would seem important to screen for PTSD symptoms early post-trauma and target these symptoms and thereby hopefully alleviate PTSD symptoms in these patients. Such interventions may also have positive effects on pain-related disability. In particular, it would seem important to be aware of whether PTSD symptoms decrease or increase within the first three months post-injury and intervene if the patient does not follow a recovering trajectory, as these two subgroups will be observably different at this time point according to the present study. Of note, the finding that pain-related catastrophizing and fear-avoidance beliefs were not predictors of group membership does not rule out their (or other process-related variables') relevance. For instance, a recent study by a part of the present author group found these factors to mediate the relationship between PTSD symptoms and pain (Andersen et al., 2016). Hence, we do not argue for a strictly diagnostic focus in clinical interventions, but rather an integrated one with inclusion of some of these more trans-diagnostic and underlying mechanisms.

Besides a number of strengths in the present study, there are also important limitations to take into consideration. First, it is important to note that PTSD symptoms were measured by self-report questionnaires, as answers may be inflated by other symptomatology such as pain, especially on the non-specific symptoms. Even though the HTQ has shown good validity compared to diagnostic interviews (Mollica et al., 1992), a

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clinician-administered interview would have reduced this risk of false positives. Also, we cannot be certain that the participants answered the HTQ based on the event causing their whiplash, as would have been clear using a diagnostic interview. This is secured to the degree possible by asking specifically for accident-related symptoms. Second, it is important to be aware of high bivariate correlations that may stem from a conceptual overlap in many of these factors. Third, the current study used DSM-IV and not DSM-5, but as the focus was on PTSD symptoms as measured by the core symptoms (Maercker et al., 2013) and not the diagnosis, it is considered satisfactory. Fourth, no information on the sample prior to the trauma was collected, even though pre-trauma vulnerabilities may play a significant role (Bendix et al., 2016; Carstensen et al., 2008). Fifth, the relatively short follow-up period does not shed light upon the course of symptoms into more long-lasting chronicity. Additional assessments would also have allowed for estimation of non-linear developments, thereby enabling testing for more time-dependent fluctuations in symptoms. Earlier studies have indeed concluded that these symptom patterns are non-linear and fluctuating (Bryant et al., 2013). Sixth, only 56.6% of the potential sample responded to the initial study invitation with a further 30% attrition rate from the baseline sample to the sample that responded two or three times (i.e., the sample used for the present study), leaving the present results to be based on less than 40% of the initial total cohort. This may challenge the representativeness of the sample and the generalizability of the results. Seventh, while the majority of the used scales are extensively used in Denmark and are well-validated in other languages, proper validation work of the Danish versions is generally lacking, which is important to take note of in the interpretation of the present results. Finally, a larger sample size would have allowed for the identification of more trajectories. Here, it is important to keep in mind that we did find indicators of a possible fourth trajectory. Relatedly, both the present study and Sterling and colleagues (2010) found indication of a slight increase in symptoms in the chronic group

towards the end of the study period. Hence, studies following patients for longer and in larger samples are of importance.

Conclusions

The present study aimed to identify trajectories of PTSD symptoms following whiplash and test predictors and functional outcomes of such trajectories. Three trajectories were identified with 14.9% following a chronic trajectory, suggesting that a significant subset of people does not recover over time. This group showed enhanced levels of both psychosocial and physical pain-related disability at six months after controlling for baseline disability compared to the two remaining trajectories. Initial pain and depression predicted membership, but these predictors did not succeed in differentiating between the chronic and recovering trajectories. Hence, directly targeting of PTSD symptoms might be an important part of the puzzle to ensure recovery. The present study demonstrates the importance of PTSD symptoms and gives insights into the differential courses of recovery after whiplash, which emphasizes the need to consider PTSD symptoms in WAD-management.

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Figure legends

Table 1. Correlations of variables at time points used: PTSD symptoms T1-T3, continuous predictors at T1, and functional outcomes at T3.

Notes: *** $p < 0.001$

Table 2. Fluctuations of symptoms over time.

Table 3. Fit indices of models with 1-4 classes.

Figure 1. Sample means of PTSD symptom trajectories in the final 3-class model. Class proportions represent most likely class membership.

Table 4. Results of multinomial logistic regression model with class membership as the dependent variable and the resilient trajectory as the reference class.

Notes: ** $p < 0.005$, *** $p < 0.001$

Table 5. Functional outcomes of trajectory membership at 6 months.

	1.	2.	3.	4.	5.	6.	7.	8.	9.
1. PTSD symptoms T1									
2. PTSD symptoms T2	.818***								
3. PTSD symptoms T3	.737***	.858***							
4. Pain T1	.578***	.578***	.599***						
5. Depression T1	.692***	.632***	.651***	.537***					
6. Pain-catastrophizing T1	.589***	.552***	.579***	.628***	.623***				
7. Fear-avoidance-beliefs T1	.519***	.481***	.505***	.820***	.514***	.565***			
8. Age T1	-.080	.002	-.036	-.009	-.036	-.011	-.004		
9. Physical disability T3	.514***	.517***	.649***	.679***	.564***	.549***	.568***	.045	
10. Psychosocial disability T3	.526***	.559***	.702***	.649***	.629***	.586***	.548***	.004	.925***

Variable	Baseline – T1 Mean (SD)	3 months – T2 Mean (SD)	6 months - T3 Mean (SD)
PTSD symptoms	27.26 (10.21)	26.08 (09.66)	25.15 (09.39)
Pain intensity	03.10 (02.50)	02.20 (02.52)	01.88 (02.51)
Psychosocial disability	11.89 (13.98)	09.45 (13.92)	07.92 (13.22)
Physical disability	19.66 (21.19)	14.28 (20.21)	12.17 (19.71)
Depressive symptoms	03.95 (04.49)	03.49 (04.17)	03.19 (04.07)
Pain-catastrophizing	21.74 (08.87)	20.60 (09.26)	19.51 (08.55)
Fear-avoidance-beliefs	12.15 (10.05)	08.41 (09.56)	07.19 (09.32)

	AIC	BIC	SSA-BIC	VLMR-LRT (p-value)	LMR-LRT (p-value)	Bootstrap (p-values)
1 class	4312.96	4333.56	4314.54	-	-	-
2 classes	4265.90	4296.80	4268.28	0.088	0.099	<0.0001
3 classes	4190.70	4231.91	4193.87	0.014	0.017	<0.0001
4 classes	4164.43	4215.94	4168.40	0.394	0.408	<0.0001

	Recovering	Chronic
	OR (95% CI)	OR (95% CI)
Age	0.97 (0.93-1.01)	1.01 (0.97-1.04)
Gender	1.36 (0.38-4.86)	0.70 (0.23-2.11)
Pain	1.86 (1.26-2.76)**	1.86 (1.27-2.73)**
Pain-catastrophizing	1.01 (0.94-1.10)	1.05 (0.98-1.13)
Fear-avoidance-beliefs	0.93 (0.84-1.02)	0.97 (0.89-1.10)
Depression	1.31 (1.15-1.50)***	1.23 (1.07-1.41)**

	Resilient	Recovering	Chronic	Significant differences	<i>p</i>-values
Physical disability (mean(SD))	7.15 (13.14)	16.50(20.40)	34.79(28.72)	Chronic > Recovering	<i>p</i> =0.009
				Chronic > Resilient	<i>p</i> =0.003
Psychosocial disability (mean(SD))	4.07 (7.95)	9.60(11.99)	25.63(18.71)	Chronic > Recovering	<i>p</i> <0.001
				Chronic > Resilient	<i>p</i> =0.005

