**SUPPLEMENTARY A** Gating strategy for flow cytometry of white blood cells

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Panel **A:** Lymphocytes are gated based on low side scatter (SSC) and CD45 expression. Within the lymphocytes, CD19+ B-cells, CD3+ T-cells, CD56+CD3- natural killer (NK) cells and CD56+ T-cells are gated. Within CD3+ T-cells CD4+CD8- (CD4+ T-cells), CD4-CD8+ (CD8+ T-cells), CD4+CD8+ double positive T-cells (DPT) and CD4- D8- double negative T-cells (DNT) are gated. Within CD4+ T-cells, CD25hi T-regulatory (Treg) are gated, the remaining CD4+ T-cells are defined as conventional T-cells. CD25 and HLA-DR expression is analyzed on CD4+ conventional T-cells and CD8+ T-cells using appropriate isotype controls for gating. Panel **B:** Mononuclear cells (PBMC) are gated based on low/intermediate SSC and CD45 expression. Within the PBMC, CD14+ monocytes are gated. Activation markers TLR4 and HLA-DR expression on CD14+ monocytes is analysed and expression levels are corrected for background staining with appropriate isotype controls.

**SUPPLEMENTARY B**

|  |  |  |
| --- | --- | --- |
| **Clinical factors** | **Psychological factors** | **Lifestyle factors** |
| Pain intensity (Matute Wilander, Kåredal et al. 2014) | Mental health (Wium-Andersen, Ørsted et al. 2013) | Physical activity (Abramson and Vaccarino 2002) |
| Disability (Klyne, Barbe et al. 2022) | Stress (Segerstrom and Miller 2004) | Smoking (Shiels, Katki et al. 2014) |
| Sex (Gregus, Levine et al. 2021) | Depression (Wium-Andersen, Ørsted et al. 2013) | Alcohol use (Klyne, Barbe et al. 2017) |
| Central sensitization (Fitzcharles, Cohen et al. 2021) | Anxiety (Vogelzangs, Beekman et al. 2013) | Insomnia (Klyne, Barbe et al. 2017) |
| Number of co-morbidities (Koop, Lutke Schipholt et al. 2021) | Kinesiophobia (Koop, Lutke Schipholt et al. 2021) | BMI (Klyne, Barbe et al. 2017) |
|  | Rumination (Klyne, Barbe et al. 2017) | Visceral adipose tissue (Schlecht, Fischer et al. 2016) |
|  | Magnification (Klyne, Barbe et al. 2017) |  |
|  | Helplessness (Klyne, Barbe et al. 2017) |  |
|  | Catastrophizing (Klyne, Barbe et al. 2017) |  |

**SUPPLEMENTARY C**  Flowchart of the study

**SUPPLEMENTARY D** Differences in ex-vivo inflammatory marker concentration between healthy participants, people with non-specific neck pain and cervical radiculopathy.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Non-specific neck pain versus healthy participants** | **Cervical radiculopathy versus healthy participants** | **Non-specific neck pain versus cervical radiculopathy** |
| Ex-vivo | B1 (SE) | B1 (SE) | B1 (SE) |
| Inflammatory index | **0.54 (0.24)** | 0.55 (0.28)\*  | 0.16 (0.25) |
| Pro-inflammatory index | **0.70 (0.24)** | **0.64 (0.30)** | 0.23 (0.25) |
| Anti-inflammatory index | 0.39 (0.31)  | 0.47 (0.31)  | 0.09 (0.33) |
| Ratio pro/anti inflammatory index | 8.16 (4.77)  | 12.05 (8.30)  | -1.16 (3.65) |
| hsCRP | 0.52 (0.29)  | 0.59 (0.30)\*  | 0.27 (0.30) |
| IL-1β | **1.85 (0.57)**  | 2.42 (2.49)  | 1.33 (0.93) |
| IL-1RA | **0.33 (0.12)** | **0.35 (0.14)**  | 0.008 (0.14) |
| TNF-α | **0.36 (0.14)**  | 0.29 (0.17)  | 0.07 (0.16) |
| sTNF-R2 | -0.03 (0.09) | -0.003 (0.04)  | 0.08 (0.11) |

Table shows the differences in *ex-vivo* inflammatory indexes and inflammatory markers in healthy participants, people with non-specific neck pain and cervical radiculopathy. The *ex-vivo* values were Ln-transformed. The inflammatory index was calculated as the sum of z-standardized hsCRP, IL-1β, TNF-α, IL-1RA and sTNF-R2 divided by the number of cytokines. Pro-inflammatory index was calculated as the sum of z-standardized hsCRP, IL-1β and TNF-α. Anti-inflammatory index was calculated as the sum of z-standardized IL-1RA and STNF-R2. TNF-α, tumor necrosis factor -α; IL-1β, interleukin -1β; IL-1RA, interleukin -receptor antagonist; Bold = P < 0.05; \* = P = 0.06; 1Ln-transformed, adjusted for plate number

**SUPPLEMENTARY E**

Differences in inflammatory marker concentration after *in-vitro* stimulation of whole blood cells in healthy participants, people with non-specific neck pain and cervical radiculopathy.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Non-specific neck pain versus healthy participants** | **Non-specific neck pain versus healthy participants** | **Cervical radiculopathy versus healthy participants** | **Cervical radiculopathy versus healthy participants** | **Non-specific neck pain versus cervical radiculopathy** | **Non-specific neck pain versus cervical radiculopathy** |
| In-vitro | LPS | B1 (SE) | Normalized-B2 (SE) | B1 (SE) | Normalized-B2 (SE) | B1 (SE) | Normalized-B2 (SE) |
| Inflammatory index | LD-LPS | -0.19 (0.20) | -0.11 (0.21) | **-0.11 (0.04)** | -0.08 (0.05) | -0.07 (0.18) | -0.05 (0.19) |
| HD-LPS | -0.10 (0.22)♂ -0.21 (0.28)♀ 0.31 (0.33) | 0.004 (0.26) | -0.09 (0.06)♂ -0.32 (0.30)♀ 0.22 (0.28) | -0.02 (0.06) | 0.08 (0.21) | 0.10 (0.24) |
| Pro-inflammatory index | LD-LPS | -0.17 (0.24)♂ -0.36 (0.19)♀ 0.42 (0.48) | -0.10 (0.21) | **-0.10 (0.04)** | -0.06 (0.05) | -0.09 (0.19) | -0.07 (0.19) |
| HD-LPS | -0.04 (0.18) | 0.06 (0.26) | -0.11 (0.06)♂ -0.04 (0.33)♀ 0.28 (0.33) | -0.04 (0.06) | -0.005 (0.23) | 0.007 (0.25) |
| Anti-inflammatory index | LD-LPS | -0.24 (0.21)♂ -0.40 (0.24)♀ -0.09 (0.47) | -0.14 (0.23)  | **-0.15 (0.05)** | -0.11 (0.06) | -0.003 (0.20) | 0.007 (0.21) |
| HD-LPS | -0.27 (0.26) | -0.13 (0.31) | -0.04 (0.07) | -0.02 (0.08) | 0.30 (0.24) | 0.33 (0.29) |
| Ratio pro/anti inflammatory index | LD-LPS | -0.86 (1.93) | -0.21 (0.75) | -0.04 (0.27) | -0.22 (1.01) | -1.82 (1.79) | -3.61 (1.89) |
| HD-LPS | 7.88 (27.7) | -1.09 (3.93) | -0.29 (0.21) | -0.13 (0.25) | 9.80 (25.0) | -0.03 (3.54) |
| TNF-α | LD-LPS | -0.37 (0.23) | -0.31 (0.24) | -0.04 (0.27)  | 0.02 (0.31)  | -0.31 (0.22) | -0.30 (0.23) |
| HD-LPS | -0.23 (0.18)♂ -0.27 (0.22)**♀** 0.16 (0.30) | -0.17 (0.20) | -0.11 (0.25)  | -0.05 (0.25)  | -0.15 (0.18) | -0.14 (0.19) |
| IL-1β | LD-LPS | -0.04 (0.26) | 0.02 (0.29)  | 0.34 (0.32)  | 0.40 (0.38)  | -0.32 (0.29) | -0.31 (0.26) |
| HD-LPS | 0.12 (0.16)  | 0.18 (0.19)  | 0.17 (0.16)  | 0.22 (0.20)  | -0.001 (0.15) | 0.005 (0.18) |
| IL-1RA | LD-LPS | -0.07 (0.14)♂ -0.13 (0.14)♀ 0.27 (0.35) | -0.12 (0.16)♂ -0.36 (0.20)♀ -0.06 (0.16) | -0.03 (0.13)  | 0.03 (0.16)  | -0.005 (0.13) | 0.002 (0.15) |
| HD-LPS | -0.08 (0.10) | -0.02 (0.12)♂ -0.02 (0.16)♀ -0.20 (0.21) | -0.04 (0.11) | 0.02 (0.12)  | -0.006 (0.10) | 0.001 (0.12) |
| IL-4 | LD-LPS | - | - | - | - | - | - |
| HD-LPS | - | - | - | - | - | - |
| IL-10 | LD-LPS | -0.33 (0.21)  | -0.28 (0.22)  | -0.21 (0.21) | -0.15 (0.25)  | 0.004 (0.20) | 0.01 (0.21) |
| HD-LPS | -0.16 (0.19)  | -0.10 (0.19)  | -0.42 (0.23)  | -0.36 (0.23)  | 0.35 (0.18) | 0.35 (0.18) |
| CCL2 | LD-LPS | 0.03 (0.18) ♂ 0.13 (0.35)♀ 0.008 (0.20) | 0.08 (0.18)   | -0.23 (0.23) ♂ -0.19 (0.30)♀ -0.09 (0.26) | -0.17 (0.21)  | 0.25 (0.17) | 0.25 (0.17) |
| HD-LPS | 0.15 (0.18) ♂ 0.11 (0.21)♀ 0.31 (0.34) | 0.20 (0.19)  | -0.03 (0.24)  | 0.03 (0.26)  | 0.16 (0.17) | 0.17 (0.18) |
| CCL3  | LD-LPS | -0.20 (0.24)  | -0.14 (0.26)  | 0.02 (0.19)  | 0.07 (0.24)  | -0.13 (0.22) | -0.13 (0.23) |
| HD-LPS | -0.04 (0.14) ♂ -0.13 (0.18)♀ 0.31 (0.23) | 0.02 (0.17)  | -0.001 (0.15)  | 0.06 (0.16)  | 0.01 (0.14) | 0.02 (0.15) |
| CCL4  | LD-LPS | -0.18 (0.19)  | -0.12 (0.20)  | -0.06 (0.14) ♂ -0.15 (0.20)♀ 0.09 (0.17) | -0.005 (0.18)  | -0.08 (0.17) | -0.07 (0.19) |
| HD-LPS | -0.10 (0.10) ♂ -0.14 (0.13)♀ 0.06 (0.15) | -0.04 (0.13)  | -0.04 (0.11)  | 0.02 (0.13)  | -0.02 (0.10) | -0.01 (0.12) |

Table shows the differences in inflammatory indices and inflammatory markers after whole blood stimulation with TLR4 agonist lipopolysaccharide at concentration of 1ng/ml (LD-LPS) or 10µg/ml (HD-LPS) in healthy participants, people with non-specific neck pain and cervical radiculopathy. The inflammatory index was calculated as the sum of z-standardized (/1000 monocyte normalized) CCL2, CCL3, CCL4, TNF-α, IL-1β, IL-10 and IL-1RA divided by the number of cytokines. Pro-inflammatory index was calculated as the sum of z-standardized (/1000 monocyte normalized) CCL2, CCL3, CCL4, TNF-α and Il-1β. Anti-inflammatory index was calculated as the sum of z-standardized (/1000 monocyte normalized) IL-1RA and IL-10. TNF-α, tumor necrosis factor -α; IL-1β, interleukin -1β; IL-1RA, interleukin -receptor antagonist; IL-4, interleukin – 4; IL-10, interleukin -10; CCL2, c-c-motif ligand 2 also referred to as monocyte chemoattractant protein 1; CCL3, c-c-motif ligand 3 also referred to as macrophage inflammatory protein 1α; CCL4, c-c-motif ligand 4 also referred to as macrophage inflammatory protein 1β; LPS, lipopolysaccharide; Bold = p < 0.05. ♂ effect modification for males; ♀ effect modification for females.

1Ln-transformed, adjusted for plate number, LPS lot number, stimulation time

2Ln-transformed, normalized (/1000 monocytes), adjusted for plate number, LPS lot number, stimulation time.

**SUPPLEMENTARY F1** Association of lifestyle factors with neuroimmune responses in people with non-specific neck pain.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Physical Activitya** | **Smokingb** | **Alcohol usec** | **BMI** | **Visceral Adiposed** |
|  | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** |
| **In-vitro** |
|  Inflammatory index | LD-LPS | 0.20 | 0.11 (0.18) | -0.11 (0.15) | 0.07 (0.02) | **0.19 (0.003)** |
| HD-LPS | 0.06 (0.007) | 0.04 (0.16) | -0.06 (0.14) | 0.08 (0.02) | 0.08 (0.003) |
|  Pro-inflammatory index | LD-LPS | 0.08 (0.008) | 0.08 (0.18) | -0.16 (0.16) | 0.05 (0.02) | **0.20 (0.003)** |
| HD-LPS | 0.05 (0.007) | 0.002 (0.17) | -0.05 (0.14) | 0.07 (0.02) | 0.10 (0.003) |
|  Anti-inflammatory index | LD-LPS | 0.09 (0.008) | 0.16 (0.19) | -0.15 (0.17) | 0.13 (0.02) | 0.15 (0.004) |
| HD-LPS | 0.08 (0.008) | 0.11 (0.18) | -0.07 (0.15) | 0.09 (0.02) | 0.02 (0.003) |
|  Ratio pro/anti inflammatory index | LD-LPS | 0.10 (0.07) | 0.001 (1.60) | -0.03 (1.37) | 0.13 (0.15)♂ -0.18 (0.17) ♀ 0.22 (0.20) | 0.07 (0.01) |
| HD-LPS | **-0.22 (0.08)** | -0.05 (1.72) | -0.03 (1.46) | 0.14 (0.16) | 0.06 (0.03) |
|  TNF-α | LD-LPS | 0.06 (0.009) | 0.002 (0.21) | -0.06 (0.18) | -0.04 (0.003) | **0.25 (0.004)** |
| HD-LPS | 0.06 (0.008) | -0.07 (0.17) | 0.02 (0.15) | -0.05 (0.002) | 0.04 (0.003) |
|  IL-1β | LD-LPS | 0.05 (0.01) | 0.15 (0.24) | -0.16 (0.20) | -0.06 (0.003) | 0.14 (0.004) |
| HD-LPS | 0.04 (0.007) | -0.03 (0.17) | -0.10 (0.14) | -0.02 (0.002) | 0.05 (0.003) |
|  IL-1RA | LD-LPS | 0.11 (0.006) | 0.25 (0.14) | **-0.19 (0.12)**♂ -0.26 (0.32)♀ -0.01 (0.11) | 0.04 (0.002) | **0.22 (0.003)**♂ 0.32 (0.006)♀ 0.27 (0.002) |
| HD-LPS | 0.15 (0.005)♂ 0.21 (0.007)**♀ 0.17 (0.006)** | 0.17 (0.11) | -0.15 (0.09) | 0.005 (0.002)♂ 0.44 (0.02)♀ 0.17 (0.01) | 0.14 (0.002)♂ 0.32 (0.003)♀ 0.17 (0.002) |
|  IL-4 | LD-LPS | - | - | - | - | - |
| HD-LPS | **-** | **-** | **-** | **-** | **-** |
|  IL-10 | LD-LPS | 0.05 (0.008) | 0.13 (0.19) | -0.06 (0.16) | -0.16 (0.003) | 0.03 (0.003) |
| HD-LPS | -0.02 (0.007) | 0.006 (0.16) | 0.04 (0.07) | -0.13 (0.002) | -0.11 (0.003) |
|  CCL2  | LD-LPS | 0.05 (0.007) | 0.07 (0.16) | -0.02 (0.12) | -0.04 (0.002) | 0.02 (0.003) |
| HD-LPS | -0.06 (0.007) | 0.09 (0.16) | -0.13 (0.13) | -0.06 (0.002) | 0.08 (0.003) |
|  CCL3  | LD-LPS | 0.06 (0.010) | 0.04 (0.22) | -0.09 (0.19) | -0.04 (0.003) | **0.20 (0.004)** |
| HD-LPS | 0.03 (0.006) | -0.05 (0.15) | 0.021 (0.12) | -0.06 (0.002) | 0.08 (0.003) |
|  CCL4 | LD-LPS | 0.09 (0.008) | 0.05 (0.18) | -0.07 (0.15) | -0.04 (0.002) | **0.20 (0.003)** |
| HD-LPS | 0.11 (0.005) | 0.06 (0.12) | -0.004 (0.10) | -0.06 (0.002) | 0.14 (0.002) |
| **Ex-vivo** |
|  Inflammatory index |  | -0.03 (0.007) | 0.01 (0.14) | -0.08 (0.13) | **0.39 (0.01)** | 0.14 (0.003) |
|  Pro-inflammatory index |  | 0.04 (0.007) | -0.03 (0.15) | 0.05 (0.15) | **0.39 (0.02)** | 0.12 (0.003) |
|  Anti-inflammatory index |  | -0.08 (0.008) | 0.05 (0.18) | -0.17 (0.16) | **0.28 (0.02)** | 0.12 (0.003) |
|  Ratio pro/ anti inflammatory index |  | 0.12 (0.29) | -0.03 (5.96) | -0.07 (5.56) | 0.04 (0.61) | -0.09 (0.12) |
|  hsCRP |  | 0.01 (0.01) | 0.05 (0.26) | -0.01 (0.25) | **0.44 (0.02)** | 0.16 (0.005) |
|  TNF-α |  | 0.07 (0.006) | -0.09 (0.13) | 0.08 (0.12) | 0.12 (0.01)♂ 0.30 (0.02)♀ 0.006 (0;01) | 0.03 (0.002)**♂ 0.14 (0.005)**♀-0.12 (0.003) |
|  sTNF-R2 |  | -0.10 (0.004) | 0.06 (0.08) | -0.13 (0.08) | 0.07 (0.009) | 0.05 (0.002) |
|  Il-1β |  | 0.03 (0.03) | 0.12 (0.56) | 0.002 (0.49) | 0.22 (0.05) | 0.16 (0.01) |
|  IL-1RA |  | -0.03 (0.005) | 0.02 (0.11) | -0.15 (0.10) | **0.40 (0.01)** | 0.14 (0.002) |

Data represent standardized regression coefficient β (standard error, unstandardized B) of various lifestyle factors demonstrating an association with *ex-vivo* and *in-vitro* inflammatory indexes and of *in-vitro* and *ex-vivo* single inflammatory mediators using linear regression analysis. All single neuroimmune responses are ln-transformed. The *in-vitro* neuroimmune responses are normalized for monocyte count. Significant values are in bold font (\*p < 0.05). TNF-α, tumor necrosis factor -α; IL-1β, interleukin -1β; IL-1RA, interleukin -receptor antagonist; IL-4, interleukin – 4; IL-10, interleukin -10; CCL2 / MCP1, c-c-motif ligand 2 also referred to as monocyte chemoattractant protein 1; CCL3 / MIP1α, c-c-motif ligand 3 also referred to as macrophage inflammatory protein 1α; CCL4 / MIP1β, c-c-motif ligand 4 also referred to as macrophage inflammatory protein 1β; TNFα : IL-10, ratio between TNFα : IL-10; IL-1β : IL-1RA, ratio between IL-1β : IL-1RA; 1ng/ml (LD-LPS), 1 milliliter whole-blood stimulation with 1 nanogram TLR4 agonist lipopolysacharide; 10µg/ml (HD-LPS), 1 milliliter whole blood stimulation with 10 microgram of TLR4 agonist lipopolysacharide; ♂ effect modification for males; ♀ effect modification for females.

aRefers to 1000/metabolic equivalent of a task

bRefers to current smoker, yes:1, no:0

cRefers to consuming alcohol, yes:1, no:0

dRefers to linear distance in millimeters between the posterior aspect of peritoneum and anterior aspect of lumbar vertebra T10

**SUPPLEMENTARY F2** Association of clinical factors with neuroimmune responses in people with non-specific neck pain.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Pain intensitya** | **Disabilityb** | **Sexc** | **Central Sensitizationd** | **Number of co-morbidities** | **Insomniae** |
|  | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** |
| **In-vitro** |  |
|  Inflammatory index | LD-LPS | **0.19 (0.004)** | 0.05 (0.006) | 0.04 (0.16) | -0.06 (0.03) | **0.23 (0.06)** | 0.008 (0.17) |
| HD-LPS | **0.23 (0.003)** | 0.11 (0.005) | 0.02 (0.14) | -0.08 (0.03) | 0.18 (0.05) | 0.09 (0.15) |
|  Pro-inflammatory index | LD-LPS | 0.15 (0.004) | 0.009 (0.006) | -0.01 (0.16) | -0.05 (0.03) | **0.22 (0.06)** | -0.01 (0.17) |
| HD-LPS | **0.22 (0.004)** | 0.09 (0.005) | -0.07 (0.15) | -0.07 (0.03) | **0.18 (0.06)** | 0.06 (0.16) |
|  Anti-inflammatory index | LD-LPS | **0.25 (0.004)** | 0.14 (0.006) | 0.16 (0.17) | -0.07 (0.03) | **0.22 (0.07)** | 0.05 (0.18) |
| HD-LPS | **0.20 (0.004)** | 0.14 (0.006) | **0.20 (0.15)** | -0.08 (0.03) | 0.12 (0.06) | 0.14 (0.16) |
|  Ratio pro/anti inflammatory index | LD-LPS | 0.002 (0.04)♂ 0.05 (0.05)♀-0.09 (0.05) | -0.05 (0.05)♂ -0.29 (0.06) ♀ 0.04 (0.07) | -0.15 (1.40) | 0.006 (0.28) | 0.009 (0.55)♂ 0.08 (0.71)♀-0.21 (0.73) | -0.03 (1.48) |
| HD-LPS | **-0.21 (0.04)** | -0.11 (0.06) | -0.02 (1.51) | -0.03 (0.30) | 0.06 (0.59) | -0.02 (1.58) |
|  TNF-α | LD-LPS | 0.15 (0.005) | 0.07 (0.007) | -0.08 (0.18) | -0.03 (0.04)**♂ 0.34 (0.26)** ♀ -0.07 (0.03) | **0.20 (0.07)** | -0.08 (0.19) |
| HD-LPS | 0.19 (0.004) | 0.10 (0.005) | -0.14 (0.15) | -0.04 (0.030)♂ 0.38 (0.15)♀ -0.07 (0.03) | 0.10 (0.06) | 0.009 (0.16) |
|  IL-1β | LD-LPS | **0.20 (0.005)** | 0.14 (0.008) | 0.09 (0.21) | -0.03 (0.04) | 0.18 (0.08) | -0.008 (0.22) |
| HD-LPS | **0.22 (0.004)** | 0.13 (0.005) | 0.04 (0.15) | -0.02 (0.03) | 0.15 (0.06) | 0.10 (0.16) |
|  IL-1RA | LD-LPS | **0.23 (0.003)** | 0.09 (0.005)♂ -0.03 (0.01)**♀ 0.16 (0.004)** | **0.18 (0.12)** | 0.04 (0.02) | **0.33 (0.05)** | 0.05 (0.30) |
| HD-LPS | **0.21 (0.002)** | 0.12 (0.004) | **0.23 (0.10)** | -0.01 (0.02) | **0.27 (0.04)** | 0.09 (0.10) |
|  IL-4 | LD-LPS | - | **-** | - | - | - | - |
| HD-LPS | - | **-** | - | - | - | **-** |
|  IL-10 | LD-LPS | **0.19 (0.004)** | 0.15 (0.006) | 0.08 (0.17) | -0.16 (0.03) | 0.05 (0.06) | 0.04 (0.17) |
| HD-LPS | 0.11 (0.004) | 0.10 (0.005) | 0.10 (0.14) | -0.12 (0.03) | -0.08 (0.05) | 0.13 (0.15) |
|  CCL2  | LD-LPS | 0.04 (0.004) | -0.10 (0.005) | -0.06 (0.14) | -0.04 (0.03)**♂ 0.45 (0.24)**♀ -0.08 (0.03) | 0.02 (0.05) | 0.05 (0.15) |
| HD-LPS | 0.06 (0.004) | 0.006 (0.005) | -0.05 (0.14) | -0.05 (0.03) | 0.04 (0.05) | -0.05 (0.14) |
|  CCL3  | LD-LPS | 0.08 (0.005) | -0.03 (0.007) | 0.02 (0.20) | -0.05 (0.04)♂ 0.41 (0.21)♀-0.19 (0.20) | **0.21 (0.07)** | -0.004 (0.20) |
| HD-LPS | 0.15 (0.003) | 0.06 (0.005) | -0.07 (0.13) | -0.07 (0.03) | 0.15 (0.05) | 0.06 (0.14) |
|  CCL4 | LD-LPS | 0.12 (0.004) | -0.04 (0.006) | -0.004 (0.16) | -0.05 (0.03) | **0.25 (0.06)** | 0.002 (0.16) |
| HD-LPS | **0.21 (0.003)** | 0.04 (0.004) | -0.03 (0.10) | -0.08 (0.02) | **0.25 (0.04)** | 0.09 (0.11) |
| **Ex-vivo** |  |
|  Inflammatory index |  | **0.23 (0.003)** | -0.01 (0.005) | -0.007 (0.14) | -0.12 (0.13) | 0.09 (0.05) | -0.06 (0.15) |
|  Pro inflammatory index |  | 0.17 (0.004) | -0.11 (0.005) | -0.08 (0.15) | -0.14 (0.14) | 0.05 (0.06) | 0.08 (0.16) |
|  Anti-inflammatory index |  | **0.22 (0.004)** | 0.07 (0.006) | 0.06 (0.17) | -0.07 (0.16) | 0.10 (0.07) | -0.16 (0.18) |
|  Ratio pro/ anti inflammatory index |  | 0.06 (0.15) | 0.006 (0.21) | 0.09 (5.73) | -0.14 (0.14) | -0.15 (2.28) | -0.14 (6.03) |
|  hsCRP |  | 0.16 (0.006) | -0.14 (0.009) | 0.04 (0.25) | -0.16 (0.24) | 0.07 (0.098) | **0.18 (0.25)** |
|  TNF-α |  | 0.07 (0.003)♂ 0.14 (0.006)♀ 0.06 (0.003) | -0.03 (0.004) | **-0.19 (0.12)** | -0.09 (0.12) | -0.03 (0.05) | -0.03 (0.13) |
|  sTNF-R2 |  | **0.23 (0.002)** | 0.07 (0.003) | -0.02 (0.08) | -0.03 (0.08) | 0.13 (0.03) | -0.11 (0.09) |
|  Il-1β |  | 0.16 (0.01) | 0.09 (0.02) | -0.15 (0.49) | 0.03 (0.47) | -0.33 (0.18) | -0.08 (0.50) |
|  IL-1RA |  | 0.13 (0.003) | 0.06 (0.004) | 0.12 (0.11) | -0.09 (0.10) | 0.03 (0.04) | -0.16 (0.11) |

Data represents standardized regression coefficient β (standard error, unstandardized B) of various lifestyle factors demonstrating an association with *ex-vivo* and *in-vitro* inflammatory indexes and of *in-vitro* and *ex-vivo* single inflammatory mediators using linear regression analysis. All single neuroimmune responses are ln-transformed. The *in-vitro* neuroimmune responses are normalized for monocyte count. Significant values are in bold font (\*p < 0.05) TNF-α, tumor necrosis factor -α; IL-1β, interleukin -1β; IL-1RA, interleukin -receptor antagonist; IL-4, interleukin – 4; IL-10, interleukin -10; CCL2 / MCP1, c-c-motif ligand 2 also referred to as monocyte chemoattractant protein 1; CCL3 / MIP1α, c-c-motif ligand 3 also referred to as macrophage inflammatory protein 1α; CCL4 / MIP1β, c-c-motif ligand 4 also referred to as macrophage inflammatory protein 1β; TNFα : IL-10, ratio between TNFα : IL-10; IL-1β : IL-1RA, ratio between IL-1β : IL-1RA; 1ng/ml (LD-LPS), 1 milliliter whole-blood stimulation with 1 nanogram TLR4 agonist lipopolysacharide; 10µg/ml (HD-LPS), 1 milliliter whole blood stimulation with 10 microgram of TLR4 agonist lipopolysacharide; ♂ effect modification for males; ♀ effect modification for females.

aRefers to pain intensity measured on the visual analogue scale, 0-100

bRefers to score on the neck disability index, 0-100

cMale:0 Female:1

dRefers to total score on the central sensitisation questionnaire higher than 40

eRefers having insomnia (pittsburg sleep quality index score above 5)

**SUPPLEMENTARY F3** Association of psychological factors with neuroimmune responses in people with non-specific neck pain.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Mental Healtha** | **Stressb** | **Depressionc** | **Anxietyd** | **Kinesiophobiae** | **Pain rumination** | **Pain magnification** | **Pain helplessness** | **Catastrophizingjf**  |
|  | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** |
| **In-vitro** |
|  Inflammatory index | LD-LPS | -0.06 (0.005) | 0.15 (0.009) | 0.04 (0.009) | **0.23 (0.01)** | 0.03 (0.17) | 0.06 (0.02) | 0.03 (0.03) | -0.03 (0.01) | 0.03 (0.007) |
| HD-LPS | -0.03 (0.004) | 0.003 (0.008) | -0.08 (0.008) | 0.13 (0.009) | 0.05 (0.15) | 0.11 (0.02) | 0.11 (0.02) | 0.06 (0.01) | 0.10 (0.006) |
|  Pro-inflammatory index | LD-LPS | -0.04 (0.005) | 0.14 (0.009) | 0.01 (0.009) | **0.19 (0.01)** | 0.007 (0.17) | 0.04 (0.02) | -0.006 (0.03) | -0.07 (0.01) | -0.005 (0.007) |
| HD-LPS | -0.01 (0.004) | 0.004 (0.008) | -0.11 (0.008) | 0.10 (0.01) | 0.06 (0.16) | 0.13 (0.02) | 0.07 (0.02) | 0.04 (0.01) | 0.08 (0.006) |
|  Anti-inflammatory index | LD-LPS | -0.10 (0.005) | 0.15 (0.009) | 0.11 (0.009) | **0.18 (0.01)** | 0.07 (0.18) | 0.09 (0.02) | 0.11 (0.03) | 0.05 (0.02) | 0.10 (0.007) |
| HD-LPS | -0.07 (0.005) | -0.002 (0.009) | 0.008 (0.009) | 0.17 (0.01) | 0.02 (0.17) | 0.06 (0.02) | 0.16 (0.03) | 0.08 (0.01) | 0.10 (0.007) |
|  Ratio pro/anti inflammatory index | LD-LPS | 0.14 (0.04) | -0.17 (0.08) | -0.05 (0.08) | -0.14 (0.09) | 0.04 (1.49) | 0.005 (0.17)♂ 0.05 (0.22)♀-0.25 (0.22) | 0.001 (0.24) | 0.01 (0.13)♂ 0.07 (0.17)♀ -0.09 (0.18) | 0.002 (0.06) |
| HD-LPS | 0.06 (0.04) | 0.05 (0.08) | **-0.24 (0.08)** | -0.16 (0.10) | 0.03 (1.58) | -0.15 (0.18) | -0.11 (0.25) | -0.17 (0.13) | -0.17 (0.06) |
|  TNF-α | LD-LPS | 0.06 (0.005) | 0.08 (0.01) | -0.04 (0.01)♂ 0.22 (0.03)**♀ -0.12 (0.01)** | 0.12 (0.01) | 0.06 (0.19) | 0.07 (0.02) | -0.02 (0.03)♂ 0.27 (0.07)**♀ -0.13 (0.04)** | -0.04 (0.02) | 0.02 (0.008) |
| HD-LPS | 0.02 (0.004) | 0.04 (0.008) | -0.12 (0.008) | 0.08 (0.01) | 0.06 (0.16) | 0.15 (0.02 ) | 0.06 (0.03) | 0.07 (0.01)**♂ 0.18 (0.03)**♀ 0.06 (0.02) | 0.10 (0.006) |
|  IL-1β | LD-LPS | -0.20 (0.006) | 0.17 (0.01) | 0.08 (0.01) | 0.18 (0.01) | 0.14 (0.22) | 0.15 (0.03) | 0.007 (0.04) | 0.03 (0.02) | 0.08 (0.009) |
| HD-LPS | -0.04 (0.004) | -0.03 (0.008) | -0.11 (0.008) | 0.04 (0.01) | 0.08 (0.16) | 0.17 (0.02) | 0.06 (0.02) | 0.09 (0.01) | 0.12 (0.006) |
|  IL-1RA | LD-LPS | -0.10 (0.004)♂ -0.25 (0.01)♀ 0.03 (0.003) | 0.05 (0.007) | 0.02 (0.007) | 0.18 (0.008) | 0.005 (0.13) | 0.08 (0.02) | 0.07 (0.02) | 0.07 (0.01) | 0.10 (0.005) |
| HD-LPS | -0.05 (0.003)♂ -0.17 (0.006)♀0.06 (0.003) | -0.16 (0.005) | -0.08 (0.005) | 0.08 (0.007) | -0.01 (0.10) | 0.12 (0.01) | 0.12 (0.02) | 0.12 (0.009) | 0.14 (0.004) |
|  IL-4 | LD-LPS | - | - | - | - | - | - | - | - | - |
| HD-LPS | - | - | - | - | - | - | - | - | - |
|  IL-10 | LD-LPS | -0.07 (0.005) | **0.21 (0.009)** | 0.17 (0.009) | **0.29 (0.01)** | 0.11 (0.17) | 0.06 (0.02) | 0.12 (0.03) | 0.01 (0.02) | 0.07 (0.007) |
| HD-LPS | -0.07 (0.004) | 0.16 (0.008) | 0.09 (0.008) | **0.19 (0.009)** | 0.04 (0.15) | -0.02 (0.02) | 0.14 (0.02) | 0.008 (0.01) | 0.03 (0.006) |
|  CCL2  | LD-LPS | 0.01 (0.004) | 0.05 (0.008) | 0.008 (0.008)♂ 0.52 (0.02)♀ -0.04 (0.008) | 0.13 (0.009) | -0.07 (0.15) | -0.04 (0.02) | 0.04 (0.03) | -0.03 (0.01) | -0.03 (0.006) |
| HD-LPS | -0.04 (0.004) | 0.06 (0.008) | 0.09 (0.007)♂ 0.32 (0.02)♀ -0.08 (0.008) | 0.08 (0.009) | 0.08 (0.14) | 0.01 (0.02) | 0.03 (0.02) | 0.03 (0.01) | 0.03 (0.006) |
|  CCL3  | LD-LPS | -0.003 (0.006) | 0.12 (0.01) | 0.001 (0.01)♂ 0.29 (0.04)**♀ -0.16 (0.009)** | 0.15 (0.01) | -0.03 (0.21) | 0.003 (0.02) | -0.05 (0.03) | -0.11 (0.02) | -0.05 (0.009) |
| HD-LPS | 0.04 (0.004) | -0.01 (0.007) | -0.16 (0.007) | 0.06 (0.009) | 0.02 (0.14) | 0.08 (0.02) | 0.04 (0.02) | -0.02 (0.01) | 0.03 (0.005) |
|  CCL4 | LD-LPS | -0.02 (0.005) | 0.11 (0.009) | 0.005 (0.009)♂ 0.26 (0.03)**♀-0.13 (0.007)** | **0.18 (0.010)** | -0.07 (0.17) | -0.01 (0.02) | -0.002 (0.03) | -0.10 (0.01) | -0.05 (0.007) |
| HD-LPS | -0.01 (0.003) | -0.04 (0.006) | -0.12 (0.005) | 0.13 (0.007) | -0.001 (0.11) | 0.06 (0.01) | 0.11 (0.02) | -0.01 (0.009) | 0.05 (0.004) |
| **Ex-vivo** |
|  Inflammatory index |  | 0.18 (0.004) | -0.19 (0.007) | -0.14 (0.007) | -0.05 (0.009) | -0.09 (0.14) | **-0.21 (0.02)** | -0.15 (0.02) | -0.17 (0.01) | **-0.20 (0.006)** |
|  Pro inflammatory index |  | 0.18 (0.004) | -0.19 (0.008) | -0.15 (0.008) | -0.08 (0.01) | -0.08 (0.16) | **-0.27 (0.02)** | **-0.25 (0.02)** | **-0.26 (0.01)** | **-0.28 (0.006)** |
|  Anti-inflammatory index |  | 0.13 (0.005) | -0.14 (0.009) | -0.09 (0.009) | -0.02 (0.01) | -0.08 (0.17) | -0.11 (0.02) | -0.02 (0.03) | -0.05 (0.02) | -0.08 (0.007) |
|  Ratio pro/ anti inflammatory index |  | 0.09 (0.16) | 0.06 (0.31) | 0.04 (0.30) | -0.008 (0.39) | 0.09 (5.99) | -0.02 (0.69) | 0.05 (0.95) | 0.05 (0.51) | 0.03 (0.25) |
|  hsCRP |  | **0.20 (0.007)** | **-0.19 (0.01)** | -0.09 (0.01) | -0.10 (0.02) | 0.01 (0.26) | **-0.25 (0.03)** | **-0.20 (0.04)** | -0.18 (0.02) | **-0.23 (0.01)** |
|  TNF-α |  | 0.09 (0.003)♂**0.28 (0.009)**♀-0.05 ().004) | -0.11 (0.007) | -0.15 (0.006) | -0.04 (0.008) | -0.14 (0.126) | -0.17 (0.01)**♂-0.15 (0.03)**♀-0.20 (0.02) | -0.17 (0.02) | **-0.23 (0.01)** | **-0.21 (0.005)** |
|  sTNF-R2 |  | 0.07 (0.002) | -0.11 (0.004) | -0.07 (0.004) | -0.02 (0.005) | -0.09 (0.08) | -0.05 (0.01) | -0.04 (0.01) | -0.09 (0.007) | -0.06 (0.003) |
|  Il-1β |  | 0.27 (0.02) | -0.12 (0.02) | -0.09 (0.02) | -0.25 (0.03) | -0.23 (0.59) | 0.002 (0.49) | -0.16 (0.07) | -0.24 (0.09) | -0.12 (0.05) |
|  IL-1RA |  | 0.15 (0.003) | -0.11 (0.006) | -0.08 (0.006) | -0.01 (0.007) | -0.04 (0.11) | -0.12 (0.01) | 0.006 (0.02) | 0.01 (0.01) | -0.06 (0.005) |

Data represent standardized regression coefficient-β (standard error, unstandardized B) of various psychological factors demonstrating an association with several neuroimmune responses *ex-vivo* and after *in-vitro* whole blood stimulation using linear regression models. All neuroimmune responses are Ln-transformed and *in-vitro* responses are normalized for monocyte count. Significant values are in bold font (\*p < 0.05). TNF-α, tumor necrosis factor -α; IL-1β, interleukin -1β; IL-1RA, interleukin -receptor antagonist; IL-4, interleukin – 4; IL-10, interleukin -10; CCL2 / MCP1, c-c-motif ligand 2 also referred to as monocyte chemoattractant protein 1; CCL3 / MIP1α, c-c-motif ligand 3 also referred to as macrophage inflammatory protein 1α; CCL4 / MIP1β, c-c-motif ligand 4 also referred to as macrophage inflammatory protein 1β; TNFα : IL-10, ratio between TNFα : IL-10; IL-1β : IL-1RA, ratio between IL-1β : IL-1RA; 1ng/ml (LD-LPS), 1 milliliter whole-blood stimulation with 1 nanogram TLR4 agonist lipopolysacharide; 10µg/ml (HD-LPS), 1 milliliter whole blood stimulation with 10 microgram of TLR4 agonist lipopolysacharide; ♂ effect modification for males; ♀ effect modification for females.

aRefers to mental health inventory -5 score

bRefers to score on the depression, anxiety and stress scale 21 subsection stress

cRefers to the score on the depression, anxiety and stress scale 21 subsection depression

dRefers to the score on the depression, anxiety and stress scale 21 subsection anxiety

eRefers to total score on the tampa scale questionnaire higher than 37

fRefers to the total score on the pain catastrophizing scale

**SUPPLEMENTARY G1** Association of lifestyle factors with neuroimmune responses in people with a cervical radiculopathy

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Physical Activitya**  | **Smokingb** | **Alcohol usec** | **BMI** | **Visceral Adiposed**  |
|  | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** |
| **In-vitro** |
|  Inflammatory index | LD-LPS | -0.18 (0.02) | 0.19 (0.34) | 0.03 (0.35) | 0.12 (0.04) | 0.10 (0.005) |
| HD-LPS | -0.13 (0.02) | 0.07 (0.32) | -0.17 (0.32) | 0.22 (0.03)♂ 0.25 (0.06)♀ 0.15 (0.06) | 0.14 (0.005)♂ -0.09 (0.01)♀ 0.16 (0.01) |
|  Pro-inflammatory index | LD-LPS | -0.23 (0.02) | 0.15 (0.35) | 0.13 (0.35) | 0.11 (0.04) | 0.09 (0.006) |
| HD-LPS | -0.17 (0.02) | -0.06 (0.34) | -0.04 (0.34) | 0.29 (0.03) | 0.20 (0.005) |
|  Anti-inflammatory index | LD-LPS | -0.05 (0.03) | 0.25 (0.38) | -0.19 (0.39) | 0.13 (0.04) | 0.11 (0.006) |
| HD-LPS | -0.01 (0.02) | 0.35 (0.34) | -0.42 (0.34) | 0.008 (0.04)♂ 0.26 (0.07)♀ -0.35 (0.06) | -0.04 (0.006)♂ -0.002 (0.01)♀ -0.33 (0.01) |
|  Ratio pro/anti inflammatory index | LD-LPS | -0.25 (0.11) | -0.16 (1.62) | 0.04 (1.6) | -0.20 (0.16) | -0.13 (0.03) |
| HD-LPS | 0.07 (0.22) | -0.24 (3.28) | 0.22 (3.33) | 0.12 (0.34) | 0.19 (0.05) |
|  TNF-α | LD-LPS | -0.15 (0.04) | -0.11 (0.53) | 0.14 (0.53) | 0.29 (0.05) | 0.27 (0.008) |
| HD-LPS | 0.02 (0.03) | **-0.51 (0.37)** | 0.06 (0.43) | 0.40 (0.04) | 0.32 (0.006) |
|  IL-1β | LD-LPS | -0.23 (0.04) | 0.04 (0.54) | -0.05 (0.55) | 0.14 (0.05) | 0.05 (0.009) |
| HD-LPS | -0.16 (0.02) | -0.17 (0.31) | -0.13 (0.31) | 0.29 (0.03) | 0.17 (0.005) |
|  IL-1RA | LD-LPS | -0.11 (0.02) | 0.07 (0.25) | -0.15 (0.25) | 0.37 (0.02) | 0.31 (0.004) |
| HD-LPS | -0.05 (0.01) | 0.22 (0.20) | -0.38 (0.19) | 0.35 (0.02) | 0.26 (0.003) |
|  IL-4 | LD-LPS | - | - | - | - | - |
| HD-LPS | **-** | **-** | **-** | **-** | **-** |
|  IL-10 | LD-LPS | 0.02 (0.03) | 0.36 (0.37) | -0.18 (0.39) | -0.15 (0.04) | -0.13 (0.006) |
| HD-LPS | 0.03 (0.02) | 0.32 (0.035) | -0.27 (0.36) | -0.33 (0.03)♂ -0.53 (0.07)**♀ -0.39 (0.05)** | -0.31 (0.005)♂ -0.51 (0.01)**♀ -0.47 (0.008)** |
|  CCL2  | LD-LPS | -0.14 (0.02) | **0.50 (0.26)** | 0.06 (0.30) | -0.29 (0.03)♂ -0.71 (0.02)♀ -0.12 (0.05) | -0.19 (0.005) |
| HD-LPS | -0.32 (0.02) | **0.63 (0.29)** | -0.02 (0.39) | -0.19 (0.04) | -0.12 (0.006) |
|  CCL3  | LD-LPS | -0.29 (0.02) | -0.02 (0.36) | 0.19 (0.36) | 0.09 (0.04) | 0.04 (0.006) |
| HD-LPS | -0.08 (-0.006) | -0.30 (0.24) | 0.02 (0.26) | 0.28 (0.03) | 0.16 (0.004) |
|  CCL4 | LD-LPS | -0.05 (0.02) | 0.14 (0.28) | 0.14 (0.29) | 0.19 (0.03) | 0.15 (0.004) |
| HD-LPS | -0.06 (0.01)♂ -0.003 (0.02)♀ -0.07 (0.05) | 0.14 (0.21) | -0.07 (0.21) | 0.26 (0.02) | 0.17 (0.003) |
| **Ex-vivo** |
|  Inflammatory index |  | -0.23 (0.02) | -0.10 (0.27) | -0.33 (0.26) | 0.31 (0.03) | **0.43 (0.004)** |
|  Pro-inflammatory index |  | -0.07 (0.02) | -0.16 (0.21) | -0.33 (0.21) | 0.38 (0.02) | 0.37 (0.003) |
|  Anti-inflammatory index |  | -0.27 (0.03) | -0.04 (0.38) | -0.28 (0.38) | 0.22 (0.04) | 0.39 (0.005) |
|  Ratio pro/anti inflammatory index |  | -0.13 (0.33) | 0.29 (4.72) | 0.29 (4.72) | -0.34 (0.47) | -0.33 (0.07) |
|  hsCRP |  | -0.11 (0.03)  | -0.10 (0.39)  | -0.26 (0.39)  | **0. 36 (0.04)** | 0.29 (0.01) |
|  TNF-α |  | **-0.41 (0.01)** | -0.19 (0.20) | -0.03 (0.22) | **0.21 (0.02)** | 0.40 (0.003) |
|  sTNF-R2 |  | -0.28 (0.01) | 0.02 (0.11) | -0.18 (0.11) | 0.18 (0.01) | 0.38 (0.002) |
|  Il-1β |  | - | - | - | - | - |
|  IL-1RA |  | -0.20 (0.01) | -0.10 (0.19) | -0.32 (0.18) | 0.20 (0.02) | -0.17 (0.03) |

Data represent standardized regression coefficient β (standard error, unstandardized B) of various lifestyle factors demonstrating an association with *ex-vivo* and *in-vitro* inflammatory indexes and of *in-vitro* and *ex-vivo* single inflammatory mediators using linear regression analysis. All single neuroimmune responses are ln-transformed. The *in-vitro* neuroimmune responses are normalized for monocyte count. Significant values are in bold font (\*p < 0.05). TNF-α, tumor necrosis factor -α; IL-1β, interleukin -1β; IL-1RA, interleukin -receptor antagonist; IL-4, interleukin – 4; IL-10, interleukin -10; CCL2 / MCP1, c-c-motif ligand 2 also referred to as monocyte chemoattractant protein 1; CCL3 / MIP1α, c-c-motif ligand 3 also referred to as macrophage inflammatory protein 1α; CCL4 / MIP1β, c-c-motif ligand 4 also referred to as macrophage inflammatory protein 1β; TNFα : IL-10, ratio between TNFα : IL-10; IL-1β : IL-1RA, ratio between IL-1β : IL-1RA; 1ng/ml (LD-LPS), 1 milliliter whole-blood stimulation with 1 nanogram TLR4 agonist lipopolysacharide; 10µg/ml (HD-LPS), 1 milliliter whole blood stimulation with 10 microgram of TLR4 agonist lipopolysacharide; ♂ effect modification for males; ♀ effect modification for females.

aRefers to 1000/metabolic equivalent of a task

bRefers to current smoker, yes:1, no:0

cRefers to consuming alcohol, yes:1, no:0

dRefers to linear distance in millimeters between the posterior aspect of peritoneum and anterior aspect of lumbar vertebra T10

**SUPPLEMENTARY G2** Association of clinical factors with neuroimmune responses in people with a cervical radiculopathy

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Pain intensitya** | **Disabilityb** | **Sexc** | **Central Sensitizationd** | **Number of co-morbidities** | **Insomniae**  |
|  | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** |
| **In-vitro** |  |
|  Inflammatory index | LD-LPS | 0.25 (0.01) | 0.2 (0.01) | -0.10 (0.35) | -0.19 (0.37) | 0.04 (0.14) | -0.30 (0.37) |
| HD-LPS | 0.15 (0.01)♂ 0.30 (0.01)♀ 0.05 (0.03) | **0.42 (0.01)**♂ 0.20 (0.01)♀ 0.77 (0.02) | -0.31 (0.31) | 0.11 (0.34) | 0.16 (0.12) | -0.27 (0.33) |
|  Pro-inflammatory index | LD-LPS | 0.23 (0.01) | 0.01 (0.01) | -0.10 (0.36) | -0.15 (0.38) | 0.10 (0.14) | -0.25 (0.37) |
| HD-LPS | 0.15 (0.01) | 0.36 (0.01)♂ 0.13 (0.01)♀ 0.74 (0.02) | -0.29 (0.33) | 0.11 (0.36) | 0.17 (0.13) | -0.18 (0.36) |
|  Anti-inflammatory index | LD-LPS | 0.16 (0.01) | 0.04 (0.01) | -0.10 (0.40) | -0.27 (0.41) | -0.11 (0.16) | -0.36 (0.40) |
| HD-LPS | 0.11 (0.01)♂ 0.35 (0.01)♀ -0.14 (0.03) | **0.47 (0.01)**♂ 0.28 (0.01)♀ 0.67 (0.02) | -0.19 (0.36) | 0.10 (0.39)♂ -0.46 (0.38)♀ **1.16 (0.57)** | 0.10 (0.14) | -0.41 (0.36) |
|  Ratio pro/anti inflammatory index | LD-LPS | -0.13 (0.06) | -0.06 (0.06) | 0.19 (1.64) | -0.03 (1.77) | -0.17 (0.39) | -0.23 (1.74) |
| HD-LPS | -0.29 (0.12) | **-0.47 (0.10)** | -0.17 (3.39) | -0.24 (3.54) | 0.15 (1.34) | 0.06 (3.68) |
|  TNF-α | LD-LPS | 0.37 (0.02) | -0.07 (0.02) | 0.08 (0.54) | -0.46 (0.52) | -0.26 (0.20) | -0.06 (0.58) |
| HD-LPS | 0.03 (0.02) | 0.18 (0.01) | -0.05 (0.43) | -0.16 (0.45) | 0.05 (0.17) | -0.007 (0.46) |
|  IL-1β | LD-LPS | 0.38 (0.02) | -0.06 (0.02) | 0.11 (0.55) | -0.38 (0.55) | 0.01 (0.22) | -0.09 (0.59) |
| HD-LPS | 0.13 (0.01) | 0.29 (0.01) | -0.12 (0.31) | 0.02 (0.33) | 0.16 (0.12) | -0.02 (0.34) |
|  IL-1RA | LD-LPS | 0.32 (0.009) | 0.22 (0.008) | -0.21 (0.25) | -0.42 (0.25)♂ 0.98 (0.24)♀ -0.62 (0.26) | -0.25 (0.09) | -0.32 (0.26) |
| HD-LPS | **0.51 (0.006)** | **0.54 (0.006)** | -0.23 (0.20) | -0.29 (0.21) | -0.09 (0.08) | -0.34 (0.21) |
|  IL-4 | LD-LPS | - | **-** | - | - | - | - |
| HD-LPS | - | **-** | - | - | - | **-** |
|  IL-10 | LD-LPS | 0.12 (0.02) | -0.15 (0.01) | 0.04 (0.41) | -0.05 (0.43) | 0.06 (0.16) | -0.30 (0.42) |
| HD-LPS | -0.34 (0.01) | 0.19 (0.01) | -0.22 (0.37) | 0.45 (0.36)♂ 1.07 (0.85)♀ 0.04 (0.35) | 0.24 (0.14) | -0.30 (0.38) |
|  CCL2  | LD-LPS | -0.22 (0.01) | 0.31 (0.01) | -0.28 (0.29) | **0.59 (0.27)**♂ 0.57 (0.62)♀ | **0.49 (0.10)** | -0.30 (0.31) |
| HD-LPS | 0.23 (0.01) | 0.10 (0.01) | -0.18 (0.39) | 0.13 (0.41) | 0.08 (0.15) | -0.19 (0.41) |
|  CCL3  | LD-LPS | 0.15 (0.01) | -0.16 (0.01) | -0.02 (0.37) | -0.24 (0.38) | 0.12 (0.14) | -0.18 (0.39) |
| HD-LPS | -0.07 (0.009) | 0.27 (0.008) | -0.29 (0.25) | 0.13 (0.27) | 0.27 (0.09) | -0.09 (0.28) |
|  CCL4 | LD-LPS | 0.18 (0.01) | 0.03 (0.01) | -0.25 (0.28) | -0.06 (0.31) | 0.01 (0.12) | -0.32 (0.30) |
| HD-LPS | 0.21 (0.007) | **0.44 (0.006)**♂ 0.93 (0.009)♀ 0.29 (0.008) | -0.39 (0.20) | 0.26 (0.22)♂ 1.11 (0.36)♀ -0.04 (0.27) | 0.04 (0.08) | -0.32 (0.22) |
| **Ex-vivo** |  |
|  Inflammatory index |  | 0.01 (0.22) | 0.11 (0.01) | -0.04 (0.28) | -0.34 (0.26) | -0.28 (0.11) | -0.03 (0.29) |
|  Pro-inflammatory index |  | **0.42 (0.008)** | 0.32 (0.008) | -0.007 (0.22) | -0.29 (0.21) | -0.25 (0.09) | 0.16 (0.23) |
|  Anti-inflammatory index |  | 0.08 (0.02) | -0.01 (0.01) | -0.06 (0.39) | -0.30 (0.37) | -0.25 (0.16) | -0.13 (0.41) |
|  Ratio pro/anti inflammatory index |  | -0.17 (0.18) | -0.25 (0.17) | 0.43 (4.38) | -0.29 (0.21) | 0.26 (1.89) | 0.03 (5.21) |
|  hsCRP |  | **0.45 (0.01)** | 0.38 (0.01) | 0.05 (0.41) | -0.29 (0.38) | -0.21 (0.16) | **0.13 (0.43)** |
|  TNF-α |  | 0.05 (0.01) | 0.07 (0.01) | -0.10 (0.21) | -0.24 (0.21) | -0.32 (0.08) | 0.02 (0.23) |
|  sTNF-R2 |  | -0.16 (0.004) | -0.13 (0.004) | -0.10 (0.11) | -0.28 (0.11) | -0.21 (0.05) | -0.24 (0.11) |
|  Il-1β |  | - | - | - | - | - | - |
|  IL-1RA |  | -0.30 (0.01) | 0.10 (0.01) | 0.01 (0.19) | -0.26 (0.19) | -0.23 (0.08) | 0.01 (0.20) |

Data represent standardized regression coefficient β (standard error, unstandardized B) of various clinical factors demonstrating an association with *ex-vivo* and *in-vitro* inflammatory indexes and of *in-vitro* and *ex-vivo* single inflammatory mediators using linear regression analysis. All single neuroimmune responses are ln-transformed. The *in-vitro* neuroimmune responses are normalized for monocyte count. Significant values are in bold font (\*p < 0.05) TNF-α, tumor necrosis factor -α; IL-1β, interleukin -1β; IL-1RA, interleukin -receptor antagonist; IL-4, interleukin – 4; IL-10, interleukin -10; CCL2 / MCP1, c-c-motif ligand 2 also referred to as monocyte chemoattractant protein 1; CCL3 / MIP1α, c-c-motif ligand 3 also referred to as macrophage inflammatory protein 1α; CCL4 / MIP1β, c-c-motif ligand 4 also referred to as macrophage inflammatory protein 1β; TNFα : IL-10, ratio between TNFα : IL-10; IL-1β : IL-1RA, ratio between IL-1β : IL-1RA; 1ng/ml (LD-LPS), 1 milliliter whole-blood stimulation with 1 nanogram TLR4 agonist lipopolysacharide; 10µg/ml (HD-LPS), 1 milliliter whole blood stimulation with 10 microgram of TLR4 agonist lipopolysacharide; ♂ effect modification for males; ♀ effect modification for females.

aRefers to pain intensity measured on the visual analogue scale, 0-100

bRefers to score on the neck disability index, 0-100

cMale:0 Female:1

dRefers to total score on the central sensitisation questionnaire higher than 40

eRefers having insomnia (pittsburg sleep quality index score above 5)

**SUPPLEMENTARY G3** Association of psychological factors with neuroimmune responses in people with a cervical radiculopathy

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Mental Healtha**  | **Stressb** | **Depressionc** | **Anxietyd** | **Kinesiophobiae** | **Pain rumination** | **Pain magnification** | **Pain helplessness** | **Catastrophizingf** |
|  | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** |
| **In-vitro** |
|  Inflammatory index | LD-LPS | -0.13 (0.01) | -0.02 (0.02) | 0.10 (0.02) | 0.07 (0.02)♂ -0.41 (0.03)♀ **0.93 (0.02)** | 0.32 (0.37)♂ 0.27 (0.52)♀ **0.82 (0.56)** | 0.27 (0.04) | **0.53 (0.06)** | 0.05 (0.03) | 0.28 (0.02) |
| HD-LPS | -0.11 (0.01) | 0.23 (0.02) | 0.25 (0.02) | 0.24 (0.02)♂ -0.25 (0.02)♀ **0.77 (0.02)** | 0.37 (0.33)♂ 0.26 (0.39)♀ **0.75 (0.55)** | 0.14 (0.04) | 0.15 (0.06) | 0.33 (0.03) | 0.28 (0.01) |
|  Pro-inflammatory index | LD-LPS | -0.10 (0.01) | -0.002 (0.02) | 0.12 (0.02) | 0.07 (0.02)♂ 0.37 (0.42)♀ **0.75 (0.62)** | 0.39 (0.36)♂ -0.41 (0.03)♀ **0.94 (0.02)** | 0.25 (0.04) | **0.59 (0.06)** | 0.08 (0.03) | 0.29 (0.02) |
| HD-LPS | -0.07 (0.01) | 0.21 (0.02) | 0.25 (0.02) | 0.22 (0.02)♂ -0.28 (0.02)♀ **0.80 (0.02)** | 0.41 (0.34) | 0.15 (0.04) | 0.26 (0.06) | 0.36 (0.03) | 0.33 (0.02) |
|  Anti-inflammatory index | LD-LPS | -0.17 (0.01) | -0.07 (0.20) | 0.05 (0.02) | 0.06 (0.02) | 0.13 (0.43) | 0.27 (0.05) | 0.33 (0.07) | 0.001 (0.04) | 0.19 (0.02) |
| HD-LPS | -0.16 (0.01)♂ 0.23 (0.01)♀ **-0.94 (0.01)** | 0.23 (0.02)♂ -0.37 (0.02)♀ 0.85 (0.02) | 0.21 (0.02)♂ -0.26 (0.02)♀ **0.79 (0.03)** | 0.23 (0.02)♂ -0.10 (0.03)♀ 0.52 (0.03) | 0.18 (0.39)♂ -0.07 (0.47)♀ 0.59 (0.76) | 0.008 (0.04)♂ -0.04 (0.05)♀ 0.53 (0.09) | -0.15 (0.07)♂ -0.54 (0.07)♀ 0.55 (0.12) | 0.16 (0.03)♂ -0.08 (0.03)♀ 0.47 (0.06) | 0.10 (0.02) |
|  Ratio pro/anti inflammatory index | LD-LPS | 0.01 (0.06) | 0.13 (0.08) | 0.23 (0.09) | -0.03 (0.09) | 0.12 (1.79) | 0.30 (0.19) | 0.09 (0.31) | 0.05 (0.15) | 0.17 (0.08) |
| HD-LPS | **0.53 (0.11)** | -0.29 (0.16) | -0.35 (0.19) | **-0.54 (0.16)** | -0.39 (3.45) | -0.37 (0.38) | **-0.55 (0.57)** | -0.49 (0.27) | **-0.55 (0.14)** |
|  TNF-α | LD-LPS | 0.007 (0.02) | -0.22 (0.03) | -0.04 (0.03) | -0.04 (0.03) | 0.16 (0.58) | 0.19 (0.06) | 0.50 (0.09) | -0.05 (0.05) | 0.18 (0.02) |
| HD-LPS | 0.17 (0.02) | 0.01 (0.02) | 0.06 (0.03) | -0.03 (0.02) | 0.12 (0.46) | -0.007 (0.05) | -0.07 (0.08) | 0.21 (0.04) | 0.11 (0.02) |
|  IL-1β | LD-LPS | 0.009 (0.02) | -0.17 (0.03) | -0.05 (0.03) | 0.01 (0.03) | 0.34 (0.57) | 0.28 (0.06) | 0.49 (0.09) | -0.06 (0.05) | 0.21 (0.03) |
| HD-LPS | 0.03 (0.01) | 0.17 (0.01)♂ 1.06 (0.02)♀ -0.43 (0.02) | 0.21 (0.02)♂ 1.13 (0.02)♀ -0.32 (0.02) | 0.20 (0.02)♂ 0.89 (0.02)♀ -0.32 (0.02) | 0.36 (0.32)♂ 0.80 (0.61)♀ 0.20 (0.41) | 0.10 (0.04) | 0.16 (0.06) | 0.36 (0.03) | 0.28 (0.01) |
|  IL-1RA | LD-LPS | -0.02 (0.009) | -0.16 (0.01)**♂ 1.14 (0.009)**♀ -0.51 (0.01) | -0.009 (0.02)**♂ 1.05 (0.009)**♀ -0.31 (0.02) | 0.009 (0.01)♂ 0.94 (0.009)♀ -0.37 (0.02) | 0.04 (0.28) | 0.31 (0.03) | 0.25 (0.05) | 0.11 (0.02) | 0.25 (0.01) |
| HD-LPS | 0.05 (0.007) | -0.07 (0.01)♂ 1.04 (0.005)♀ -0.64 (0.02) | 0.001 (0.01)♂ 0.92 (0.006)♀ -0.03 (0.02) | 0.09 (0.01) | 0.06 (0.22) | 0.16 (0.02) | -0.09 (0.04) | 0.11 (0.02) | 0.11 (0.009) |
|  IL-4 | LD-LPS | - | - | - | - | - | - | - | - | - |
| HD-LPS | - | - | - | - | - | - | - | - | - |
|  IL-10 | LD-LPS | -0.27 (0.01) | 0.05 (0.02) | 0.10 (0.02) | 0.10 (0.02) | 0.19 (0.43) | 0.15 (0.05) | 0.32 (0.07) | -0.11 (0.04) | 0.09 (0.02) |
| HD-LPS | -0.30 (0.01) | 0.43 (0.02) | 0.32 (0.02)♂ 0.60 (0.04)♀ | 0.28 (0.02) | 0.23 (0.39) | -0.04 (0.04) | -0.13 (0.07) | 0.15 (0.03) | 0.04 (0.02) |
|  CCL2  | LD-LPS | -0.20 (0.01) | **0.49 (0.01)** | 0.24 (0.02) | 0.30 (0.02) | **0.45 (0.29)** | -0.14 (0.04) | 0.23 (0.06) | 0.18 (0.03) | 0.10 (0.01) |
| HD-LPS | -0.24 (0.01) | 0.15 (0.02) | 0.04 (0.02) | 0.21 (0.02) | 0.41 (0.39) | 0.13 (0.05) | **0.56 (0.06)** | -0.12 (0.03) | 0.13 (0.02)♂ 0.30 (0.03)♀0.04 (0.02) |
|  CCL3  | LD-LPS | 0.02 (0.01) | -0.15 (0.02) | 0.04 (0.02) | -0.09 (0.02) | 0.33 (0.38) | 0.32 (0.04) | **0.55 (0.06)** | 0.06 (0.03) | 0.30 (0.02) |
| HD-LPS | 0.08 (0.009) | 0.14 (0.01) | 0.14 (0.02)♂ 0.76 (0.02)♀ -0.17 (0.02) | 0.08 (0.01)♂ 0.51 (0.02)♀ -0.21 (0.02) | 0.30 (0.27) | 0.05 (0.03) | 0.01 (0.05) | 0.38 (0.02) | 0.24 (0.01) |
|  CCL4 | LD-LPS | -0.22 (0.01) | 0.04 (0.01)**♂ 1.16 (0.01)**♀ -0.43 (0.02) | 0.25 (0.02) | 0.08 (0.02)♂ 0.88 (0.02)♀ -0.31 (0.02) | 0.18 (0.31) | 0.28 (0.03) | 0.43 (0.05) | 0.15 (0.03) | 0.31 (0.01) |
| 10ug/ml | -0.31 (0.007) | 0.29 (0.01)♂ 1.16 (0.006)♀ -0.19 (0.01) | 0.42 (0.01)♂ 1.03 (0.008)♀ 0.14 (0.02) | 0.32 (0.01)♂ 0.78 (0.01)♀ 0.05 (0.02) | 0.27 (0.22)♂ 0.73 (0.35)♀ 0.28 (0.28) | 0.26 (0.03)♂ 0.70 (0.04)♀ 0.30 (0.03) | 0.28 (0.04)♂ 0.73 (0.05)♀ 0.11 (0.05) | 0.46 (0.02)♂ 0.71 (0.03)♀ 0.23 (0.03) | 0.44 (0.009) |
| **Ex-vivo** |
|  Inflammatory index |  | **0.54 (0.009)** | -0.30 (0.01) | -0.28 (0.02) | -0.29 (0.01) | -0.36 (0.29) | -0.13 (0.03) | -0.32 (0.04) | -0.24 (0.02) | -0.24 (0.01) |
|  Pro-inflammatory index |  | **0.47 (0.008)** | -0.27 (0.01) | -0.21 (0.01) | -0.19 (0.01) | -0.29 (0.24) | -0.08 (0.02) | -0.18 (0.03) | -0.04 (0.02) | -0.10 (0.008) |
|  Anti-inflammatory index |  | **0.49 (0.01)** | -0.27 (0.02) | -0.28 (0.02) | -0.29 (0.02) | -0.34 (0.41) | -0.14 (0.04) | -0.35 (0.06) | -0.31 (0.03) | -0.28 (0.01) |
|  Ratio pro/anti inflammatory index |  | 0.31 (0.18) | -0.33 (0.22) | **-**0.35 (0.26) | **-0.46 (0.24)** | -0.09 (5.52) | 0.009 (0.52) | -0.11 (0.75) | -0.13 (0.37) | -0.10 (0.18) |
|  hsCRP |  | 0.36 (0.01) | -0.27 (0.02) | -0.21 (0.02) | -0.18 (0.02) | -0.21 (0.43) | -0.07 (0.04) | -0.19 (0.06) | 0.01 (0.03) | -0.07 (0.02) |
|  TNF-α |  | **0.47 (0.01)** | -0.24 (0.01) | -0.24 (0.01) | -0.15 (0.01) | -0.18 (0.24) | -0.17 (0.02) | -0.25 (0.03) | -0.29 (0.02*)* | -0.26 (0.01) |
|  sTNF-R2 |  | **0.47 (0.004)** | -0.24 (0.01) | 0.23 (0.01) | -0.36 (0.01) | **-0.42 (0.11)** | -0.2 (0.01) | -0.38 (0.02) | -0.27 (0.07) | -0.30(0.004) |
|  Il-1β |  | **-** | **-** | - | - | - | **-** | **-** | *-* | **-** |
|  IL-1RA |  | 0.40 (0.01) | -0.24 (0.01) | -0.27 (0.01) | -0.17 (0.01) | -0.177 (0.21) | -0.04 (0.02) | -0.24 (0.28) | -0.28 (0.01) | 0.21 (0.01) |

Data represent standardized regression coefficient-β (standard error, unstandardized B) of various psychological factors demonstrating an association with several neuroimmune responses *ex-vivo* and after *in-vitro* whole blood stimulation using linear regression models. All neuroimmune responses are Ln-transformed. The *in-vitro* neuroimmune responses are normalized for monocyte count. Significant values are in bold font (\*p < 0.05). TNF-α, tumor necrosis factor -α; IL-1β, interleukin -1β; IL-1RA, interleukin -receptor antagonist; IL-4, interleukin – 4; IL-10, interleukin -10; CCL2 / MCP1, c-c-motif ligand 2 also referred to as monocyte chemoattractant protein 1; CCL3 / MIP1α, c-c-motif ligand 3 also referred to as macrophage inflammatory protein 1α; CCL4 / MIP1β, c-c-motif ligand 4 also referred to as macrophage inflammatory protein 1β; TNFα : IL-10, ratio between TNFα : IL-10; IL-1β : IL-1RA, ratio between IL-1β : IL-1RA; 1ng/ml (LD-LPS), 1 milliliter whole-blood stimulation with 1 nanogram TLR4 agonist lipopolysacharide; 10µg/ml (HD-LPS), 1 milliliter whole blood stimulation with 10 microgram of TLR4 agonist lipopolysacharide; ♂ effect modification for males; ♀ effect modification for females.

aRefers to mental health inventory -5 score

bRefers to score on the depression, anxiety and stress scale 21 subsection stress

cRefers to the score on the depression, anxiety and stress scale 21 subsection depression

dRefers to the score on the depression, anxiety and stress scale 21 subsection anxiety

eRefers to total score on the tampa scale questionnaire higher than 37

fRefers to the total score on the pain catastrophising scale

**SUPPLEMENTARY H1** Association of lifestyle factors with neuroimmune responses in healthy participants

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Physical Activitya**  | **Smokingb** | **Alcohol usec** | **BMI** | **Visceral Adiposed**  |
|  | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** |
| **In-vitro** |
|  Inflammatory index | LD-LPS | 0.04 (0.02) | 0.31 (0.58) | -0.17 (0.32) | **-0.40 (0.03)** | -0.20 (0.007) |
| HD-LPS | 0.14 (0.02) | **0.59 (0.54)** | -0.18 (0.32) | 0.08 (0.03) | -0.16 (0.007) |
|  Pro-inflammatory index | LD-LPS | 0.04 (0.02) | 0.27 (0.60) | -0.17 (0.33) | **-0.40 (0.03)** | -0.22 (0.007) |
| HD-LPS | 0.10 (0.02) | 0.43 (0.57) | -0.24 (0.32) | 0.14 (0.03) | -0.12 (0.007) |
|  Anti-inflammatory index | LD-LPS | 0.03 (0.02) | 0.37 (0.60) | -0.15 (0.35) | **-0.38 (0.03)** | -0.16 (0.007) |
| HD-LPS | 0.16 (0.03) | **0.74 (0.67)** | -0.003 (0.45) | -0.07 (0.04) | -0.18 (0.009) |
|  Ratio pro/anti inflammatory index | LD-LPS | 0.34 (0.03) | -0.06 (1.07) | -0.18 (0.57) | 0.15 (0.06) | 0.19 (0.01) |
| HD-LPS | -0.26 (0.13) | -0.07 (4.46) | -0.10 (2.39) | -0.24 (0.23) | -0.40 (0.05) |
|  TNF-α | LD-LPS | 0.07 (0.02) | 0.03 (0.73) | -0.10 (0.39) | **-0.42 (0.03)** | -0.19 (0.008) |
| HD-LPS | 0.11 (0.02) | 0.18 (0.64) | -0.27 (0.33) | **0.52 (0.03)** | -0.05 (0.007) |
|  IL-1β | LD-LPS | -0.02 (0.04) | 0.14 (1.19) | -0.19 (0.63) | **-0.56 (0.05)** | -0.28 (0.01) |
| HD-LPS | 0.10 (0.02) | 0.32 (0.51) | -0.32 (0.26) | 0.21 (0.03) | 0.04 (0.006) |
|  IL-1RA | LD-LPS | -0.003 (0.01) | 0.33 (0.42) | -0.12 (0.24)♂ 0.13 (0.22)♀ -0.71 (0.47) | **-0.40 (0.02)** | -0.12 (0.005) |
| HD-LPS | -0.02 (0.01) | 0.55 (0.29) | -0.05 (0.17) | -0.25 (0.02) | -0.05 (0.004) |
|  IL-4 | LD-LPS | - | - | - | - | - |
| HD-LPS | **-** | **-** | **-** | **-** | **-** |
|  IL-10 | LD-LPS | 0.06 (0.02) | **0.37 (0.59)** | -0.17 (0.34) | **-0.31 (0.03)** | -0.19 (0.007) |
| HD-LPS | 0.29 (0.02) | **0.64 (0.52)** | 0.04 (0.32) | 0.13 (0.03) | -0.23 (0.007) |
|  CCL2  | LD-LPS | 0.03 (0.02) | **0.63 (0.63)** | -0.15 (0.37) | 0.31 (0.04) | 0.07 (0.008) |
| HD-LPS | -0.06 (0.02) | 0.30 (0.79) | 0.17 (0.43) | -0.39 (0.04) | 0.17 (0.009) |
|  CCL3  | LD-LPS | 0.05 (0.02) | 0.13 (0.69) | -0.09 (0.38) | **-0.51 (0.03)** | -0.18 (0.008) |
| HD-LPS | 0.21 (0.02) | 0.27 (0.39) | -0.16 (0.21) | 0.11 (0.02) | -0.18 (0.004) |
|  CCL4 | LD-LPS | 0.008 (0.01) | 0.11 (0.46) | -0.13 (0.24) | **-0.36 (0.02)** | -0.28 (0.005) |
| HD-LPS | -0.04 (0.009) | 0.19 (0.29) | -0.18 (0.15) | 0.005 (0.02) | **-0.37 (0.003)** |
| **Ex-vivo** |
| Inflammatory index |  | 0.24 (0.02) | 0.19 (0.54) | 0.08 (0.39) | 0.23 (0.04) | **0.52 (0.006)** |
|  Pro-inflammatory index |  | 0.16 (0.02) | 0.10 (0.63) | -0.05 (0.44) | 0.37 (0.04) | 0.19 (0.41) |
|  Anti-inflammatory index |  | 0.27 (0.02) | 0.25 (0.58) | 0.19 (0.41) | 0.04 (0.04) | 0.39 (0.007) |
|  Ratio pro/anti inflammatory index |  | 0.34 (0.66) | **-0.61 (17.8)** | -0.14 (16.4) | -0.34 (1.40) | -0.14 (16.4) |
|  hsCRP |  | -0.28 (0.02) | 0.11 (0.64) | 0.18 (0.47) | **0.47 (0.04)** | 0.40 (0.008) |
|  TNF-α |  | 0.44 (0.01) | -0.08 (0.37) | -0.25 (0.25) | 0.10 (0.02) | 0.55 (0.004) |
|  sTNF-R2 |  | **0.46 (0.005)** | -0.29 (0.17) | 0.21 (0.12) | -0.01 (0.01) | **0.49 (0.002)** |
|  Il-1β |  | 0.33 (0.06) | 0.29 (2.52) | 0.64 (1.84) | 0.22 (0.27) | 0.31 (0.03) |
|  IL-1RA |  | -0.05 (0.009) | **0.67 (0.22)** | 0.08 (0.21) | 0.07 (0.02) | 0.10 (0.004) |

Data represent standardized regression coefficient β (standard error, unstandardized B) of various lifestyle factors demonstrating an association with *ex-vivo* and *in-vitro* inflammatory indexes and of *in-vitro* and *ex-vivo* single inflammatory mediators using linear regression analysis. All single neuroimmune responses are ln-transformed. The *in-vitro* neuroimmune responses are normalized for monocyte count. Significant values are in bold font (\*p < 0.05). TNF-α, tumor necrosis factor -α; IL-1β, interleukin -1β; IL-1RA, interleukin -receptor antagonist; IL-4, interleukin – 4; IL-10, interleukin -10; CCL2 / MCP1, c-c-motif ligand 2 also referred to as monocyte chemoattractant protein 1; CCL3 / MIP1α, c-c-motif ligand 3 also referred to as macrophage inflammatory protein 1α; CCL4 / MIP1β, c-c-motif ligand 4 also referred to as macrophage inflammatory protein 1β; TNFα : IL-10, ratio between TNFα : IL-10; IL-1β : IL-1RA, ratio between IL-1β : IL-1RA; 1ng/ml (LD-LPS), 1 milliliter whole-blood stimulation with 1 nanogram TLR4 agonist lipopolysacharide; 10µg/ml (HD-LPS), 1 milliliter whole blood stimulation with 10 microgram of TLR4 agonist lipopolysacharide; ♂ effect modification for males; ♀ effect modification for females.

aRefers to 1000/metabolic equivalent of a task

bRefers to current smoker, yes:1, no:0

cRefers to consuming alcohol, yes:1, no:0

dRefers to linear distance in millimeters between the posterior aspect of peritoneum and anterior aspect of lumbar vertebra T10

**SUPPLEMENTARY H2** Association of clinical factors with neuroimmune responses in healthy participants

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Pain intensitya** | **Disabilityb** | **Sexc** | **Central Sensitizationd** | **Number of co-morbidities** | **Insomniad**  |
|  | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** |
| **In-vitro** |
|  Inflammatory index | LD-LPS | N/A | 0.14 (0.02) | 0.21 (0.28) | 0.18 (0.45) | **-0.42 (0.29)** | 0.04 (0.08) |
| HD-LPS | N/A | 0.32 (0.02) | 0.23 (0.28) | 0.33 (0.43) | **-0.52 (0.30)** | 0.12 (0.08) |
|  Pro-inflammatory index | LD-LPS | N/A | 0.14 (0.02) | 0.17 (0.28) | 0.16 (0.45) | **-0.45 (0.29)** | 0.02 (0.08) |
| HD-LPS | N/A | 0.27 (0.02) | 0.08 (0.29) | 0.24 (0.44) | **-0.49 (0.31)** | 0.06 (0.08) |
|  Anti-inflammatory index | LD-LPS | N/A | 0.12 (0.02) | 0.27 (0.29) | 0.21 (0.47) | **-0.35 (0.34)** | 0.08 (0.08) |
| HD-LPS | N/A | 0.32 (0.02) | **0.47 (0.34)** | 0.41 (0.56) | **-0.43 (0.45)** | 0.19 (0.10) |
|  Ratio pro/anti inflammatory index | LD-LPS | N/A | 0.06 (0.03) | -0.14 (0.50) | 0.06 (0.80) | 0.21 (0.64) | 0.05 (0.14) |
| HD-LPS | N/A | -0.02 (0.12) | 0.17 (2.08) | -0.08 (3.33) | **-0.68 (1.97)** | -0.16 (0.56) |
|  TNF-α | LD-LPS | N/A | 0.003 (0.02) | 0.18 (0.33) | 0.03 (0.55) | -0.23 (0.42) | -0.08 (0.09) |
| HD-LPS | N/A | 0.25 (0.02) | -0.06 (0.31) | 0.26 (0.47) | -0.20 (0.39) | -0.13 (0.08) |
|  IL-1β | LD-LPS | N/A | 0.15 (0.03) | 0.32 (0.53) | 0.17 (0.88) | **-0.39 (0.64)** | 0.09 (0.15) |
| HD-LPS | N/A | 0.32 (0.01) | 0.03 (0.25) | 0.27 (0.37) | -0.27 (0.31) | 0.19 (0.07) |
|  IL-1RA | LD-LPS | N/A | 0.06 (0.01) | 0.35 (0.19) | 0.15 (0.33) | -0.25 (0.26) | 0.07 (0.06) |
| HD-LPS | N/A | 0.21 (0.008) | **0.50 (0.13)** | 0.29 (0.23) | -0.28 (0.19) | 0.23 (0.04) |
|  IL-4 | LD-LPS | - | **-** | - | - | - | - |
| HD-LPS | - | **-** | - | - | **-** | - |
|  IL-10 | LD-LPS | N/A | 0.17 (0.02) | 0.16 (0.30) | 0.24 (0.45) | **-0.41 (0.28)** | 0.08 (0.08) |
| HD-LPS | N/A | 0.31 (0.02) | 0.25 (0.27) | 0.36 (0.42) | -0.41 (0.33) | 0.08 (0.08) |
|  CCL2  | LD-LPS | N/A | 0.27 (0.02) | -0.27 (0.32) | 0.25 (0.51) | **-0.47 (0.38)** | 0.13 (0.09) |
| HD-LPS | N/A | 0.06 (0.02) | -0.08 (0.39) | 0.002 (0.61) | -0.33 (0.47) | 0.04 (0.10) |
|  CCL3  | LD-LPS | N/A | 0.09 (0.02) | 0.23 (0.31) | 0.10 (0.52) | -0.29 (0.39) | 0.02 (0.09) |
| HD-LPS | N/A | 0.23 (0.01) | 0.15 (0.19) | 0.16 (0.29) | -0.32 (0.23) | 0.15 (0.05) |
|  CCL4 | LD-LPS | N/A | 0.03 (0.01) | 0.20 (0.21) | 0.06 (0.35) | **-0.35 (0.23)** | -0.06 (0.06) |
| HD-LPS | N/A | -0.16 (0.03) | 0.001 (0.008) | 0.21 (0.13) | **-0.42 (0.14)** | 0.06 (0.22) |
| **Ex-vivo** |
|  Inflammatory index |  | N/A | 0.21 (0.02) | -0.13 (0.30) | 0.21 (0.52) | 0.19 (0.43) | -0.40 (0.08) |
|  Pro-inflammatory index |  | N/A | 0.24 (0.02) | -0.16 (0.34) | 0.19 (0.59) | 0.25 (0.49) | -0.39 (0.09) |
|  Anti-inflammatory index |  | N/A | 0.14 (0.02) | -0.06 (0.33) | 0.19 (0.56) | 0.10 (0.47) | -0.34 (0.09) |
|  Ratio pro/anti inflammatory index |  | N/A | 0.10 (0.81) | -0.20 (12.64) | 0.20 (0.59) | -0.12 (18.6) | 0.12 (3.69) |
|  hsCRP |  | N/A | 0.16 (0.02) | -0.001 (0.37) | 0.03 (0.64) | 0.33 (0.51) | -0.27 (0.10) |
|  TNF-α |  | N/A | 0.27 (0.01) | -0.22 (0.20) | 0.29 (0.34) | 0.10 (0.29) | -0.29 (0.06) |
|  sTNF-R2 |  | N/A | -0.09 (0.006) | -0.31 (0.09) | -0.15 (0.17) | 0.14 (0.14) | -0.35 (0.03) |
|  Il-1β |  | N/A | -0.34 (0.15) | -0.39 (1.45) | N/A | 0.64 (1.84) | -0.02 (1.10) |
|  IL-1RA |  | N/A | 0.30 (0.01) | 0.21 (0.16) | **0.44 (0.25)** | 0.01 (0.23) | -0.16 (0.05) |

Data represent standardized regression coefficient β (standard error, unstandardized B) of various clinical factors demonstrating an association with *ex-vivo* and *in-vitro* inflammatory indexes and of *in-vitro* and *ex-vivo* single inflammatory mediators using linear regression analysis. All single neuroimmune responses are ln-transformed. The *in-vitro* neuroimmune responses are normalized for monocyte count. Significant values are in bold font (\*p < 0.05) TNF-α, tumor necrosis factor -α; IL-1β, interleukin -1β; IL-1RA, interleukin -receptor antagonist; IL-4, interleukin – 4; IL-10, interleukin -10; CCL2 / MCP1, c-c-motif ligand 2 also referred to as monocyte chemoattractant protein 1; CCL3 / MIP1α, c-c-motif ligand 3 also referred to as macrophage inflammatory protein 1α; CCL4 / MIP1β, c-c-motif ligand 4 also referred to as macrophage inflammatory protein 1β; TNFα : IL-10, ratio between TNFα : IL-10; IL-1β : IL-1RA, ratio between IL-1β : IL-1RA; 1ng/ml (LD-LPS), 1 milliliter whole-blood stimulation with 1 nanogram TLR4 agonist lipopolysacharide; 10µg/ml (HD-LPS), 1 milliliter whole blood stimulation with 10 microgram of TLR4 agonist lipopolysacharide; ♂ effect modification for males; ♀ effect modification for females.

aRefers to pain intensity measured on the visual analogue scale, 0-100

bRefers to score on the neck disability index, 0-100

cMale:0 Female:1

dRefers to total score on the central sensitisation questionnaire higher than 40

eRefers having insomnia (pittsburg sleep quality index score above 5)

**SUPPLEMENTARY H3** Association of psychological factors with neuroimmune responses in healthy partciipants

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Mental Healtha**  | **Stressb** | **Depressionc** | **Anxietyd** | **Kinesiophobiae** | **Pain rumination** | **Pain magnification** | **Pain helplessness** | **Catastrophizingf** |
|  | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** | **Standardized- adjusted** β **(SE)** |
| **In-vitro** |
|  Inflammatory index | LD-LPS | **-0.33 (0.01)** | 0.26 (0.02) | -0.05 (0.09) | 0.24 (0.06) | 0.27 (0.58) | -0.13 (0.03) | -0.10 (0.05) | -0.03 (0.04) | -0.10 (0.01) |
| HD-LPS | **-0.42 (0.01)** | 0.20 (0.02) | 0.04 (0.09) | -0.02 (0.06) | 0.19 (0.62) | -0.18 (0.03) | -0.19 (0.05) | -0.17 (0.04) | -0.19 (0.01) |
|  Pro-inflammatory index | LD-LPS | **-0.35 (0.01)** | 0.24 (0.02) | -0.06 (0.10) | 0.23 (0.06) | 0.31 (0.58) | -0.15 (0.03) | -0.13 (0.05) | -0.03 (0.04) | -0.12 (0.01) |
| HD-LPS | **-0.32 (0.01)** | 0.08 (0.02) | 0.003 (0.09) | -0.04 (0.06) | 0.18 (0.62) | -0.14 (0.03) | -0.19 (0.05) | -0.15 (0.04) | -0.17 (0.01) |
|  Anti-inflammatory index | LD-LPS | -0.28 (0.01) | 0.28 (0.02) | -0.02 (0.10) | 0.25 (0.06) | 0.17 (0.66) | -0.07 (0.03) | -0.03 (0.06) | -0.02 (0.05) | -0.05 (0.02) |
| HD-LPS | **-0.49 (0.02)** | 0.38 (0.03) | 0.11 (0.13) | 0.03 (0.08) | 0.16 (0.84) | -0.21 (0.03) | -0.14 (0.07) | -0.16 (0.06) | -0.19 (0.02) |
|  Ratio pro/anti inflammatory index | LD-LPS | 0.06 (0.02) | **-0.49 (0.03)** | -0.03 (0.17) | -0.20 (0.10) | **-0.48 (0.97)** | -0.15 (0.05) | -0.05 (0.09) | -0.33 (0.07) | 0.06 (0.03) |
| HD-LPS | -0.12 (0.10) | 0.09 (0.14) | -0.46 (0.61) | 0.05 (0.44) | **0.88 (2.22)** | -0.25 (0.18) | -0.05 (0.37) | -0.02 (0.31) | -0.15 (0.10) |
|  TNF-α | LD-LPS | -0.27 (0.02) | 0.04 (0.02) | -0.10 (0.11) | 0.001 (0.07) | 0.10 (0.75) | -0.25 (0.03) | -0.15 (0.06) | -0.008 (0.05) | -0.17 (0.02) |
| HD-LPS | -0.10 (0.02) | -0.08 (0.02) | 0.14 (0.10) | -0.20 (0.06) | -0.11 (0.67) | 0.12 (0.03) | -0.06 (0.05) | -0.002 (0.05) | 0.05 (0.02) |
|  IL-1β | LD-LPS | -0.24 (0.03) | 0.32 (0.04) | -0.02 (0.19) | 0.34 (1.13) | -0.21 (0.05) | -0.19 (0.10) | -0.08 (0.08) | -0.19 (0.03) | -0.003 (0.01) |
| HD-LPS | -0.08 (0.01) | -0.07 (0.02) | 0.05 (0.08) | -0.06 (0.05) | -0.09 (0.54) | -0.11 (0.02) | -0.17 (0.04) | 0.16 (0.04) | -0.15 (0.01) |
|  IL-1RA | LD-LPS | 0.23 (0.01) | 0.33 (0.01) | -0.03 (0.07) | 0.27 (0.04) | 0.08 (0.45) | -0.10 (0.02) | -0.04 (0.04) | 0.04 (0.03) | -0.05 (0.01) |
| HD-LPS | -0.13 (0.007)♂ -0.05 (0.006)♀ -0.17 (0.02) | 0.32 (0.01) | -0.12 (0.05) | 0.22 (0.03) | 0.12 (0.33) | -0.24 (0.01) | -0.08 (0.03) | -0.11 (0.02) | -0.18 (0.007) |
|  IL-4 | LD-LPS | - | - | - | - | - | - | - | - | - |
| HD-LPS | - | - | - | - | - | - | - | - | - |
|  IL-10 | LD-LPS | **-0.30 (0.01)** | 0.19 (0.02) | -0.01 (0.10) | 0.20 (0.06) | 0.23 (0.63) | -0.04 (0.03) | -0.02 (0.06) | -0.08 (0.05) | -0.05 (0.02) |
| HD-LPS | **-0.66 (0.01)** | 0.29 (0.02) | 0.29 (0.09) | -0.17 (0.06) | 0.13 (0.61) | -0.10 (0.03) | -0.14 (0.05) | -0.15 (0.04) | -0.14 (0.01) |
|  CCL2  | LD-LPS | -0.31 (0.02) | 0.19 (0.02) | -0.02 (0.11) | 0.18 (0.07) | 0.26 (0.70) | 0.22 (0.03) | 0.14 (0.06) | 0.04 (0.05) | 0.17 (0.02) |
| HD-LPS | -0.36 (0.02) | 0.28 (0.03) | 0.34 (0.08) | 0.39 (0.76) | -0.19 (0.03) | -0.04 (0.07) | 0.08 (0.06) | -0.09 (0.02) | -0,09 (0.01) |
|  CCL3  | LD-LPS | -0.29 (0.01) | 0.22 (0.02) | -0.02 (0.11) | 0.24 (0.07) | 0.19 (0.69) | -0.24 (0.03) | -0.19 (0.06) | -0.07 (0.05) | -0.19 (0.01) |
| HD-LPS | -0.33 (0.008) | 0.04 (0.01) | 0.13 (0.06) | -0.10 (0.04) | 0.05 (0.41) | -0.25 (0.02) | -0.29 (0.03) | -0.30 (0.03) | -0.30 (0.008) |
|  CCL4 | LD-LPS | -0.23 (0.01) | 0.17 (0.01) | -0.05 (0.07) | 0.13 (0.05) | **0.30 (0.41)** | -0.11 (0.02) | -0.09 (0.04) | -0.01 (0.03) | -0.09 (0.01) |
| HD-LPS | -0.06 (0.04) | -0.15 (0.006) | -0.02 (0.05) | -0.11 (0.03) | **0.33 (0.26)** | -0.006 (0.01) | -0.04 (0.02) | -0.07 (0.02) | -0.04 (0.006) |
| **Ex-vivo** |
|  Inflammatory index |  | **0.44 (0.01)** | -0.11 (0.02) | -0.21 (0.10) | 0.11 (0.07) | -0.03 (0.74) | 0.04 (0.03) | -0.03 (0.06) | 0.25 (0.05) | 0.10 (0.02) |
|  Pro- inflammatory index |  | **0.53 (0.02)** | -0.28 (0.03) | -0.23 (0.12) | -0.01 (0.08) | 0.01 (0.83) | -0.04 (0.04) | -0.07 (0.07) | 0.22 (0.05) | 0.03 (0.02) |
|  Anti-inflammatory index |  | 0.26 (0.02) | 0.08 (0.02) | -0.15 (0.11) | 0.21 (0.07) | -0.07 (0.79) | 0.12 (0.03) | 0.02 (0.07) | 0.24 (0.05) | 0.14 (0.02) |
|  Ratio pro/anti inflammatory index |  | -0.08 (0.64) | 0.12 (0.96) | 0.05 (4.54) | 0.19 (2.78) | -0.04 (31.3) | 0.07 (1.33) | 0.18 (2.53) | 0.08 (2.05) | 0.11 (0.68) |
|  hsCRP |  | 0.33 (0.02) | -0.28 (0.03) | -0.23 (0.12) | -0.17 (0.08) | 0.04 (0.89) | -0.12 (0.04) | -0.20 (0.07) | 0.19 (0.06) | -0.05 (0.02) |
|  TNF-α |  | 0.39 (0.009) | -0.12 (0.02) | -0.04 (0.07) | 0.12 (0.05) | 0.13 (0.36) | 0.15 (0.02) | 0.09 (0.04) | 0.23 (0.03) | 0.18 (0.01) |
|  sTNF-R2 |  | 0.35 (0.005) | -0.11 (0.007) | -0.27 (0.03) | 0.02 (0.02) | 0.04 (0.12) | -0.12 (0.01) | 0.02 (0.02)♂ **-0.50 (0.02)**♀ 0.23 (0.04) | 0.12 (0.02) | -0.1 (0.005) |
|  Il-1β |  | 0.65 (0.08) | 0.21 (0.10) | -0.05 (0.87) | 0.15 (0.30) | 0.03 (0.26) | 0.03 (0.28) | 0.16 (0.41) | -0.31 (0.37) | -0.05 (0.15) |
|  IL-1RA |  | 0.04 (0.008) | 0.23 (0.01) | 0.04 (0.06) | 0.29 (0.03) | 0.28 (0.02) | 0.30 (0.02) | 0.005 (0.03) | 0.23 (0.03) | 0.23 (0.03) |

Data represent standardized regression coefficient-β (standard error, unstandardized B) of various psychological factors demonstrating an association with several neuroimmune responses *ex-vivo* and after *in-vitro* whole blood stimulation using linear regression models. All neuroimmune responses are Ln-transformed. The *in-vitro* neuroimmune responses are normalized for monocyte count. Significant values are in bold font (\*p < 0.05). TNF-α, tumor necrosis factor -α; IL-1β, interleukin -1β; IL-1RA, interleukin -receptor antagonist; IL-4, interleukin – 4; IL-10, interleukin -10; CCL2 / MCP1, c-c-motif ligand 2 also referred to as monocyte chemoattractant protein 1; CCL3 / MIP1α, c-c-motif ligand 3 also referred to as macrophage inflammatory protein 1α; CCL4 / MIP1β, c-c-motif ligand 4 also referred to as macrophage inflammatory protein 1β; TNFα : IL-10, ratio between TNFα : IL-10; IL-1β : IL-1RA, ratio between IL-1β : IL-1RA; 1ng/ml (LD-LPS), 1 milliliter whole-blood stimulation with 1 nanogram TLR4 agonist lipopolysacharide; 10µg/ml (HD-LPS), 1 milliliter whole blood stimulation with 10 microgram of TLR4 agonist lipopolysacharide; ♂ effect modification for males; ♀ effect modification for females.

aRefers to mental health inventory -5 score

bRefers to score on the depression, anxiety and stress scale 21 subsection stress

cRefers to the score on the depression, anxiety and stress scale 21 subsection depression

dRefers to the score on the depression, anxiety and stress scale 21 subsection anxiety

eRefers to total score on the tampa scale questionnaire higher than 37

fRefers to the total score on the pain catastrophizing scale