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1. CONSORT checklist

Table S1: CONSORT 2010 checklist.

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	N/A
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Page 130
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	Page 131
	2b	Specific objectives or hypotheses	Pages 131 & 132
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Page 132
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Page 133
Participants	4a	Eligibility criteria for participants	Page 133
	4b	Settings and locations where the data were collected	Page 132
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Pages 132 – 135
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Pages 134 & 135
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	Page 136
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	N/A
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	N/A

Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	N/A
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	N/A
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	N/A
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	Pages 136
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	Pages 136 – 138

Results

Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Page 138
	13b	For each group, losses and exclusions after randomisation, together with reasons	Page 138
Recruitment	14a	Dates defining the periods of recruitment and follow-up	N/A
	14b	Why the trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Page 138 & 139
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Page 138 & 139
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Pages 139 – 151
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Page 152
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A

Discussion

Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Page 154

Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Pages 153 & 154
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Pages 153 & 154
Other information			
Registration	23	Registration number and name of trial registry	N/A
Protocol	24	Where the full trial protocol can be accessed, if available	N/A
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Page 155

2. Plots of model assumptions

a. Outcome: surface area of secondary hyperalgesia

Figure S1: Plots of model assumptions for the conventional mixed-effects linear regression investigating the relationship between Childhood Trauma Questionnaire-Short Form (CTQ-SF) and surface area of secondary hyperalgesia.

b. Outcome: magnitude of secondary hyperalgesia

Figure S2: Plots of model assumptions for the conventional mixed-effects linear regression investigating the relationship between Childhood Trauma Questionnaire-Short Form (CTQ-SF) and magnitude of secondary hyperalgesia.

c. <u>Outcome: temporal summation</u>

Figure S3: Plots of model assumptions for the conventional linear regression investigating the relationship between Childhood Trauma Questionnaire-Short Form (CTQ-SF) and temporal summation at the lumbar site.
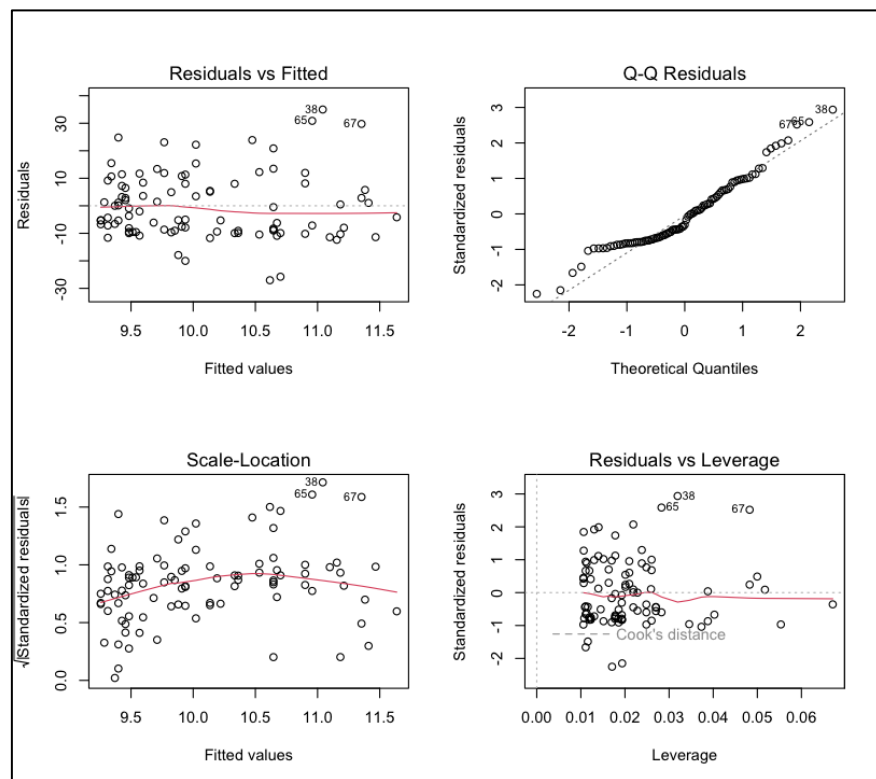
Figure S4: Plots of model assumptions for the conventional linear regression investigating the relationship between Childhood Trauma Questionnaire-Short Form (CTQ-SF) and temporal summation at the deltoid site.

d. Outcome: conditioned pain modulation
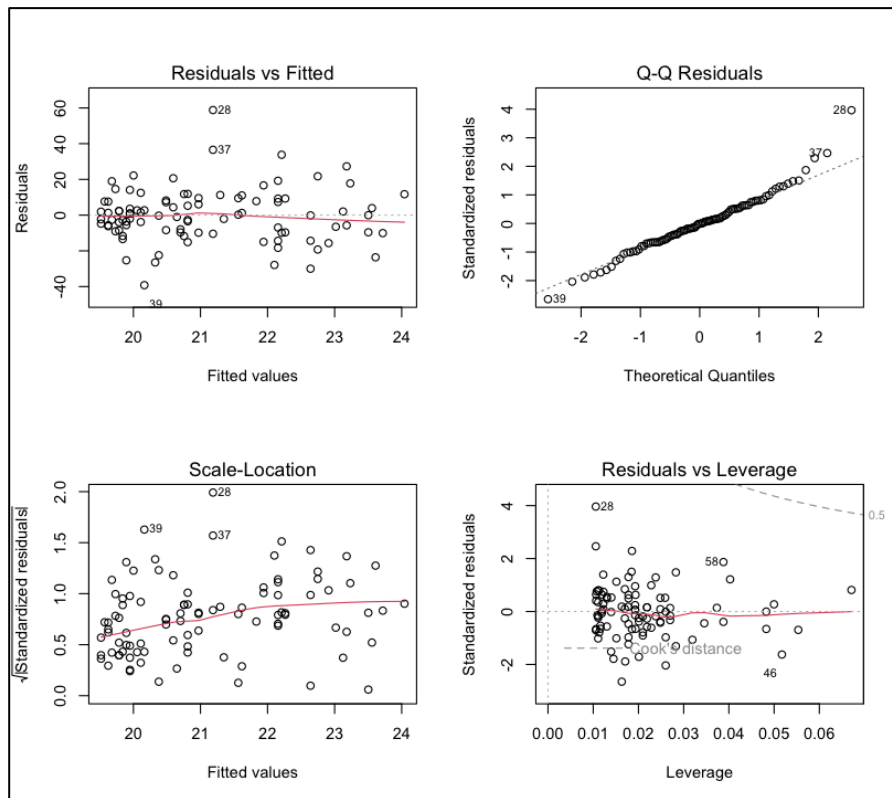
Figure S5: Plots of model assumptions for the conventional linear regression investigating the relationship between Childhood Trauma Questionnaire-Short Form (CTQ-SF) and conditioned pain modulation at the lumbar site.
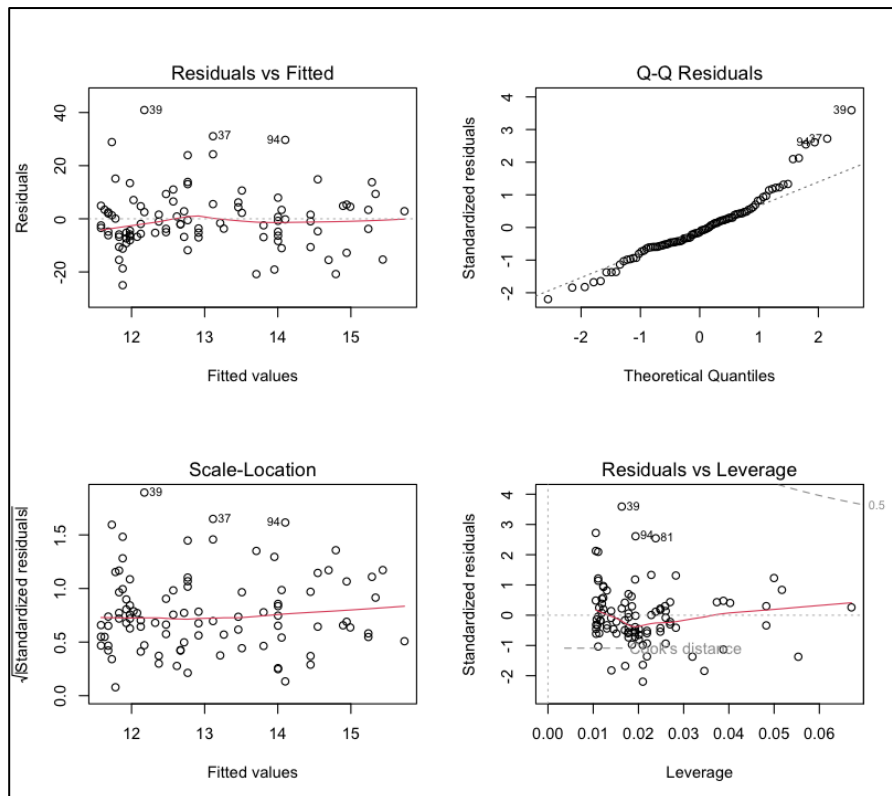
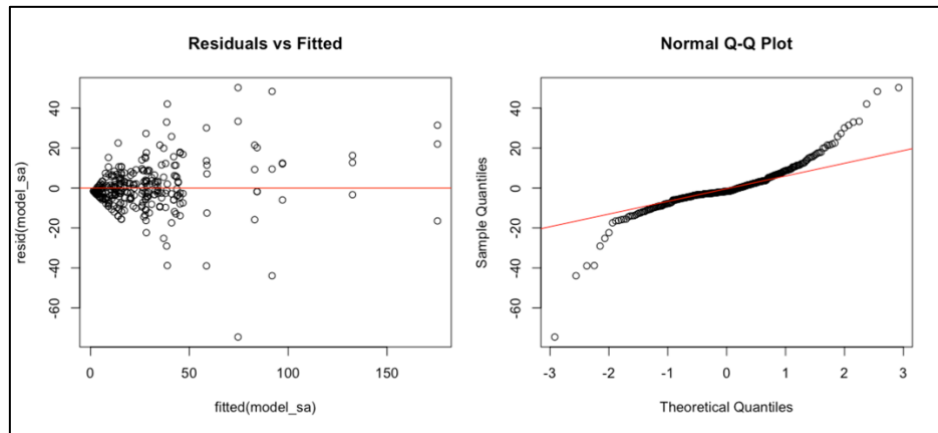*Figure S6: Plots of model assumptions for the conventional linear regression investigating the relationship between Childhood Trauma Questionnaire-Short Form (CTQ-SF) and conditioned pain modulation at the deltoid site.*

3. Exploratory analyses

3.1   Predictor: Perceived stress scale

a.   Outcome: surface area of secondary hyperalgesia

The unadjusted model found no evidence of an association between the PSS and the surface area of SH (β= 0.06 [95%CI: -0.51; 0.63], p = 0.83). When sex was included as an interaction term, both the unadjusted (β= 0.33 [95%CI: -0.70; 1.36], p = 0.53) and the covariate-adjusted models (β= 0.15 [95%CI: -0.94; 1.25], p = 0.78) found no evidence of an association between PSS and the surface area of SH, and no evidence of an effect of sex, nor an interaction between PSS and sex (Fig S8 and Table S2).

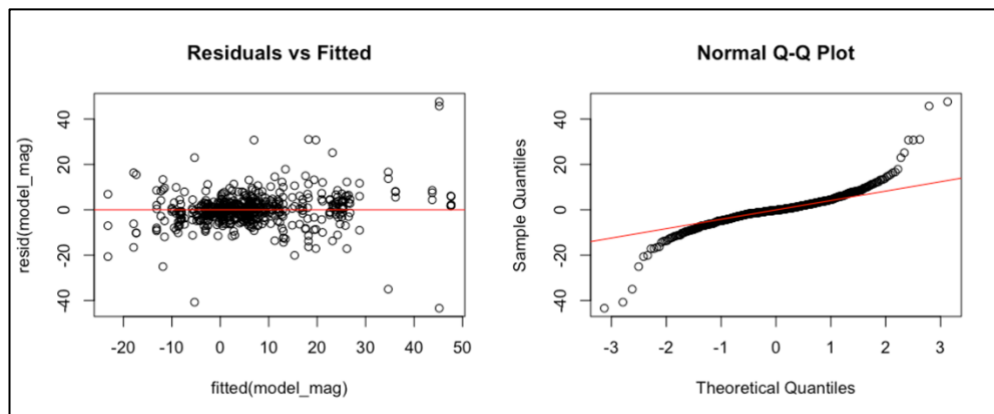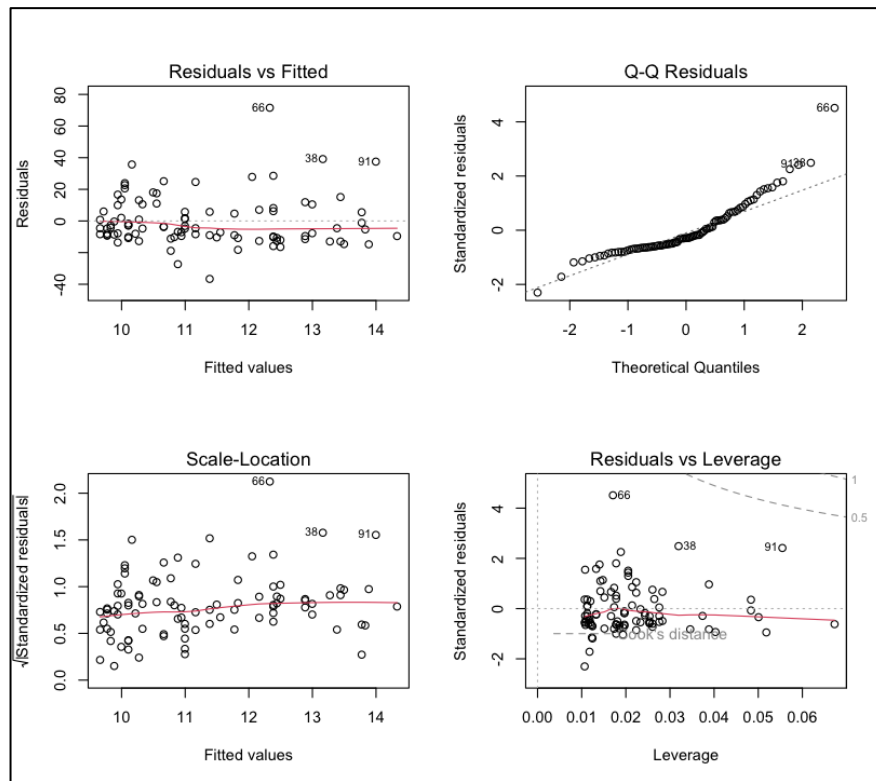*Figure S7: Plots of model assumptions for the conventional mixed-effects linear regression investigating the relationship between the Perceived Stress Scale (PSS) and the surface area of secondary hyperalgesia.*

Figure S8: Plot of the association between the Perceived Stress Scale (PSS) and the surface area of secondary hyperalgesia. Plots show the observed values (dots) and the predicted regression line and 95% confidence interval (ribbon) for the covariate-adjusted model for the full cohort (plot a) and with sex as an interaction term (plot b).

Table S2: Summary of the relationship between recent stress (Perceived stress Scale: PSS) and surface area of induced secondary hyperalgesia.

Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	*p*	Estimates	95% CI	*p*	Estimates	95% CI	*p*
Intercept	20.59	10.09; 31.09	**<0.001**	17.43	-0.11; 34.97	0.05	14.90	-13.72; 43.52	0.31
PSS score	0.06	-0.51; 0.63	0.83	0.33	-0.70; 1.36	0.53	0.15	-0.94; 1.25	0.78
Sex (female)				4.59	-17.51; 26.70	0.68	-2.31	-25.39; 20.78	0.84
PSS score x sex (female)				-0.38	-1.63; 0.87	0.55	-0.11	-1.38; 1.16	0.87
Age							0.52	0.05; 1.00	**0.03**
Mean SPARS rating of HFS induction							-0.08	-0.45; 0.29	0.65
HFS current intensity							-40.78	-90.24; 8.68	0.11
CTQ-SF total score							0.16	-0.03; 0.35	0.10
PSQI score							-0.23	-1.51; 1.06	0.73
Diagnosis of major depressive disorder							0.67	-15.18; 16.52	0.93
Recent COVID-19 infection							6.99	-10.24; 24.33	0.43
Recent acute illness							-5.43	-14.70; 3.84	0.35
Diagnosis of chronic illness							-8.19	-22.20; 5.82	0.25
Random effects									
σ^2			81.80			81.50			80.64
τ_{00}			338.66$_{study\ id}$			343.43$_{study\ id}$			333.08$_{study\ id}$
ICC			0.81			0.81			0.81
N			95$_{study\ id}$			95$_{study\ id}$			95$_{study\ id}$
Observations			285			285			285
Marginal R^2 / Conditional R^2			0.000/0.806			0.005/0.809			0.132/0.831

PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; HFS = high-frequency electrical stimulation; PSQI = Pittsburgh Sleep Quality Index.

b. Outcome: magnitude of secondary hyperalgesia

The unadjusted model found no evidence of an association between PSS and the magnitude of SH (β= 0.05 [95%CI: -0.25; 0.35], p = 0.45). When sex was included as an interaction term, both the unadjusted (β= -0.02 [95%CI: -0.57; 0.54], p = 0.95) and the covariate-adjusted models (β= 0.30 [95%CI: -0.28; 0.88], p = 0.32) found no evidence of an association between PSS and the magnitude of SH, and no evidence of an effect of sex, nor an interaction between PSS and sex (Fig S10 and Table S3).
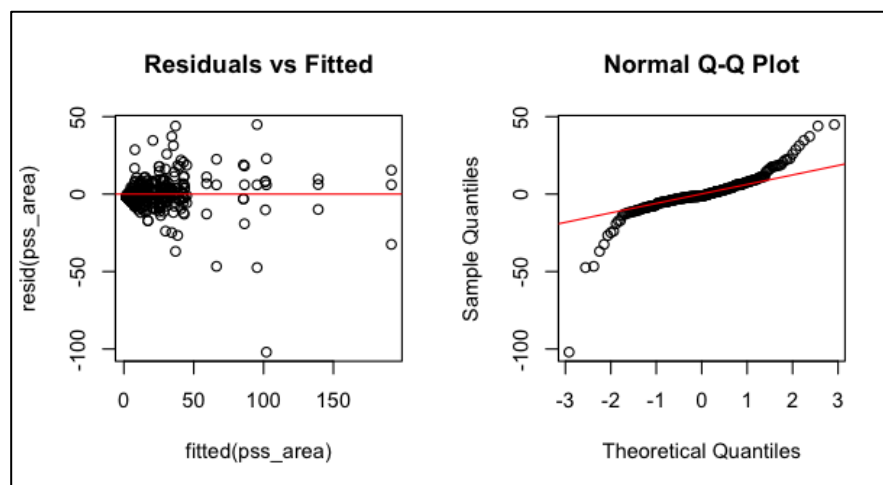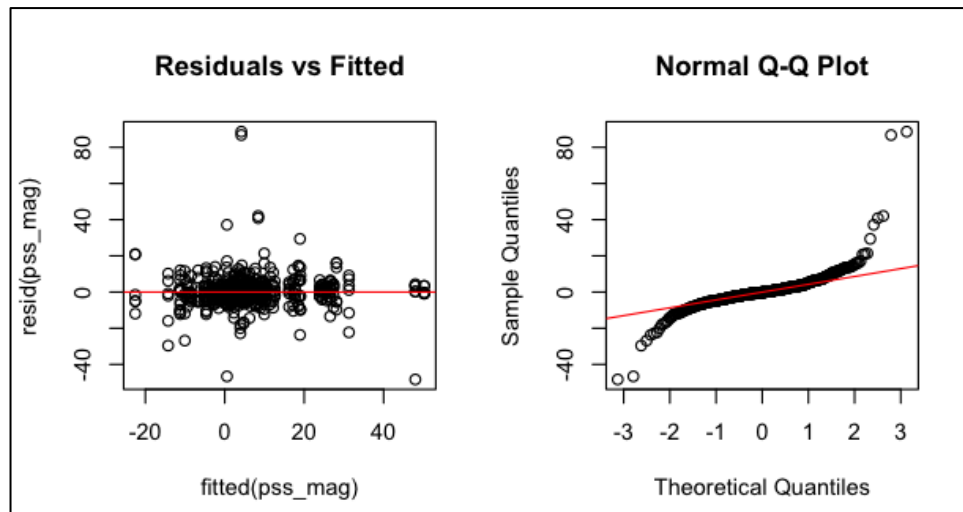

Figure S9: Plots of model assumptions for the conventional mixed-effects linear regression investigating the relationship between the Perceived Stress Scale (PSS) and the magnitude of secondary hyperalgesia.
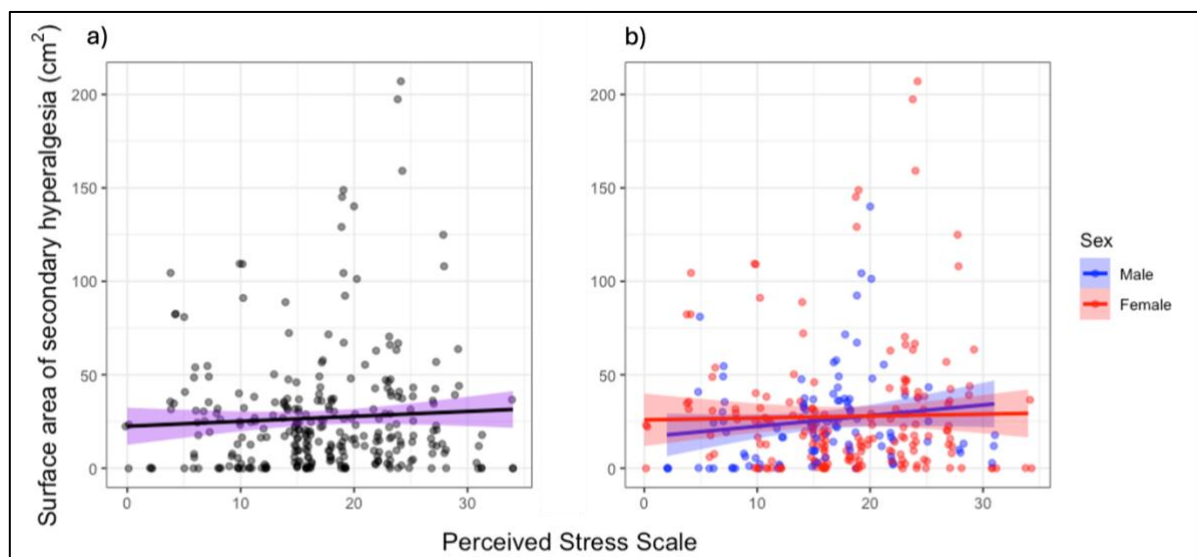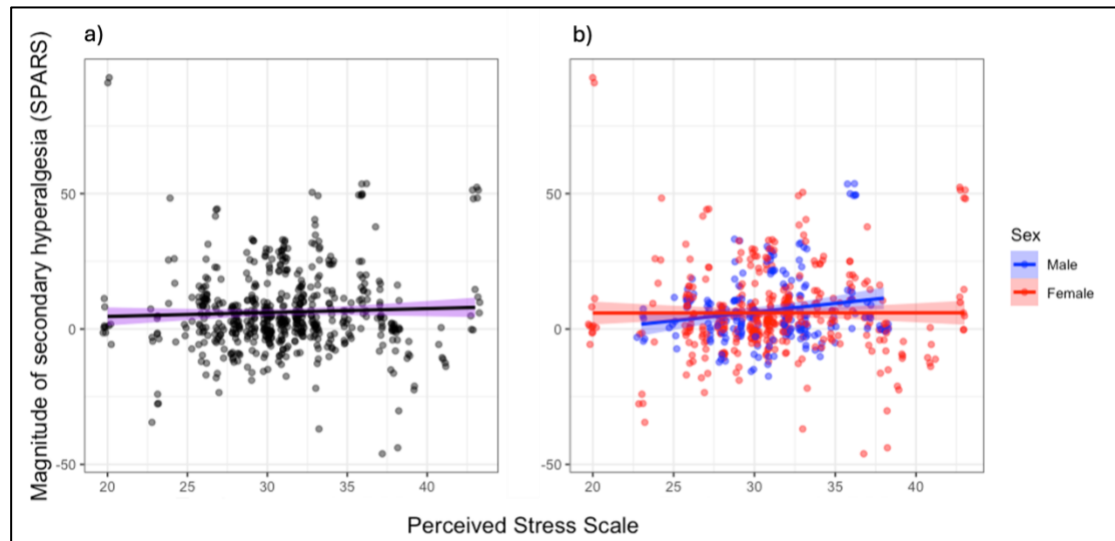

Figure S10: Plot of the association between the Perceived Stress Scale (PSS) and the magnitude of secondary hyperalgesia. Plots show the observed values (dots) and the predicted regression line and 95% confidence interval (ribbon) for the covariate-adjusted model for the full cohort (plot a) and with sex as an interaction term (plot b). Y axes have been truncated but range from -100 to +100.

Table S3: Summary of the relationship between recent stress (Perceived stress Scale: PSS) and magnitude of induced secondary hyperalgesia.

| Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	*p*	Estimates	95% CI	*p*	Estimates	95% CI	*p*
Intercept	3.86	-1.66; 9.39	0.17	5.40	-3.98; 14.78	0.26	5.74	-9.48; 20.95	0.46
PSS score	0.05	-0.25; 0.35	0.45	-0.02	-0.57; 0.54	0.95	0.30	-0.28; 0.88	0.32
Sex (female)				-2.47	-14.28; 9.35	0.68	-5.26	-17.53; 7.01	0.40
PSS score x sex (female)				0.10	-0.56; 0.77	0.76	0.26	-0.42; 0.93	0.45
Age							0.12	-0.13; 0.37	0.35
Mean SPARS rating of HFS induction							-0.17	-0.37; 0.03	0.09
HFS current intensity							17.91	-8.38; 44.20	0.18
CTQ-SF total score							-0.03	-0.13; 0.07	0.61
PSQI score							-0.43	-1.11; 0.26	0.22
Diagnosis of major depressive disorder							5.14	-3.28; 13.57	0.23
Recent COVID-19 infection							4.61	-4.55; 13.77	0.32
Recent acute illness							-5.45	-10.38; -0.53	**0.03**
Diagnosis of chronic illness							4.76	-2.68; 12.21	0.21
Random effects									
σ^2	30.38			30.37			30.45		
τ_{00}	$0.00_{modality:study\_id}$			$0.00_{modality:study\_id}$			$0.00_{modality:study\_id}$		
	96.79_{study_id}			101.34_{study_id}			97.10_{study_id}		
N	$2_{modality}$			$2_{modality}$			$2_{modality}$		
	95_{study_id}			95_{study_id}			95_{study_id}		
Observations	570			570			570		
Marginal R^2 / Conditional R^2	0.004/NA			0.011/NA			0.464/NA		

PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; HFS = high-frequency electrical stimulation; PSQI = Pittsburgh Sleep Quality Index.

c. Outcome: temporal summation

The unadjusted model satisfied the underlying assumptions of linear regression (Figs S11 and S12) and found no evidence of an association between the PSS and TS at either the lumbar (β=0.23 [95%CI: -0.65; 1.11], p = 0.60) or the deltoid site (β=0.19 [95%CI: -0.29; 0.88], p = 0.59). When sex was included as an interaction term, both the unadjusted and the covariate-adjusted models found no evidence of an association between PSS and TS at either the lumber or the deltoid site, and there was no evidence of an effect of sex, or an effect of the interaction between PSS and sex (Fig S13 and Tables S4 and S5).
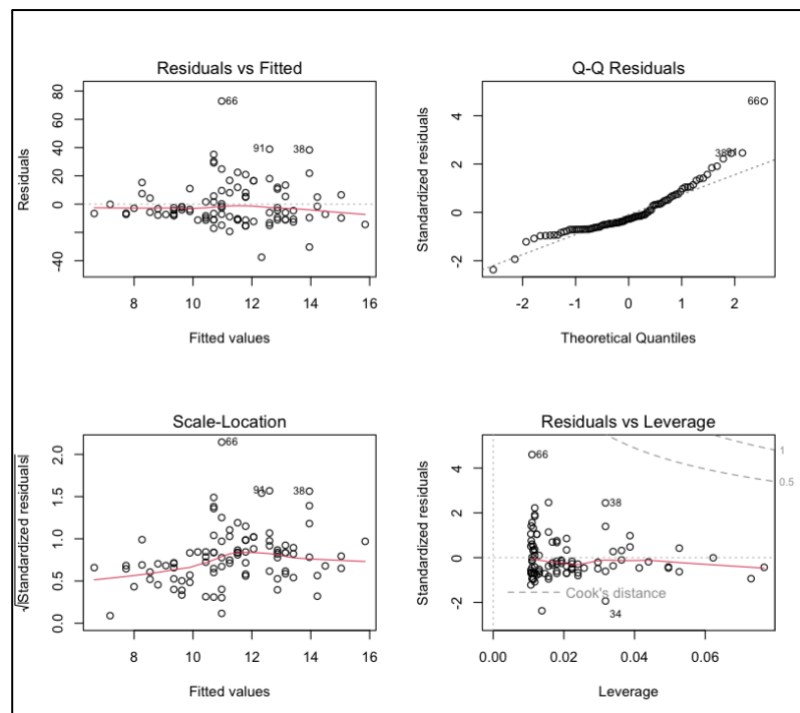

Figure S11: Plots of model assumptions for the conventional linear regression investigating the relationship between Perceived Stress Scale (PSS) and temporal summation at the lumbar site.
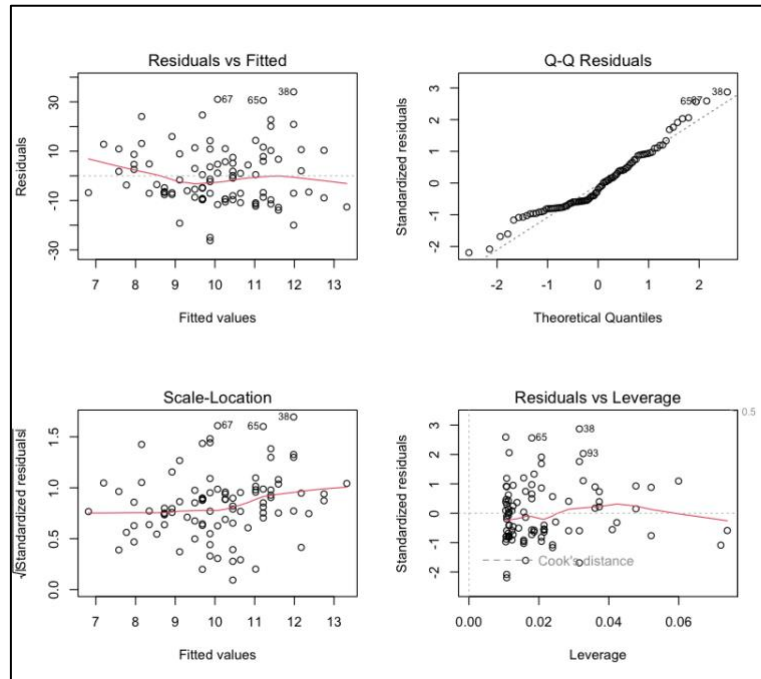
Figure S12: Plots of model assumptions for the conventional linear regression investigating the relationship between Perceived Stress Scale (PSS) and temporal summation at the deltoid site

Figure S13: Plot of the association between the Perceived Stress Scale (PSS) and temporal summation. Plots show the observed values (dots) and the predicted regression line and 95% confidence interval (ribbon) for the covariate-adjusted model for the full cohort (plots a and b) and with sex as an interaction term (plots c and d). Y axes have been truncated but range from -100 to +100.

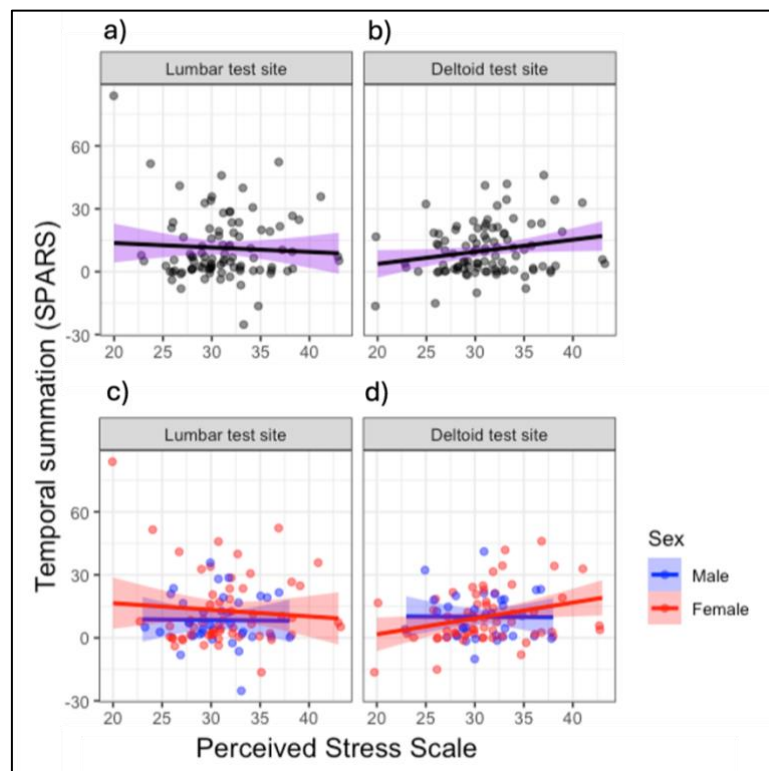*Table S4: Summary of the relationship between recent stress (Perceived stress Scale: PSS) and temporal summation at the lumbar test site. * Temporal summation data at the lumbar site were missing for one participant due to a technical error with saving the data.*

Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	p	Estimates	95% CI	p	Estimates	95% CI	p
Intercept	6.65	-2.12; 15.41	0.135	7.93	-6.39; 22.26	0.27	21.94	3.15; 40.73	**0.02**
PSS score	0.27	-0.20; 0.74	0.257	0.03	-0.81; 0.88	0.94	0.23	-0.65; 1.11	0.60
Sex (female)				-0.75	-19.01; 17.52	0.94	-1.12	-19.72; 17.47	0.91
PSS score x sex (female)				0.28	-0.74; 1.31	0.59	0.32	-0.71; 1.36	0.54
Age							-0.32	-0.71; 0.08	0.11
CTQ-SF total score							0.02	-0.13; 0.18	0.77
PSQI score							-0.83	-1.87; 0.21	0.12
Diagnosis of major depressive disorder							2.38	-9.67; 16.24	0.62
Recent COVID-19 infection							-0.43	-13.39; 12.53	0.95
Recent acute illness							-7.91	-14.92; -0.90	**0.03**
Diagnosis of chronic illness							4.75	-6.92; 16.43	0.42
Observations*		94			94			94	
R² / R² adjusted		0.014/0.003			0.031/-0.002			0.125/0.020	
PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; PSQI = Pittsburgh Sleep Quality Index.									

Table S5: Summary of the relationship between recent stress (Perceived stress Scale: PSS) and temporal summation at the deltoid test site.

Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	p	Estimates	95% CI	p	Estimates	95% CI	p
Intercept	6.81	0.31; 13.32	**0.04**	8.76	-2.15; 19.67	0.11	16.61	1.96; 31.26	**0.03**
PSS score	0.19	-0.16; 0.54	0.28	0.08	-0.56; 0.72	0.81	0.19	-0.49; 0.88	0.56
Sex (female)				-3.05	-16.79; 10.70	0.66	-3.97	-18.40; 10.45	0.59
PSS score x sex (female)				0.17	-0.61; 0.94	0.67	0.21	-0.60; 1.01	0.61
Age							-0.15	-0.45; 0.15	0.33
CTQ-SF total score							-0.00	-0.12; 0.12	0.97
PSQI score							-0.52	-1.33; 0.29	0.21
Diagnosis of major depressive disorder							5.16	-4.93; 15.26	0.31
Recent COVID-19 infection							-3.08	-13.12; 6.97	0.54
Recent acute illness							-3.35	-8.81; 2.11	0.23
Diagnosis of chronic illness							2.42	-6.33; 11.27	0.59
Observations		95			95			95	
R² / R² adjusted		0.012/0.002			0.015/-0.018			0.068/-0.043	
PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; PSQI = Pittsburgh Sleep Quality Index.									

d. Outcome: conditioned pain modulation

The unadjusted model satisfied the underlying assumptions of linear regression (Figs S14 and S15) and found no evidence of an association between PSS and CPM at either the lumbar (β=0.36 [95%CI: -0.41; 1.14], *p* = 0.53) or the deltoid site (β=-0.38 [95%CI: -0.99; 0.24], *p* = 0.32). When sex was included as an interaction term, both the unadjusted and the covariate-adjusted models found no evidence of an association between PSS and CPM at either the lumbar or the deltoid site, and there was no evidence of an effect of sex, or an effect of the interaction between PSS and sex (Fig S16 and Tables S6 and S7).
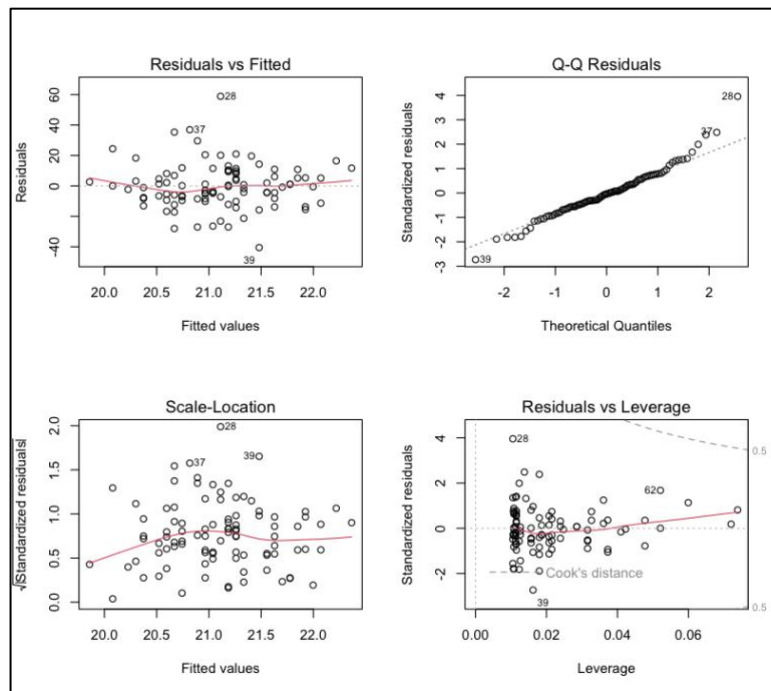
Figure S14: Plots of model assumptions for the conventional linear regression investigating the relationship between Perceived Stress Scale (PSS) and conditioned pain modulation at the lumbar site.

Figure S15: Plots of model assumptions for the conventional linear regression investigating the relationship between Perceived Stress Scale (PSS) and conditioned pain modulation at the deltoid site.

Figure S16: Plot of the association between the Perceived Stress Scale (PSS) and conditioned pain modulation. Plots show the observed values (dots) and the predicted regression line and 95% confidence interval (ribbon) for the covariate-adjusted model for the full cohort (plots a and b) and with sex as an interaction term (plots c and d).

Table S6: Summary of the relationship between recent stress (Perceived stress Scale: PSS) and conditioned pain modulation at the lumbar test site.

Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	*p*	Estimates	95% CI	*p*	Estimates	95% CI	*p*
Intercept	22.37	14.29; 30.44	**<0.001**	17.15	4.22; 30.08	**0.01**	0.74	-15.77; 17.25	0.93
PSS score	-0.07	-0.51; 0.36	0.74	0.56	-0.20; 1.33	0.15	0.36	-0.41; 1.14	0.53
Sex (female)				5.66	-10.63; 21.96	0.49	5.56	10.70; 21.82	0.50
PSS score x sex (female)				-0.81	-1.73; 0.11	0.08	-0.80	1.70; 0.11	0.08
Age							0.29	-0.06; 0.63	0.10
CTQ-SF total score							0.08	-0.05; 0.22	0.24
PSQI score							0.55	-0.36; 1.46	0.23
Diagnosis of major depressive disorder							5.62	-5.77; 17.00	0.33
Recent COVID-19 infection							8.99	-2.33; 20.31	0.12
Recent acute illness							5.78	-0.37; 11.94	0.07
Diagnosis of chronic illness							-8.73	18.71; 1.25	0.09
Observations			95			95			95
R² / R² adjusted		0.001/-0.010			0.092/0.062			0.223/0.130	
PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; PSQI = Pittsburgh Sleep Quality Index.									

Table S7: Summary of the relationship between recent stress (Perceived stress Scale: PSS) and conditioned pain modulation at the deltoid test site.
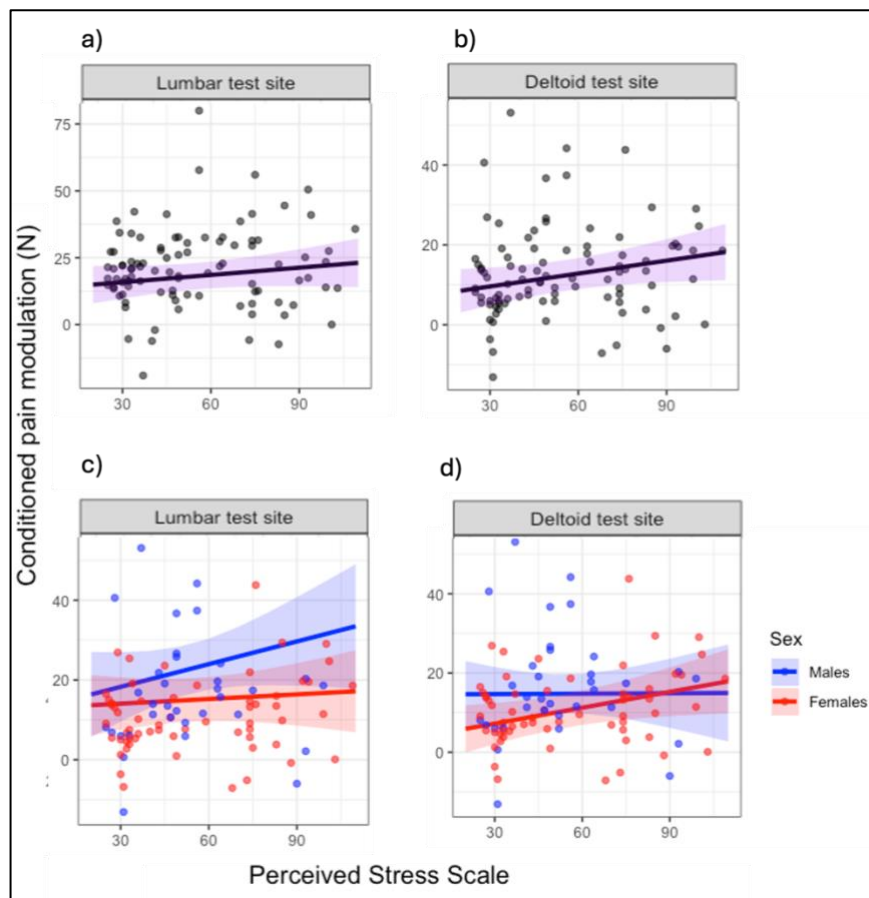
Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	*p*	Estimates	95% CI	*p*	Estimates	95% CI	*p*
Intercept	17.56	11.40; 23.71	**<0.001**	21.42	11.35; 31.50	**<0.001**	16.07	2.85; 29.28	**0.02**
PSS score	-0.26	-0.60; 0.07	0.12	-0.30	-0.90; 0.29	0.31	-0.38	-0.99; 0.24	0.32
Sex (female)				-7.41	-20.10; 5.29	0.25	-7.03	-20.04; 5.99	0.29
PSS score x sex (female)				0.14	-0.58; 0.85	0.70	0.15	-0.57; 0.88	0.68
Age							-0.01	-0.28; 0.27	0.95
CTQ-SF total score							0.10	-0.01; 0.21	0.07
PSQI score							0.00	-0.73; 0.73	1.00
Diagnosis of major depressive disorder							4.54	-4.58; 13.65	0.33
Recent COVID-19 infection							8.17	-0.89; 17.23	0.08
Recent acute illness							0.80	-4.13; 5.73	0.75
Diagnosis of chronic illness							-3.94	-11.93; 4.05	0.33
Observations			95			95			95
R² / R² adjusted		0.026/0.016			0.074/0.043			0.163/0.064	
PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; PSQI = Pittsburgh Sleep Quality Index.									

3.2 Predictor: stressful life events score (composite score of childhood adversity and recent stress)

a. Outcome: surface area of secondary hyperalgesia

The unadjusted model found no evidence of an association between the stressful life events score and the surface area of SH (β= -3.53 [95%CI: -8.34; 1.28], p = 0.15). When sex was included as an interaction term, both the unadjusted (β= -7.90 [95%CI: -16.97; 1.17], p = 0.09) and the covariate-adjusted models (β= -7.46 [95%CI: -16.91; 1.99], p = 0.12) found no evidence of an association between the stressful life events score and the surface area of SH, and no evidence of an effect of sex, nor an interaction between the stressful life events score and sex (Fig S18 and Table S8).
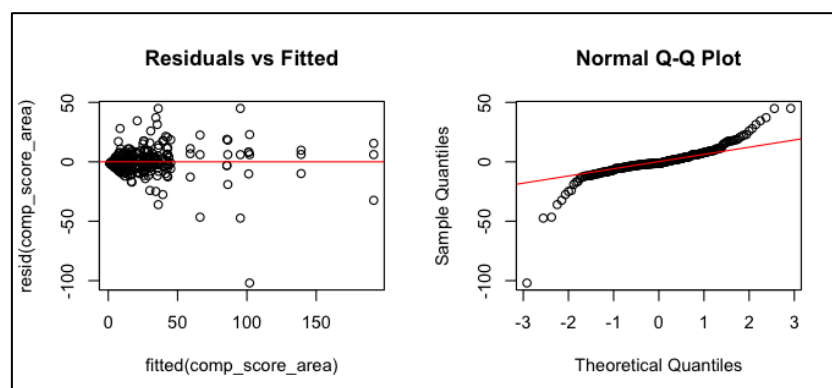

Figure S17: Plots of model assumptions for the conventional mixed-effects linear regression investigating the relationship between the stressful life events score and the surface area of secondary hyperalgesia.
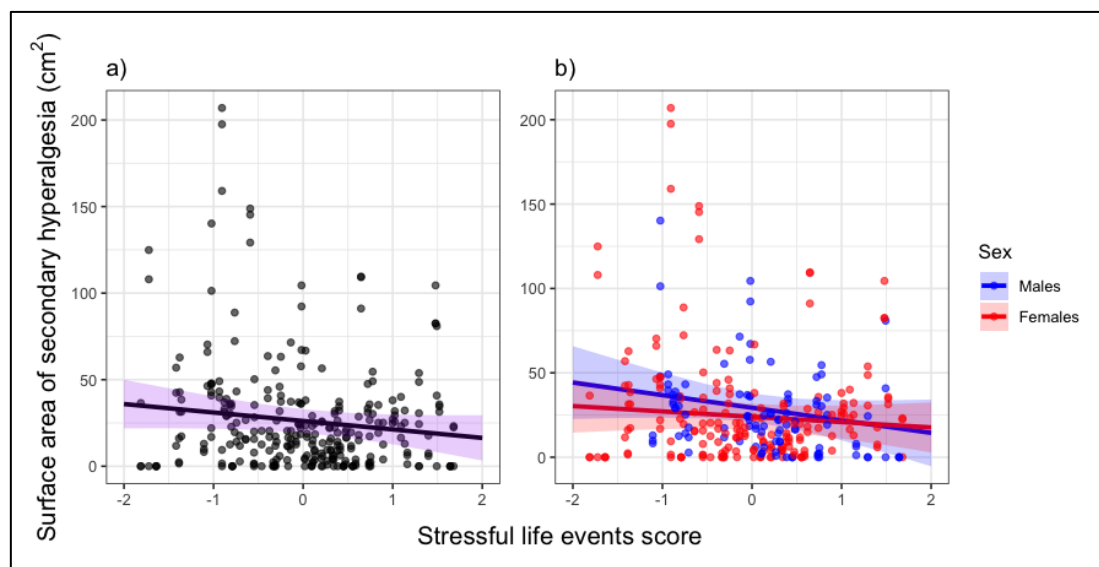

Figure S18: Plot of the association between the stressful life events score and the surface area of secondary hyperalgesia. Plots show the observed values (dots) and the predicted regression line and 95% confidence interval (ribbon) for the covariate-adjusted model for the full cohort (plot a) and with sex as an interaction term (plot b).

Table S8: Summary of the relationship between the stressful life events score and surface area of induced secondary hyperalgesia.

Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	p	Estimates	95% CI	p	Estimates	95% CI	p
Intercept	21.79	17.84; 25.73	**<0.001**	23.89	17.21; 30.58	**<0.001**	27.16	3.48; 50.84	**0.03**
Stressful life events score	-3.53	-8.34; 1.28	0.15	-7.90	-16.97; 1.17	0.09	-7.46	-16.91; 1.99	0.12
Sex (female)				-2.90	-11.19; 5.40	0.49	-5.34	-14.18; 3.49	0.24
Stressful life events score x sex (female)				6.14	-4.57; 16.84	0.26	4.30	-6.35; 14.94	0.43
Age							0.55	0.09; 1.01	**0.02**
Mean SPARS rating of HFS induction							-0.08	-0.44; 0.28	0.65
HFS current intensity							-4.00	-8.81; 0.81	0.10
PSQI score							-0.35	1.51; 0.82	0.56
Diagnosis of major depressive disorder							1.53	-13.80; 16.86	0.84
Recent COVID-19 infection							6.50	-10.34; 23.35	0.45
Recent acute illness							-5.68	-14.63; 3.26	0.21
Diagnosis of chronic illness							-7.78	21.55; 5.98	0.27
Random effects									
σ^2			82.34			81.81			81.02
τ_{00}			335.72 $_{study\ id}$			331.28 $_{study\ id}$			315.34 $_{study\ id}$
ICC			0.80			0.80			0.80
N			95 $_{study\ id}$			95 $_{study\ id}$			95 $_{study\ id}$
Observations			285			285			285
Marginal R^2 / Conditional R^2			0.020/0.807			0.032/0.808			0.133/0.823
PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; HFS = high-frequency electrical stimulation; PSQI = Pittsburgh Sleep Quality Index.									

b. Outcome: magnitude of secondary hyperalgesia

The unadjusted model found no evidence of an association between the stressful life events score and the magnitude of SH (β= -0.44 [95%CI: -2.98; 2.10], $p$ = 0.73). When sex was included as an interaction term, both the unadjusted (β= 1.35 [95%CI: -3.56; 6.27], p = 0.59) and the covariate-adjusted models (β= -0.40 [95%CI: -5.58; 4.78], p = 0.88) found no evidence of an association between the stressful life events score and the magnitude of SH, and no evidence of an effect of sex, nor an interaction between the stressful life events score and sex (Fig S20 and Table S9).
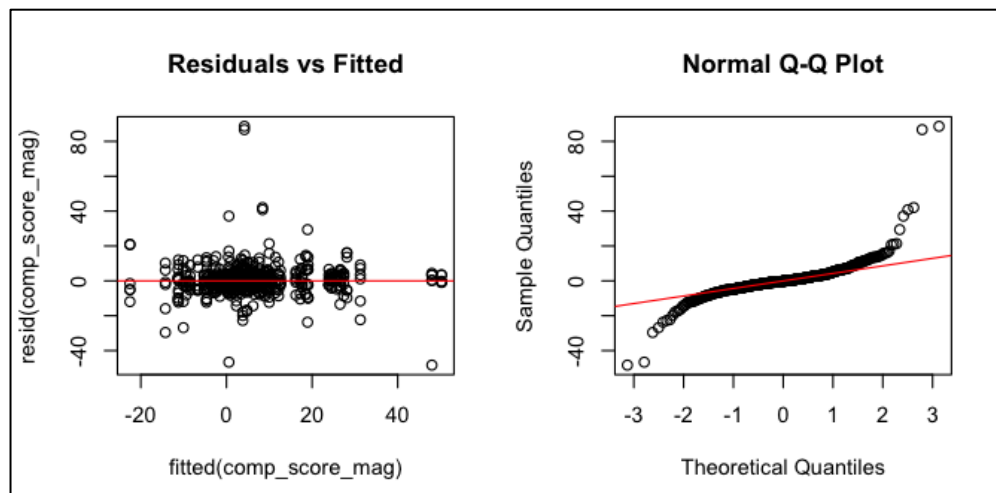
Figure S19: Plots of model assumptions for the conventional mixed-effects linear regression investigating the relationship between the stressful life events score and the magnitude of secondary hyperalgesia.
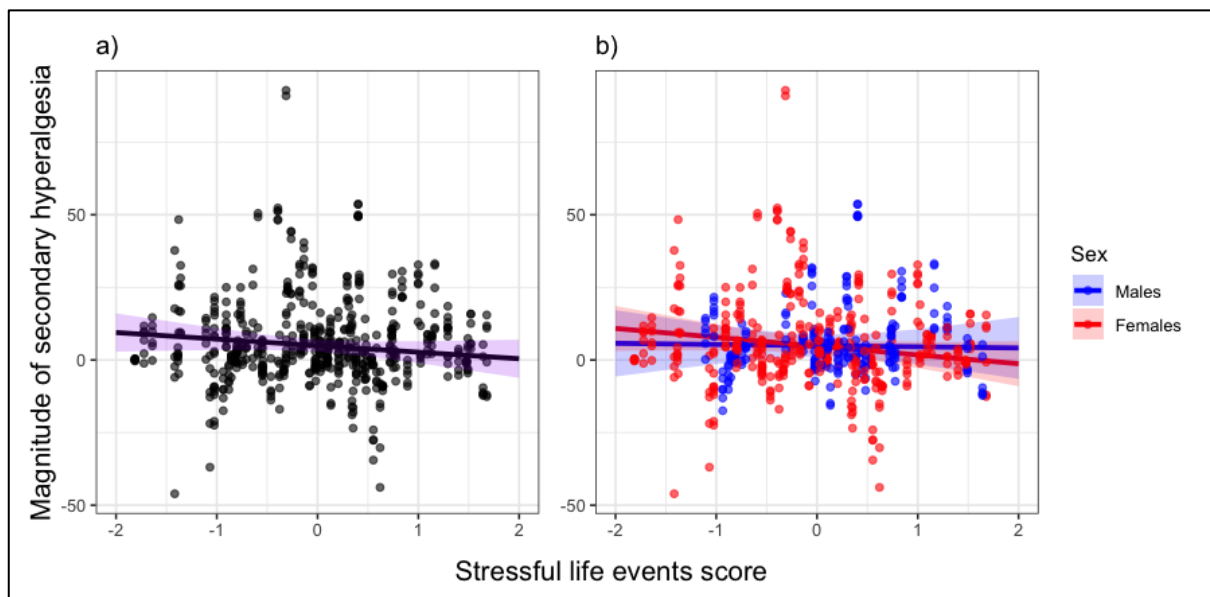
Figure S20: Plot of the association between the stressful life events score and the magnitude of secondary hyperalgesia. Plots show the observed values (dots) and the predicted regression line and 95% confidence interval (ribbon) for the covariate-adjusted model for the full cohort (plot a) and with sex as an interaction term (plot b). Y axes have been truncated but range from -100 to +100.

Table S9: Summary of the relationship between the stressful life events score and magnitude of induced secondary hyperalgesia.

Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	*p*	Estimates	95% CI	*p*	Estimates	95% CI	*p*
Intercept	4.71	2.62; 6.79	**<0.001**	4.97	1.35; 8.59	**0.007**	8.02	-4.96; 21.00	0.23
Stressful life events score	-0.44	-2.98; 2.10	0.73	1.35	-3.56; 6.37	0.59	-0.40	-5.58; 4.78	0.88
Sex (female)				-0.56	-5.05; 3.93	0.81	-0.15	-5.00; 4.69	0.95
Stressful life events score x sex (female)				-2.57	-8.37; 3.23	0.38	-2.64	-8.48; 3.20	0.37
Age							0.06	-0.19; 0.31	0.63
Mean SPARS rating of HFS induction							-0.16	-0.36; 0.03	0.11
HFS current intensity							1.93	-0.71; 4.56	0.15
PSQI score							-0.31	-0.85; 0.43	0.51
Diagnosis of major depressive disorder							4.02	-4.28; 12.42	0.35
Recent COVID-19 infection							5.20	-4.03; 14.44	0.27
Recent acute illness							-4.62	-9.53; 0.28	0.07
Diagnosis of chronic illness							3.44	-4.10; 10.99	0.37
Random effects									
σ^2	30.38			30.42			30.45		
τ_{00}	$0.00_{modality:study\_id}$			$0.00_{modality:study\_id}$			$0.00_{modality:study\_id}$		
	96.73_{study_id}			100.63_{study_id}			98.26_{study_id}		
N	$2_{modality}$			$2_{modality}$			$2_{modality}$		
	95_{study_id}			95_{study_id}			95_{study_id}		
Observations	570			570			570		
Marginal R^2 / Conditional R^2	0.004/NA			0.036/NA			0.407/NA		

PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; HFS = high-frequency electrical stimulation; PSQI = Pittsburgh Sleep Quality Index.

c. Outcome: temporal summation

The unadjusted model satisfied the underlying assumptions of linear regression (Figs S21 and S22) and found no evidence of an association between the stressful life events scale and TS at either the lumbar (β=-2.12 [95%CI: -9.93; 5.69], *p* = 0.59) or the deltoid site (β=-2.11 [95%CI: -8.21; 3.99], *p* = 0.49). When sex was included as an interaction term, both the unadjusted and the covariate-adjusted models found no evidence of an association between PSS and TS at either the lumber or the deltoid site, and there was no evidence of an effect of sex, or an effect of the interaction between PSS and sex (Fig S23 and Tables S10 and S11).
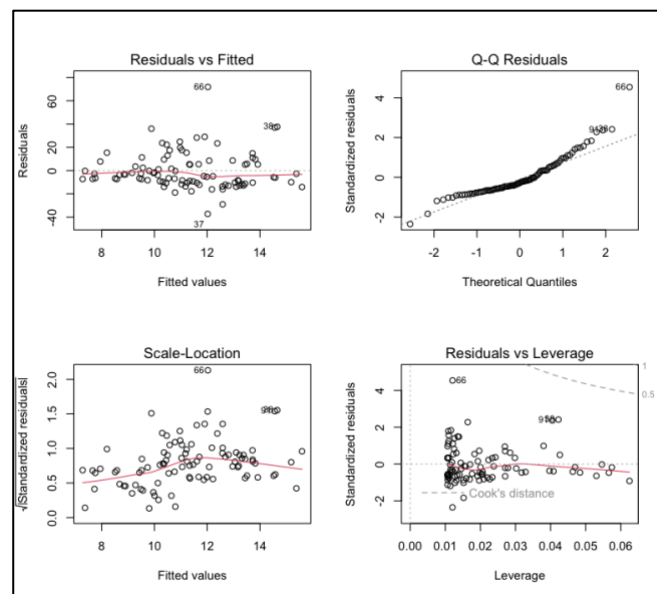
Figure S21: Plots of model assumptions for the conventional linear regression investigating the relationship between the stressful life events score and temporal summation at the lumbar site.
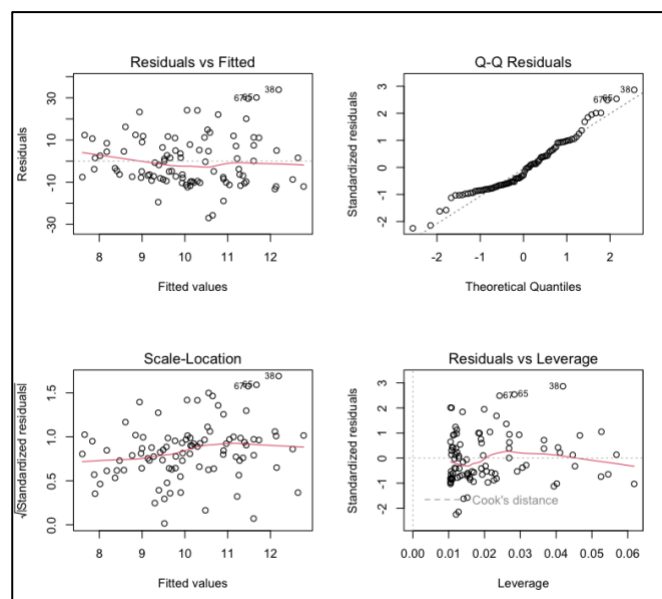
Figure S22: Plots of model assumptions for the conventional linear regression investigating the relationship between the stressful life events score and temporal summation at the deltoid site
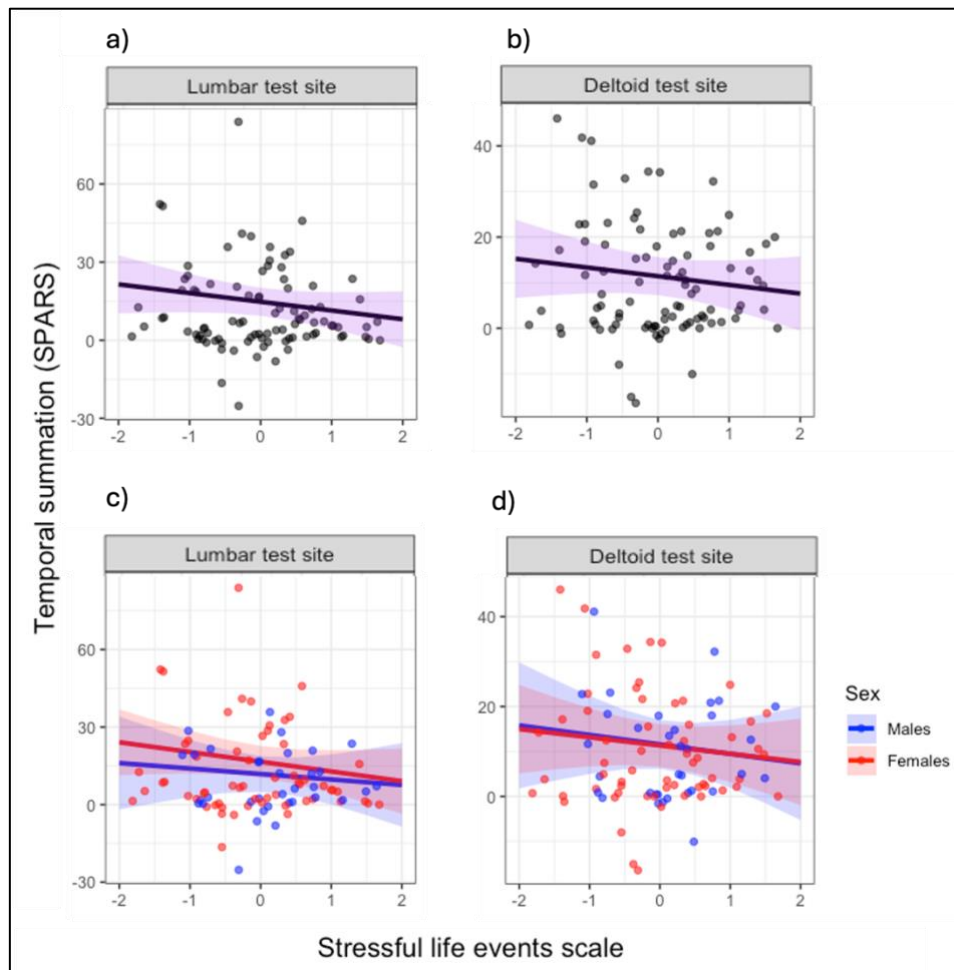
Figure S23: Plot of the association between the stressful life events score and temporal summation. Plots show the observed values (dots) and the predicted regression line and 95% confidence interval (ribbon) for the covariate-adjusted model for the full cohort (plots a and b) and with sex as an interaction term (plots c and d). Y axes have been truncated but range from -100 to +100.

Table S10: Summary of the relationship between the stressful life events score and temporal summation at the lumbar test site. * Temporal summation data at the lumbar site were missing for one participant due to a technical error with saving the data.

Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	p	Estimates	95% CI	p	Estimates	95% CI	p
Intercept	11.28	8.02; 14.54	**<0.001**	8.49	2.95; 14.03	**0.003**	26.13	11.30; 40.97	**0.001**
Stressful life events score	-2.38	-6.39; 1.62	0.24	-0.08	-7.60; 7.45	0.98	-2.12	-9.93; 5.69	0.59
Sex (female)				4.14	-2.77; 11.04	0.24	4.75	-2.41; 11.90	0.19
Stressful life events score x sex (female)				-2.77	11.71; 6.16	0.54	-1.64	-10.67; 7.39	0.72
Age							-0.35	-0.74; 0.04	0.08
PSQI score							-0.64	-1.60; 0.32	0.19
Diagnosis of major depressive disorder							2.39	-10.44; 15.21	0.71
Recent COVID-19 infection							-0.33	-13.32; 12.66	0.96
Recent acute illness							-7.47	-14.40; -0.54	**0.04**
Diagnosis of chronic illness							4.77	-7.01; 16.54	0.42
Observations*		94			94			94	
R² / R² adjusted		0.015/0.004			0.033/0.001			0.116/0.022	
PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; PSQI = Pittsburgh Sleep Quality Index.									

Table S11: Summary of the relationship between the stressful life events score and temporal summation at the deltoid test site.

Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	p	Estimates	95% CI	p	Estimates	95% CI	p
Intercept	10.09	7.63; 12.55	**<0.001**	10.17	5.93; 14.40	**<0.001**	19.21	7.64; 30.79	**0.001**
Stressful life events score	-1.48	-4.48; 1.51	0.33	-1.11	-6.86; 4.64	0.70	-2.11	-8.21; 3.99	0.49
Sex (female)				-0.16	-5.41; 5.10	0.95	-0.26	-5.85; 5.33	0.93
Stressful life events score x sex (female)				-0.54	-7.32; 6.24	0.88	0.29	-6.69; 7.27	0.94
Age							-0.18	-0.48; 0.12	0.23
PSQI score							-0.35	-1.10; 0.39	0.35
Diagnosis of major depressive disorder							4.48	-5.53; 14.49	0.38
Recent COVID-19 infection							-3.15	-13.22; 6.92	0.54
Recent acute illness							-2.98	-8.39; 2.43	0.28
Diagnosis of chronic illness							2.69	-6.24; 11.61	0.55
Observations		95			95			95	
R² / R² adjusted		0.010/-0.000			0.011/-0.022			0.055/-0.045	
PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; PSQI = Pittsburgh Sleep Quality Index.									

d. Outcome: conditioned pain modulation

The unadjusted model satisfied the underlying assumptions of linear regression (Figs S24 and S24) and found no evidence of an association between PSS and CPM at either the lumbar (β=-5.68 [95%CI: -12.57; 1.21], *p* = 0.11) or the deltoid site (β=1.50 [95%CI: -4.06; 7.05], *p* = 0.59). When sex was included as an interaction term, both the unadjusted and the covariate-adjusted models found no evidence of an association between PSS and CPM at either the lumbar or the deltoid site, and there was no evidence of an effect of sex, or an effect of the interaction between PSS and sex (Fig S26 and Tables S12 and S13).
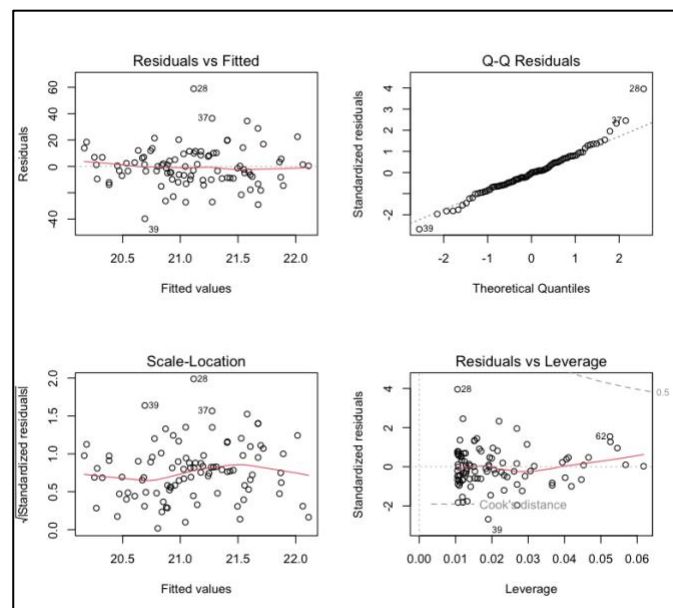

Figure S24: Plots of model assumptions for the conventional linear regression investigating the relationship between the stressful life events score and conditioned pain modulation at the lumbar site.
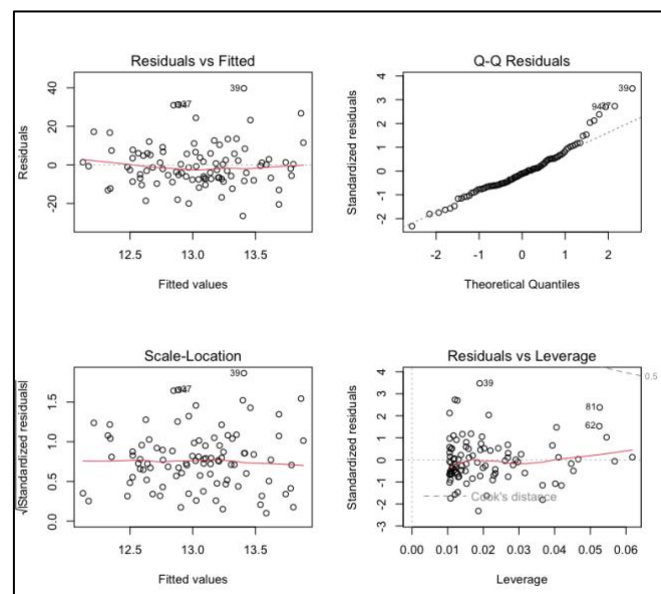

Figure S25: Plots of model assumptions for the conventional linear regression investigating the relationship between the stressful life events score and conditioned pain modulation at the deltoid site.
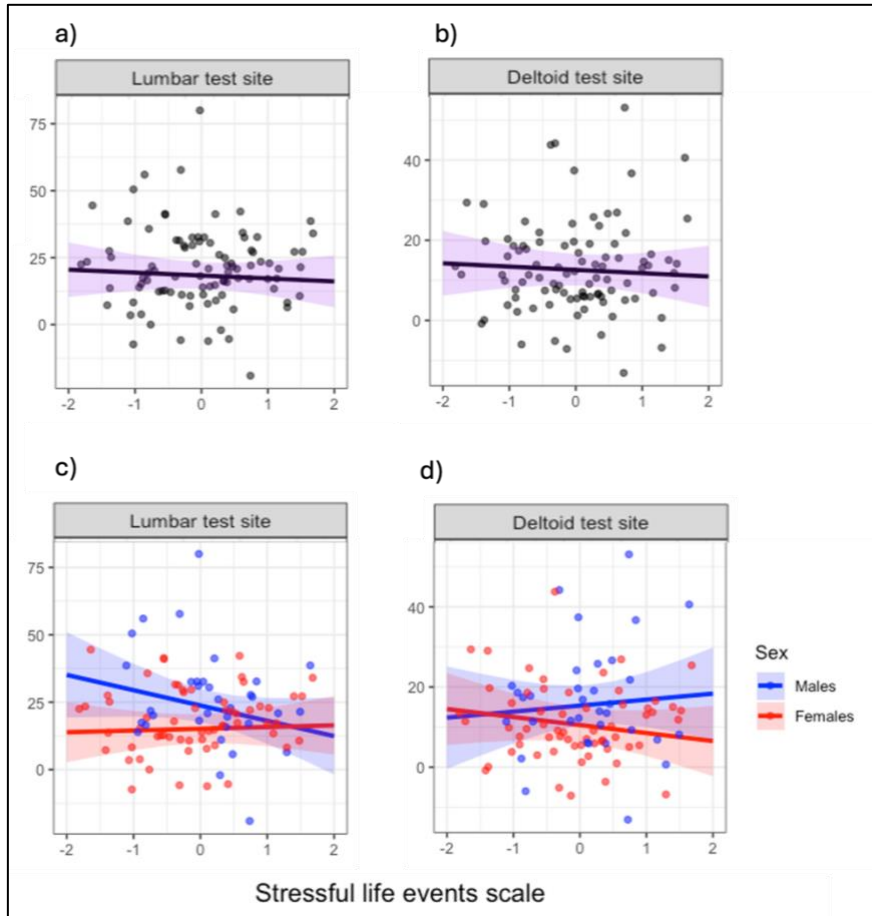
Figure S26: Plot of the association between the stressful life events score and conditioned pain modulation. Plots show the observed values (dots) and the predicted regression line and 95% confidence interval (ribbon) for the covariate-adjusted model for the full cohort (plots a and b) and with sex as an interaction term (plots c and d).

Table S12: Summary of the relationship between stressful life events score and conditioned pain modulation at the lumbar test site.

Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	p	Estimates	95% CI	p	Estimates	95% CI	p
Intercept	21.10	18.05; 24.15	**<0.001**	26.96	21.98; 31.94	**<0.001**	13.14	0.07;26.21	0.05
Stressful life events score	-0.56	-4.27; 3.16	0.77	-6.72	-13.48; 0.04	0.05	-5.68	-12.57; 1.21	0.11
Sex (female)				-8.51	-14.69; -2.33	**0.01**	-8.63	-14.94; -2.32	**0.01**
Stressful life events score x sex (female)				7.75	-0.22;15.73	0.06	6.32	-1.56; 14.21	0.12
Age							0.31	-0.02; 0.65	0.07
PSQI score							0.27	-0.58; 1.11	0.53
Diagnosis of major depressive disorder							7.03	-4.27; 18.34	0.22
Recent COVID-19 infection							8.54	-2.84; 19.92	0.14
Recent acute illness							5.19	-0.02; 11.30	0.10
Diagnosis of chronic illness							-8.31	-18.39; 1.77	0.11
Observations			95			95			95
R^2 / R^2 adjusted		0.001/-0.010			0.102/0.072			0.209/0.126	
PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; PSQI = Pittsburgh Sleep Quality Index.									

Table S13: Summary of the relationship between stressful life events score and conditioned pain modulation at the deltoid test site.

Predictors	Unadjusted model of main effect			Unadjusted model with sex interaction term			Adjusted model with sex interaction term		
	Estimates	95% CI	p	Estimates	95% CI	p	Estimates	95% CI	p
Intercept	13.04	10.69; 15.39	**<0.001**	16.36	12.44; 20.28	**<0.001**	15.87	5.33; 26.41	**0.004**
Stressful life events score	0.50	-2.3; 3.37	0.73	2.07	-3.25; 7.40	0.44	1.50	-4.06; 7.05	0.59
Sex (female)				-5.40	-10.27; -0.53	**0.03**	-4.84	-9.93; 0.25	0.06
Stressful life events score x sex (female)				-2.78	-9.06; 3.50	0.38	-3.50	-9.85; 2.86	0.28
Age							0.04	-0.23; 0.31	0.76
PSQI score							-0.22	-0.90; 0.46	0.52
Diagnosis of major depressive disorder							5.52	-3.60; 14.64	0.23
Recent COVID-19 infection							8.45	-0.72; 17.63	0.07
Recent acute illness							0.18	-4.74; 5.11	0.94
Diagnosis of chronic illness							-4.53	-12.66; 3.60	0.27
Observations			95			95			95
R^2 / R^2 adjusted		0.001/-0.009			0.064/0.033			0.136/0.045	
PSS = Perceived Stress Scale; CTQ-SF = Childhood Trauma Questionnaire-short form; PSQI = Pittsburgh Sleep Quality Index.									