Spinal pain in employees exposed to abusive supervision: Evidence of a sex and CRHRI CTC haplotype interaction

Ann-Christin Sannes, Andrine Risøy, Jan Olav Christensen, Morten Birkeland Nielsen, and Johannes Gjerstad

Abstract

Previous findings suggest that exposure to social stress in the form of abusive supervision may increase the risk of musculoskeletal disorders. In the present study, we examined the link between abusive supervision, the CRHRI genotype and spinal pain. The data were collected through a national survey drawn from the National Central Employee Register by Statistics Norway. A total of 1226 individuals returned both the questionnaire and the saliva kit. Abusive supervision was measured by a 5-item version of the Tepper's 2000 scale. Spinal pain was measured by 3 items (neck-, upper and low back pain). Genotyping with regard to CRHRI rs242941, rs242939 and rs1876828 was carried out using Taqman assay, and Phase v.2.1.1 was used to define the CRHRI allele combinations. The analyses revealed that abusive supervision was associated with spinal pain. In particular, we observed a strong effect of abusive supervision on spinal pain in female +CTC/+CTC carriers (p = 0.002). Moreover, using +CTC/+CTC as a reference, +CTC−CTC and −CTC−CTC both showed protective effects (p = 0.024, p = 0.002, respectively). Also, our data demonstrated a clear sex and CRHRI CTC haplotype interaction (p = 0.013). No such gene-environment interaction was seen in men. Our data demonstrated that the CRHRI CTC haplotype may exacerbate the effect of abusive supervision on spinal pain in female employees. Hence, the present study supports the theory that both gender and the CRHRI genotype, may moderate the pain responses to social stressors.

Keywords

Social stress, spinal pain, CRHRI, glucocorticoid receptors, sex

Introduction

In the Norwegian adult population, as many as 80% experience musculoskeletal pain. A considerable portion of such pain states may be spinal pain, i.e. neck-, upper back- and low back pain. The experience of pain involves activation of several brain areas such as hippocampus, amygdala and the prefrontal cortex. These areas are also important in the response to stressful experiences. Social stress, in the form of abusive supervision in the workplace, has been recognised to be especially detrimental. Thus, it seems likely that being exposed to abusive supervision also may affect the sensory processes in the brain relevant to pain.

Abusive supervision is defined as subordinates’ perceptions of the supervisor engaging in sustained displays of hostile verbal and nonverbal behaviour, excluding physical contact. Abusive supervision is a form of hindrance stressor (i.e. a constraint to a subordinate’s personal achievement and goal progress), leading to various negative outcomes for exposed subordinates. As many as 10–16% report being subjected to such behaviours. Experiencing abusive supervision may be linked to e.g. workplace deviance, decreased task performance and reduced creativity. Evidence exists that being exposed to abusive supervision increases the risk of health complaints.
Although little is known about the mechanisms underlying the effect of abusive supervision, it seems clear that such stressors do affect the hypothalamic-pituitary-adrenal (HPA) axis. Moreover, such strong stressful experiences could influence the hypothalamic release of corticotropin-releasing hormone (CRH), disturb pituitary release of the adrenocorticotrophic hormone (ACTH), which in turn control glucocorticoid synthesis of the adrenal cortex. Thus, it seems likely that strong social stressors through circulating glucocorticoids, may affect neuroinflammatory processes including pain.

One of the genetic factors involved in the response to activation of the HPA axis is the gene encoding corticotropin-releasing hormone type 1 receptor (CRHR1). Located at 17q21.31, this G-protein coupled receptor binds neuropeptides of the CRH family and is therefore a significant regulator of the HPA axis. In particular, this receptor may be important for the stress-induced negative feedback triggered by high cortisol levels, which in turn is crucial for the HPA deactivation and coping. Additionally, CRHR1 is expressed in several of the brain areas important in cognitive function and supraspinal nociceptive processing.

So far, research on the CRHR1 haplotype block comprising of SNPs rs242941, rs242939, rs1876828 has focused only on depression. However, given the link between social stress, HPA axis activation, CRHR1 and nociceptive processing in the brain, it seems likely that this haplotype may be involved in the experience of pain. Moreover, women and men may be different regarding pain mechanisms. Hence, our aim was to investigate associations between abusive supervision, the CRHR1 haplotype rs242941/rs242939/rs1876828, gender and spinal pain in the general working population.

Method

Data collection

As previously described, the data were based on a sample of 5000 employees randomly drawn from The Norwegian Central Employee Register collected by Statistics Norway. Briefly, inclusion criteria were adults from 18 to 60 years of age, working at least 80% of full-time employment. Questionnaires were distributed by post in 2015. A total of 1608 persons (32%) returned the questionnaire. Additionally, saliva collection kits were sent to consenting subjects (1226 returned the saliva sample kit). Ethical approval was obtained by the Regional Committee for Medical Research for Eastern Norway (REK 2014/1725).

Statistical analysis

In line with previous studies, the average of the 5 items in the questionnaire was used to score abusive supervision. An average was also calculated from the 3 questions regarding pain. The association between abusive supervision and spinal pain moderated by gender and the CRHR1 haplotype was examined using linear regression. First, the linear regression analyses were stratified by gender. In these analyses, the main effects (without any interaction term) were assessed in step 1, whereas the possible effect of the two-way interaction; abusive supervision × haplotype was assessed in step 2. Next, a linear regression analysis of the full sample with gender also included in the interaction term (three-way interaction) was conducted to assess any gender interaction.

Instruments

The respondents were asked to indicate the frequency of occurrence of several supervisor behaviours characteristic of abusive supervision. A 5-item version of the Tepper’s “Abusive Supervision Scale”, with response categories ranging from 0 to 4 (‘never’, ‘rarely’, ‘once in a while’, ‘quite often’ and ‘very often or always’), was used. Items consisted of “critiques me in front of others”, “tells me my thoughts and feelings are stupid”, “says I am useless”, “negative remarks about me in front of others” and “ridicule me”. Cronbach’s alpha for abusive supervision was 0.87. Moreover, the participants were asked to answer questions indicating their level of spinal (neck-, upper and low back) pain the last 12 months. The response categories was ranged from 0 to 3 (‘not bothered,’ ‘a little bothered,’ ‘considerably bothered,’ ‘seriously bothered’).

Genotyping/haplotyping

Extraction of genomic DNA from saliva was performed using OrageneRNA sample collection kit (DNA Genotech Inc. Kanata, Ontario, Canada). As previously described, single nucleotide polymorphism (SNP) genotyping with regard to rs242941, rs242939 and rs1876828 were carried out using predesigned TaqMan SNP genotyping assays (Applied Biosystems, Foster City, CA, USA). In accordance with the procedure in our earlier studies, an ABI 79000HT sequence detection system was used. Phase v.2.1.1 was used to define the CRHR1 haplotypes. The haplotyping was categorised into those individuals with two copies of CTC, those with one copy of CTC and all others. Approximately 10% of the samples were re-genotyped and the concordance rate was 100%. See Supplementary Table 1a for haplotype combinations, Supplementary Table 1b for haplotype grouping and Supplementary Table 2 for Hardy-Weinberg Equilibrium and p-value for all SNPs.
difference revealed in the previous analysis. All statistical analyses were conducted using Stata SE 16.0. Significance was accepted at the $p < 0.05$ level.

**Results**

In total, 342 (46%) men and 403 (54%) women were successfully genotyped for the CRHR1 haplotype (Tables 1 and 2). The distribution within the male cohort was 86 (25.1%) with two copies of the CTC allele, 180 (52.6%) with one copy of the CTC allele and 76 (22.2%) without CTC. For females the distribution was 114 (28.3%), 208 (51.6%) and 81 (20.1%), respectively. For men the mean experienced abusive supervision and spinal pain were 0.23 (SD = 0.41) and 0.68 (SD = 0.57) for the +CTC/+CTC individuals, 0.16 (SD = 0.42) and 0.72 (SD = 0.65) for +CTC/-CTC individuals, and 0.19 (SD = 0.40) and 0.69 (SD = 0.60) for -CTC/-CTC individuals (see Table 1). The mean experienced abusive supervision and spinal pain for women were 0.18 (SD = 0.47) and 0.82 (SD = 0.67) for the +CTC/+CTC individuals, 0.18 (SD = 0.40) and 0.84 (SD = 0.70) for +CTC/-CTC individuals, and 0.15 (SD = 0.36) and 0.76 (SD = 0.63) for -CTC/-CTC individuals (see Table 2).

The analysis of the male subjects (Table 3 left, step 1) showed a significant association between abusive supervision and spinal pain (Coef = 0.274, $p$-value = 0.001). However, no significant association was observed between the CRHR1 haplotype and spinal pain. Further, including an interaction term (abusive supervision $\times$ CRHR1) in the model did not indicate any differences in experienced spinal pain for the different haplotypes given abusive supervision (Table 3 left, step 2 & Figure 1(a)).

In contrast to the male subjects, the female subjects (Table 3 right, step 1) did not show a significant association between abusive supervision, or the haplotype, and

**Table 1.** Characteristics of the male subjects by CRHR1 haplotype (rs242941, rs242939, rs1876828); +CTC/+CTC, +CTC/-CTC and -CTC/-CTC.

| Range        | +CTC/+CTC |      |     | +CTC/-CTC |      |     | -CTC/-CTC |      |     | Sum |
|--------------|----------|------|-----|----------|------|-----|----------|------|-----|-----|
| Subjects     | 86       | 25.1 | 0.68| 0.05     | 180  | 52.6| 0.72     | 0.04 | 0.69| 0.05|
| Spinal pain  | 0 to 3   | 45.9 | 0.82| 0.03     | 49   | 57  | 0.23     | 0.03 | 0.19| 0.04|
| Abusive supervision | 0 to 4 | 44.3 | 0.79| 0.02     | 49   | 57  | 0.16     | 0.02 | 0.19| 0.04|
| Age          | ≤High school | 37  | 43  | 0.82     | 0.05 | 66  | 37       | 0.72 | 0.04| 0.69| 0.05|
| Education    | ≥Higher education | 49  | 57  | 0.18     | 0.04 | 114 | 63       | 0.16 | 0.02| 0.19| 0.04|
| Smoking      | No       | 31   | 36  | 0.82     | 0.05 | 137 | 76       | 0.72 | 0.04| 0.76| 0.06|
|              | Yes      | 54   | 62  | 45.9     | 0.82 | 43  | 24       | 44.9 | 0.59| 45.0| 0.94|

N: number of subjects, SEM: standard error of mean.

**Table 2.** Characteristics of the female subjects by CRHR1 haplotype (rs242941, rs242939, rs1876828); +CTC/+CTC, +CTC/-CTC and -CTC/-CTC.

| Range        | +CTC/+CTC |      |     | +CTC/-CTC |      |     | -CTC/-CTC |      |     | Sum |
|--------------|----------|------|-----|----------|------|-----|----------|------|-----|-----|
| Subjects     | 114      | 28.3 | 0.82| 0.05     | 208  | 51.6| 0.84     | 0.04 | 81  | 20.1| 403|
| Spinal pain  | 0 to 3   | 45   | 39  | 0.82     | 0.05 | 69  | 33       | 0.18 | 0.04| 0.02| 0.15| 0.03|
| Abusive supervision | 0 to 4 | 44.3 | 0.79| 0.18     | 0.04 | 139 | 67       | 0.18 | 0.04| 0.15| 0.03|
| Age          | ≤High school | 45  | 39  | 44.3     | 0.79 | 69  | 33       | 44.9 | 0.53| 42.8| 0.87|
| Education    | ≥Higher education | 69  | 61  | 44.3     | 0.79 | 139 | 67       | 44.9 | 0.53| 42.8| 0.87|
| Smoking      | No       | 91   | 80  | 0.82     | 0.05 | 180 | 86       | 0.84 | 0.04| 0.76| 0.06|
|              | Yes      | 23   | 20  | 44.3     | 0.79 | 28  | 14       | 44.9 | 0.53| 42.8| 0.87|

N: number of subjects, SEM: standard error of mean.
spinal pain in the initial analysis. However, when including the interaction term (abusive supervision × CRHR1) a significant association was seen (Table 3 right, step 2 & Figure 1(b)). In women with one or no copies of the CTC allele the effect of abusive supervision was weaker (Coef = −0.409, p-value = 0.024) or much weaker (Coef = −0.737, p-value = 0.002) than in women with two copies of the allele.

Moreover, gender was included in the interaction term (abusive supervision × haplotype × gender) in a third analysis, which confirmed gender differences (Table 4). Women without the CTC allele showed significantly less spinal pain compared to men without the CTC allele (Coef = −0.668, p-value = 0.013).

Discussion

The present study showed a clear association between abusive supervision and spinal pain. Interestingly, this association was moderated by the CRHR1 rs242941, rs242939, rs1876828 CTC haplotype in women. No such gene-environment interaction was seen in men. Thus, our data demonstrated that one or two copies of the CTC allele may reduce resilience to social stress in men.
the form of abusive supervision, but only in women. This shows that the CRHR1 haplotype may moderate the pain responses to social stressors in employees, and adds to the existing evidence linking stress and pain.\(^{26,30,31}\) Moreover, environmental stressors have long been connected to both etiology and pathophysiology of physical health.\(^{32}\)

The HPA axis is one of the primary neurobiological systems activated in response to experienced stressors. In addition to the effect circulating glucocorticoids have on the brain,\(^{33}\) the precursor CRH also have neuromodulatory properties.\(^{34}\) One of the extra-hypothalamic areas with high expression of CRH is the amygdala. Among other tasks, the amygdala is involved in the emotional-affective dimension of pain.\(^{35}\) Especially important is the presence in the central nucleus, which serves as the amygdala output nucleus.\(^{36}\) This area receives unfiltered nociceptive input as a part of the spino-parabrachial-amygdaloid pain pathway.\(^{35,36}\) Earlier observations suggest that central sensitisation may enhance the excitability in the amygdala regions in musculoskeletal pain conditions.\(^{37,38}\)

Previous research indicates that increased CRH in the amygdala can trigger pain-like behaviour,\(^{36}\) and also links pain to the function of the opioid receptors in the amygdala.\(^{4}\) Moreover, earlier data show that the opioid receptor genotype OPRM1 rs1799971 G allele increases the pain intensity in women, but have the opposite effect in men.\(^{34}\) Hence, sex differences in nociceptive processing in the amygdala,\(^{39-42}\) that also affect the HPA axis and subsequent emotional responses to stress including pain, seems likely. Given the central distribution of the CRHR1 receptors, it is tempting to speculate that the CRHR1 rs242941, rs242939, rs1876828 haplotype may affect such processes.

In any case, our data suggest that spinal pain in women is associated with genetic susceptibility. In accordance with earlier observations, the present study supports the theory that women are less affected by the psychosocial work environment,\(^{31}\) but more affected by genetic factors than men.\(^{43}\) However, such sex differences may be dependent on choice of outcome. Although women who experience abusive supervision with two CTC alleles report more pain than men with the same genotype, these men may have other manifestations not studied in the present study. The cellular mechanism underlying the impact the CRHR1 haplotype CTC allele on spinal pain and other health outcomes remains to be investigated.

**Limitations**

The outcome in the present study was the average of three items regarding neck-, upper- and low back pain over the last 12 months. Thus the information given by the subjects is not immune to recall bias.\(^{44}\) Additionally the level of abusive supervision is fairly low in this cohort. This may be related to the low occurrence of such behaviour in the Norwegian working population.\(^{45}\) Also, due to the cross-sectional nature of this study, no information regarding cause and effect can be concluded. Further, we cannot disregard common-method bias due to self-report bias as the subjects reported both the exposure and the outcome.\(^{46}\) However, as the subjects were informed that all information was treated anonymously it likely does not have any great impact.\(^{46}\) Finally, the average response rate for the questionnaire was 32%. Although somewhat low, this response rate is in line with the current trends in survey research.\(^{47}\) Furthermore, response rate is assumed to have little impact on the internal validity of a study and it is therefore unlikely that the response rate in this study have a major effect on the established association.\(^{48}\)

**Conclusion**

The present data showed that the association between abusive supervision and spinal pain was moderated by the CTC allele in women. No such gene-environment interaction was observed in men. Moreover, women with CTC appeared to be less resilient than men with the same haplotype when exposed to abusive supervision. Hence, the present data emphasize that individual differences may be important in understanding how interpersonal relations between leaders and employees affect physical health. Additionally, our results may...
assist in further understanding of the gender dependent responses to social stressors in the workplace. Still, as abusive supervision was associated with higher levels of spinal pain in both genders, the present data show that organizations will benefit from preventive measures that can prevent the occurrence of this kind of leadership. We conclude that both sex and the CRHR1 haplotype moderates spinal pain in response to abusive supervision.

Acknowledgment
We thank Tiril Schjølberg for the haplotyping and Mina Eriksen for technical support in the lab.

Author Contributions
ACS, AR, JOC, MBN and JG designed the research and analysed the data. ACS and JG wrote the manuscript with comments from AR, JOC and MBN.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Norwegian foundation: Et liv i bevegelse (ELIB).

ORCID iD
Ann-Christin Sannes https://orcid.org/0000-0002-3918-8149

Supplemental Material
Supplemental material for this article is available online.

References
1. Ihlebaek C, Brage S, Natvig B, Bruusgaard D. [Occurrence of musculoskeletal disorders in Norway]. Tidsskr nor Laegeforen 2010; 130: 2365–2368.
2. Kinge JM, Knudsen AK, Skirbekk V, Volset SE. Musculoskeletal disorders in Norway: prevalence of chronicity and use of primary and specialist health care services. BMC Musculoskelet Disord 2015; 16: 75–75.
3. Ihlebaek C, Hansson TH, Laerum E, Brage S, Eriksen HR, Holm SH, Svendsrod R, Indahl A. Prevalence of low back pain and sickness absence: a “borderline” study in Norway and Sweden. Scand J Public Health 2006; 34: 555–558.
4. Zubieta JK, Smith YR, Bueller JA, Xu Y, Kilbourn MR, Jewett DM, Meyer CR, Koepp RA, Stohler CS. Regional mu opioid receptor regulation of sensory and affective dimensions of pain. Science 2001; 293: 311–315.
5. Khalid S, Tubbs RS. Neuroanatomy and neuropsychology of pain. Cureus 2017; 9: e1754.
6. Usunoff K, Popratiloff A, Schmitt O, Wree A. Functional neuroanatomy of pain. Adv Anat Embryol Cell Biol 2006; 184: 1–115.
7. Ong WY, Stohler CS, Herr DR. Role of the prefrontal cortex in pain processing. Mol Neurobiol 2019; 56: 1137–1166.
8. Martinko M, Harvey P, Brees J, Mackey J. A review of abusive supervision research. J Org Behav 2013; 34: S120–S137.
9. Tepper B. Consequences of abusive supervision. 2000; 43: 178–190.
10. Huang J, Guo G, Tang D, Liu T, Tan L. An eye for an eye? Third parties’ silence reactions to peer abusive supervision: the mediating role of workplace anxiety, and the moderating role of core self-evaluation. Int J Environ Res Public Health 2019; 16: 5027.
11. Tepper B, Duffy M, Hoobler J, Enslie M. Moderators of the relationships between coworkers’ organizational citizenship behavior and fellow employees’ attitudes. J Appl Psychol 2004; 89: 455–465.
12. Peltokorpi V, Ramaswami A. Abusive supervision and subordinates’ physical and mental health: the effects of job satisfaction and power distance orientation. Int J Human Resour Manag 2021; 32: 893–919.
13. Smith SM, Vale WW. The role of the hypothalamic-pituitary-adrenal axis in neuroendocrine responses to stress. Dialogues Clin Neurosci 2006; 8: 383–395.
14. Lowrance SA, Ionadi A, McKay E, Douglas X, Johnson JD. Sympathetic nervous system contributes to enhanced corticosterone levels following chronic stress. Psychoneuroendocrinology 2016; 68: 163–170.
15. Lenijes EGWM, Griep EN, Boersma JW, Romijn FPTHM, de Kloer ER. Glucocorticoid receptors, fibromyalgia and low back pain. Psychoneuroendocrinology 1997; 22: 603–614.
16. Rijsdijk M, van Wijck AJM, Kalkman CJ, Yaksh TL. The effects of glucocorticoids on neuropathic pain: a review with emphasis on intrathecal methylprednisolone acetate delivery. Anesth Analg 2014; 118: 1097–1112.
17. Kranzler HR, Feinn R, Nelson EC, Covault J, Anton RF, Farrer L, Gelernter J. A CRHR1 haplotype moderates the effect of adverse childhood experiences on lifetime risk of major depressive episode in African-American women. Am J Med Genet B Neuropsychiatr Genet 2011; 156: 960–968.
18. Evans AN, Liu Y, Macgregor R, Huang V, Aguiler A. Regulation of hypothalamic corticotropin-releasing hormone transcription by elevated glucocorticoids. Mol Endocrinol 2013; 27: 1796–1807.
19. Sjöstedt E, Zhong W, Fagerberg L, Karlsson M, Mitsios N, Adori C, Oksvold P, Edfors F, Limiszewska A, Hikmet F, Huang J, Du Y, Lin L, Dong Z, Yang L, Liu X, Jiang H, Xu X, Wang J, Yang H, Bolund L, Mardinoglu A, Zhang C, von Feilitzen K, Lindskog C, Pontén F, Luo Y, Hökfelt T, Uhlén M,Mulder J. An atlas of the protein-coding genes in the human, pig, and mouse brain. Science 2020; 367: eay5947.
20. Liu Z, Zhu F, Wang G, Xiao Z, Tang J, Liu W, Wang H, Liu H, Wang X, Wu Y, Cao Z, Li W. Association study of corticotropin-releasing hormone receptor1 gene
polymorphisms and antidepressant response in major depressive disorders. *Neurosci Lett* 2007; 414: 155–158.
21. Licinio J, O’Kirwan F, Irizarry K, Merriman B, Thakur S, Jepson R, Lake S, Tantisira KG, Weiss ST, Wong ML. Association of a corticotropin-releasing hormone receptor 1 haplotype and antidepressant treatment response in Mexican-Americans. *Mol Psychiatry* 2004; 9: 1075–1082.
22. Engineer N, Darwin L, Nishigandh D, Ngianga-Bakwin K, Smith SC, Grammatopoulos DK. Association of glucocorticoid and type 1 corticotropin-releasing hormone receptors gene variants and risk for depression during pregnancy and post-partum. *J Psychiatr Res* 2013; 47: 1166–1173.
23. Liu Z, Liu W, Yao L, Yang C, Xiao L, Wan Q, Gao K, Wang H, Zhu F, Wang G, Xiao Z. Negative life events and corticotropin-releasing-hormone receptor1 gene in recurrent major depressive disorder. *Sci Rep* 2013; 3: 1548.
24. Olsen MB, Jacobsen LM, Schistad EI, Pedersen LM, Rygh LJ, Røe C, Gjerstad J. Pain intensity the first year after lumbar disc herniation is associated with the A118G polymorphism in the opioid receptor mu 1 gene: evidence of a sex and genotype interaction. *J Neurosci* 2012; 32: 9831–9834.
25. Fillingim RB, Kaplan L, Nishigandh D, Ngianga-Bakwin K, Smith SC, Grammatopoulos DK. Association of glucocorticoid and type 1 corticotropin-releasing hormone receptors gene variants and risk for depression during pregnancy and post-partum. *J Psychiatr Res* 2013; 47: 1166–1173.
26. Liu Z, Liu W, Yao L, Yang C, Xiao L, Wan Q, Gao K, Wang H, Zhu F, Wang G, Xiao Z. Negative life events and corticotropin-releasing-hormone receptor1 gene in recurrent major depressive disorder. *Sci Rep* 2013; 3: 1548.
27. Abdul Hamid R, Juhdi N, Ismail M, Abdullah NA, Hamid A. Abusive supervision and workplace deviance as moderated by spiritual intelligence: an empirical study of Selangor employees. *Malaysian J Soc Space* 2016; 12: 191–202.
28. Tepper B, Simon L, Park HM. Abusive supervision. *Annu Rev Organ Psychol Organ Behav* 2017; 4: 123–152.
29. Rajalingam D, Jacobsen DP, Nielsen MB, Einarsen SV, Gjerstad J. Exposure to workplace bullying, distress, and insomnia: the moderating role of the miR-146a genotype. *Front Psychol* 2019; 10: 1204–1206
30. Christensen JO, Nielsen MB, Sannes AC, Gjerstad J. Leadership style, headache, and neck pain: the moderating role of the Catechol-O-Methyltransferase (COMT) genotype. *J Occup Environ Med* 2021; 63: 151–158.
31. Glambek M, Nielsen MB, Gjerstad J, Einarsen S. Gender differences in the relationship between workplace bullying and subjective back and neck pain: a two-wave study in a norwegian probability sample. *J Psychosom Res* 2018; 106: 73–75.
32. McEwen BS, Gianaros PJ. Stress- and allostatics-induced brain plasticity. *Annu Rev Med* 2011; 62: 431–445.
33. Meijer OC, Buurstedt JC, Schaaf MJM. Corticosteroid receptors in the brain: transcriptional mechanisms for specificity and context-dependent effects. *Cell Mol Neurobiol* 2019; 39: 539–549.
34. Ji G, Neugebauer V. Differential effects of CRF1 and CRF2 receptor antagonists on pain-related sensitization of neurons in the central nucleus of the amygdala. *J Neurophysiol* 2007; 97: 3893–3904.
35. Thompson J, Neugebauer V. Amygdala plasticity and pain. *Pain Res Manag* 2017; 2017: 1–12.
36. Ji G, Fu Y, Adwanikar H, Neugebauer V. Non-pain-related CRF1 activation in the amygdala facilitates synaptic transmission and pain responses. *Mol Pain* 2013; 9: 2.
37. Latremoliere A, Woolf CJ. Central sensitization: a generator of pain hypersensitivity by Central neural plasticity. *J Pain* 2009; 10: 395–926.
38. Neugebauer V, Galhardo V, Maione S, Mackey SC. Forebrain pain mechanisms. *Brain Res Rev* 2009; 60: 226–242.
39. Dai YJ, Zhang X, Yang Y, Nan HY, Yu Y, Sun Q, Yan LF, Hu B, Zhang J, Qiu ZY, Gao Y, Cui GB, Chen BL, Wang W. Gender differences in functional connectivities between insular subdivisions and selective pain-related brain structures. *J Headache Pain* 2018; 19: 24.
40. Kong J, Loggia ML, Zyloney C, Tu P, Laviolette P, Gollub RL. Exploring the brain in pain: activations, deactivations and their relation. *Pain* 2010; 148: 257–267.
41. Moulton EA, Keaser ML, Gullapalli RP, Maitra R, Greenspan JD. Sex differences in the cerebral BOLD signal response to painful heat stimuli. *Am J Physiol Regul Integr Comp Physiol* 2006; 291: R257–R267.
42. Straube T, Schmidt S, Weiss T, Mentzel HJ, Miltner WH. Sex differences in brain activation to anticipated and experienced pain in the medial prefrontal cortex. *Hum Brain Mapp* 2009; 30: 689–698.
43. Sannes A-C, Christensen JO, Nielsen MB, Gjerstad J. The association between abusive supervision and anxiety in female employees is stronger in carriers of the CRHR1 TAT haplotype. *Curr Res Behav Sci* 2021; 2: 100021.
44. Rasmussen CDN, Holtermann A, Jørgensen MB. Recall bias in low back pain among workers: effects of recall period and individual and Work-Related factors. *Spine (Phila Pa 1976)* 2018; 43: E727–E733.
45. Aasland M, Skogstad A, Notelaers G, Nielsen M, Einarsen S. The prevalence of destructive leadership behaviour. *Br J Manag* 2010; 21: 438–452.
46. Podsakoff P, MacKenzie S, Lee J-Y, Podsakoff N. Common method biases in behavioral research: a critical review of the literature and recommended remedies. *J Appl Psychol* 2003; 88: 879–903.
47. Stedman RC, Connelly NA, Heberlein TA, Decker DJ, Allred SB. The end of the (research) world as we know it? Understanding and coping with declining response rates to mail surveys. *Soc Natural Resour* 2019; 32: 1139–1154.
48. Schalm RL, Kelloway EK. The relationship between response rate and effect size in occupational health psychology research. *J Occup Health Psychol* 2001; 6: 160–163.