UCLouvain

Faculté des sciences de la motricité

Etude de l'activité physique sur la sensibilisation centrale : comparaison entre sport d'endurance et rugby.

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1. Introduction

Physical activity (PA) impacts clinical and experimental pain. It is recognized as a key non-pharmacological strategy for the prevention and management of both acute and chronic pain (Chimenti et al., 2018). Several large-scale population-based studies have suggested a consistent inverse relationship between PA and the prevalence of chronic pain. For instance, the HUNT 3 study, which is a study including 46.533 Norwegians, has shown that persons doing regular recreational exercise have significantly lower odds of reporting chronic pain, with a 10–12% reduction among younger adults and up to 38% among older women, depending on the frequency and intensity of activity (Landmark et al., 2011). Similarly, data based on the seventh wave of the Tromsø study, which included overall 40.051 participants (Jacobsen et al., 2012), has revealed an inverse relationship between PA and the prevalence of chronic pain (Fjeld et al., 2023). While PA decreases the odds of reporting chronic pain, the inverse is also thought to be true as physical inactivity has been identified as a significant risk factor for its development (Sluka et al., 2013). Moreover, it has also been shown that experimentally induced pain can be reduced by acute bouts of exercise (Naugle et al., 2012).

Evidence suggests that the type of sport practiced plays a crucial role, as differences in pain modulation have been observed across various sport disciplines. Endurance athletes typically show higher pain tolerance, especially to thermal stimuli or cold pressor tests, and report lower pain intensity compared to non-athletes (Geisler et al., 2021; Peier et al., 2024; Pettersen et al., 2020; Tesarz et al., 2012a). Given that contact sports involve both sustained PA and regular exposure to nociceptive inputs, athletes from these disciplines constitute an ideal population to investigate pain tolerance. Indeed, they display enhanced pain tolerance, likely due to this repeated exposure and the development of coping strategies (Thornton et al., 2024, 2017). Although a study directly comparing endurance vs contact athletes reported greater tolerance in endurance athletes (Egan, 1987), another one did not find such effect (Ellison and and Freischlag, 1975). Evidence also suggests that the level of practice plays a role. Several studies showed that athletes reported higher pain tolerance than non-athlete (O'Farrell et al., 2022; Ryan and Kovacic, 1966; Tesarz et al., 2012b).

It also appears that pain tolerance increases with athletic involvement, with competitive athletes displaying greater tolerance than club-level athletes who themselves show higher tolerance than non-competitive individuals (Scott and Gijsbers, 1981).

PA modulates pain through several mechanisms. Regular PA modulates central pain inhibitory pathways and immune function, promoting a protective response to peripheral insults (Sluka et al., 2018). Moreover, regular exercise has been shown to reduce neuroinflammation by inhibiting microglial activation and promoting the release of anti-inflammatory cytokines such as IL-10 and IL-4 (Lesnak and Sluka, 2020; Mee-inta et al., 2019). This anti-inflammatory effect could contribute to decreased central sensitization (CS).

CS is defined by the International Association for the Study of Pain (IASP) as an "increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input" (IASP). It is believed to be involved in most chronic pain conditions through mechanisms of synaptic plasticity and heightened neuronal excitability within central pain pathways following repeated or intense nociceptive stimuli (Ji et al., 2018; Latremoliere and Woolf, 2009). Although CS cannot be studied directly in humans, it can be induced experimentally and assessed through the manifestation of secondary hyperalgesia (SH). Hyperalgesia refers to an increased pain perception to a stimulus that is normally painful. It is commonly categorized into two types: primary and secondary hyperalgesia (Treede et al., 1992). Primary hyperalgesia occurs at the site of tissue injury and is thought to result from peripheral sensitization, involving changes in the sensitivity of primary afferent nociceptors due to inflammatory mediators and local tissue damage (Julius and Basbaum, 2001; Sandkühler, 2009). In contrast, SH occurs in an area surrounding and distant from the initial injury site and is considered to reflect changes within the central nervous system. Specifically, an increase in the excitability of dorsal horn neurons and a reduction in descending inhibition (Sandkühler, 2009; Woolf, 2011). One experimental technique used to elicit SH is high frequency stimulation (HFS) of the skin. Typically, HFS is applied to the volar forearm via a specially designed electrode that preferentially activates cutaneous nociceptive afferents. The stimulation triggers increased pinprick sensitivity in the surrounding uninjured skin, reflecting SH (Klein et al., 2004).

However, despite the clinical importance of CS and the evidence regarding the impact of PA on pain, the relationship between CS and PA remains unclear. It is then relevant to explore whether PA can modulate CS and if different types of sport lead to similar effects. Moreover, the systematic underrepresentation of women in such research underlines the importance of including both sexes in future studies to see if sex differences exist.

This study aimed to determine whether SH develops similarly in rugby players and endurance athletes in relation to the level of practice, if contact sports are associated with specific adaptations modulating CS (e.g., exposure to repeated nociceptive stimuli) that are not related to adaptations specifically induced by physical training. After inducing CS with HFS, we will compare the differences in SH. We hypothesize that (1) high-level athletes will exhibit reduced SH compared to lower-level athletes, (2) rugby players will show reduced SH compared to endurance athletes.

2. Materials and Methods

2.1. Ethics and study design

This cross-sectional study was conducted with the approval of the independent ethics committee Comité Hospitalo-facultaire UCLouvain (B4032021000122) and adheres to the latest version of the Declaration of Helsinki.

This work comprised two data acquisition phases. First in phase 1 (rugby phase), 24 female rugby players were recruited from September 2021 to January 2022. Second in phase 2 (endurance phase), 60 participants were recruited from April 2023 to December 2024. Participants recruited in the second phase included both males and females and were categorized as either trained in endurance, recreationally active, or sedentary. The data acquisition of the second phase is part of a larger, still ongoing, research project where 78 participants are planned to be recruited. All participants were compensated for their participation.

2.2. Participants and recruitment

In rugby phase, two groups of age-matched female rugby players were recruited (total sample n = 24; Lemmens et al., 2022). The athlete group (ATH) was formed

with 12 players from the Belgian national rugby team and an intermediate group (INT) comprised 12 amateur players.

In endurance phase, three groups of sex- and age-matched volunteers were recruited based on their physical activity levels (total sample n = 60). The athlete group (ATH) was formed with endurance-trained athletes, the intermediate group (INT) comprised individuals who engaged in physical activity in line with World Health Organization recommendations ("WHO Guidelines on Physical Activity and Sedentary Behaviour," 2020) and the sedentary group (SED) included individuals who did not engage in regular physical activity or who did but below the WHO recommendations ("WHO Guidelines on Physical Activity and Sedentary Behaviour," 2020). The eligibility criteria applied in both phases are summarized in table 1. Participants were considered eligible if they presented all inclusion criteria and none of the exclusion criteria.

2.3. Experimental design

Rugby phase

Participants were welcomed in a comfortable and quiet room. After giving their informed consent, participants were asked to provide personal data (age, height, weight, education level, and menstrual cycle phase if applicable) and to complete five questionnaires (see 2.4.1. Questionnaires). Then, the skin of the volar forearms was cleaned with ether and alcohol and participants were familiarized with the mechanical pinprick sensitivity assessment (MPS; see 2.4.5. evaluation of sensitivity to mechanical pinprick stimulation). The sites to be tested were marked on both forearms and the MPS was assessed (T0). Then, instructions about the conditioning high frequency stimulation protocol (HFS; see 2.4.4. HFS protocol) were provided and the HFS electrode was attached onto the skin. Participants received five trains of HFS. After each train, they were asked to rate the intensity of the pain elicited (see 2.4.4. HFS protocol). The MPS and spatial extent of the secondary mechanical hyperalgesia (i.e., secondary hyperalgesia area, SHA) were assessed at 25 (T1), 30 (T2), and 35 (T3) min post-HFS. To prevent potential bias due to handedness in the assessment of MPS or SHA, the tested arm was counter-balanced across subjects. All procedures were conducted by a trained female

investigator (Cerise Lemmens; CL). An outline of the experimental procedures conducted in phase 1 is presented in Figure 1.A.

Endurance phase

The experiment was conducted in a quiet room with the participants comfortably seated on a chair. The temperature and humidity of the room were monitored. After giving their informed consent, participants were asked to provide personal data including birthdate, age, weight, height, level of education, sporting activities (main and secondary disciplines, along with their frequency and duration for a typical week) and to complete a set of questionnaires (see 2.4.1. Questionnaire). Then, participants were familiarized with the MPS assessment applied on hand dorsa (see 2.4.5. evaluation of sensitivity to mechanical pinprick stimulation). Next, MPS was assessed (T0) before placing the HFS electrode (see 2.4.4. HFS protocol) onto the volar forearm. After measuring the electrical detection threshold (EDT) to a single electrical stimulation (see 2.4.3. Detection threshold of electrical stimulation with a single pulse), HFS stimulation was administered (see 2.4.4. HFS protocol). The MPS and SHA area were assessed 10 min (T1), 20 min (T2), 30 min (T3) and 50 min (T4) after HFS. The arm tested first (dominant vs non-dominant) and the arm receiving the conditioning HFS were counterbalanced between the groups and participants. Procedures were conducted by two pairs of trained experimenters. The first 30 participants were tested by a pair of mixed gender experimenters (Tom Gallienne, Manon Buchallet; TG/MB), the second 30 participants were assessed by a pair of male experimenters (Arnaud Normand, Pierre-Yves Lavalleye; AN/PL). To minimize potential investigator bias, HFS conditioning and MPS/SHA area assessment were alternated between experimenters for each participant. An outline of the experimental procedures conducted in phase 2 is presented in Figure 1B.

	Rugby phase	Endurance phase
Inclusion criteria	-Age between 18 and 45 years - Being able to give written informed consent - Athletes: playing rugby at a national level - Intermediate: regular and recreational participation in rugby with a physical activity level approaching WHO recommendations.	-Men or Women - Age between 18 and 60 years - Being able to give written informed consent - Belonging to one of the following physical activity categories: • Athlete: regular participation in long-distance running training sessions (at least three times a week, for a minimum weekly duration of 4 hours); participation in an official competition during the previous year. • Intermediate: regular physical activity practice, approaching the level recommended by the WHO (150 to 300 min of moderate intensity or 75 to 150 min of vigorous intensity) • Sedentary: no regular physical activity or only very occasional physical activity, accumulating less physical activity than recommended by the WHO.
Exclusion criteria	-Evidence for a clinically significant alteration of the skin of the volar forearms - Pregnancy - Having a pacemaker or implanted cardiac defibrillator - Major neurological (including neuropathy) or psychiatric conditions - Medication taken in the last 12 hours (including corticoids, non-steroidal anti-inflammatory drugs or other pain killers) - Previous participation in studies involving the application of capsaicin or high-frequency transcutaneous electrical stimulation (HFS) - Chronic pain conditions (including migraine) - Recreative use of cannabis - Having slept less than 6 hours the night before testing.	- Evidence for a clinically significant alteration of the skin of the volar forearms - Pregnancy - Having a pacemaker or implanted cardiac defibrillator - Major neurological (including neuropathy) or psychiatric conditions - Medication taken within 12 hours or regular medication (except contraceptives) - Previous participation in studies involving the application of capsaicin or high-frequency transcutaneous electrical stimulation (HFS) - Chronic pain conditions (including migraine) - Recreative use of cannabis - Having slept less than 6 hours the night before testing. - Regular volleyball or pelota practice - Bone fracture in the year preceding the test (lower and/or upper limb)

	- Being under medication on regular basis (including anti-depressors, corticoids, NSAIDs, except contraception)	

Table 1. Eligibility Criteria.

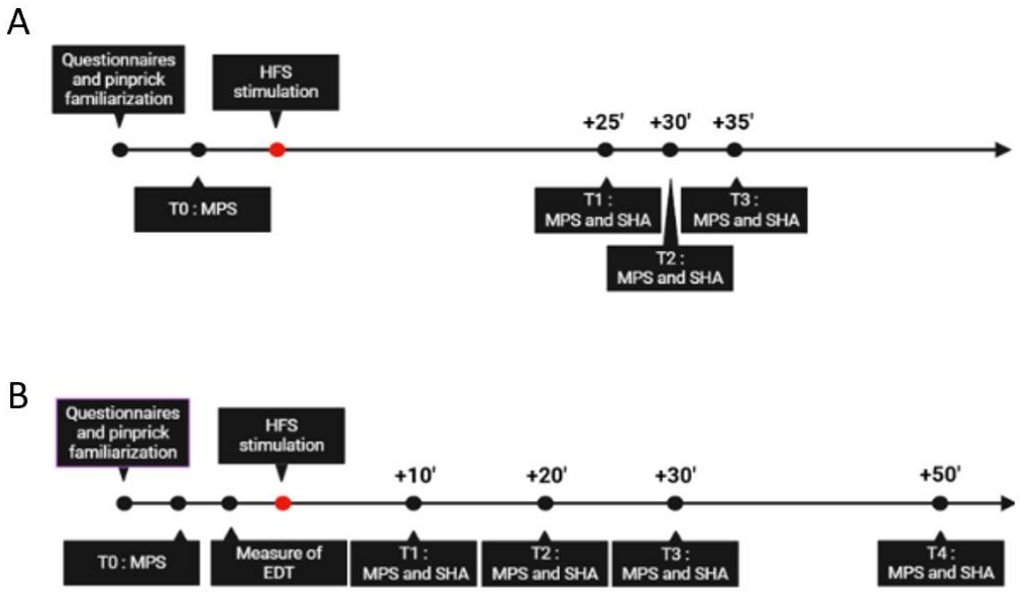

Figure 1. Experimental design. 1.A. Experimental timeline of rugby phase; the total duration of the experiment was approximately 1 h30. **1.B**. Experimental timeline of endurance phase, the duration of the experiment was approximately 2 h. Red dots represent the moment of HFS application. Abbreviations: MPS, mechanical pinprick sensitivity; HFS, High Frequency Stimulation; SHA, Secondary Hyperalgesia Area; EDT, electrical detection threshold.

2.4. Experimental procedure

2.4.1. Questionnaires

In rugby and endurance phases, the following information was collected: age, height, weight, sporting activities (frequency, intensity, competitions), and any specific lifestyle practice such as diet or meditation. The French versions of the following questionnaires were also administered:

- **International Physical Activity Questionnaire** (IPAQ) (Craig et al., 2003) to measure overall physical activity and sedentary behavior over the past seven days. The long version, consisting of 27 items was used and validated in French (Crinière et al., 2015).

- **The Flinders Handedness Survey** (FLANDERS) (Nicholls et al., 2013) to evaluate manual laterality using a questionnaire with 10 items. The French version provided by Nicholls et al., (Nicholls et al., 2013) was used although no official validation of the translation could be identified.
- **Alcohol Use Disorders Test** (AUDIT) (Saunders et al., 1993) to assess alcohol consumption over the past 12 months. The French-translated and validated version of this 10-item questionnaire was used (Gache et al., 2005).
- **State-Trait Anxiety Inventory** (STAI) (Gaudry et al., 1975) to measure anxiety levels through a 40-item questionnaire translated and validated in French (Gauthier and Bouchard, 1993). It includes two subscales: the trait anxiety scale (20 items), assessing general anxiety, and the state anxiety scale (20 items), evaluating temporary anxiety induced by specific events.
- **Karolinska Sleepiness Scale** (KSS) (Åkerstedt and and Gillberg, 1990) to assess wakefulness with a single-item scale. Participants rated their sleepiness on a scale of 1 to 10, where 1 represents "fully alert" and 10 represents "extremely sleepy, unable to stay awake". Although a French version is available and frequently used (Pertenais et al., 2019), no official validation of the translation has been conducted.

The following questionnaires were additionally administered in endurance phase:

- **Leeds Sleep Evaluation Questionnaire** (LSEQ) (Parrott and Hindmarch, 1980) to evaluate various aspects of sleep and wake-related behaviors using 10 items. Each item featured a scale with opposing extremes, where participants placed a mark. It has been validated in French (Tarrasch et al., 2003).
- **IMI2-PainCare-BioPain** (Leone et al., 2022) to assess expectations related to pain and anxiety during the experiment. This scale included two items, both presented as visual scales.

2.4.2. HFS electrode

In rugby and endurance phases, the HFS electrode consisted of a cathode with 16 blunt stainless-steel pins, each with a diameter of 0.2 mm and extending 1 mm from its base. These pins were arranged in a circle with a diameter of 1 cm, surrounded by a stainless-steel ring serving as the anode. The inner and outer diameters of the anode were 2.2 cm and 4 cm respectively. The electrode, which is made at the Centre for Sensory-Motor Interaction (Aalborg University, Aalborg, Denmark), is specifically designed to recruit small nerve fibres present in the superficial layers of the skin. A schematic representation of the electrode can be found in Figure 2.A.

2.4.3. Preparation of HFS protocol and electrical stimulation detection threshold

After cleaning the skin with ether, the HFS electrode was placed 10 cm distally from the cubital fossa on the midline of the volar forearm (Figure 2.B.) and secured onto the skin with adhesive tape. Stimulations were delivered with a constant-current electrical stimulator (Digitimer DS5, Welwyn Garden City, UK), controlled through a custom MATLAB script (The MathWorks Inc., Natick, USA). Participants were notified before any stimulation.

Only during endurance phase, EDT was measured. This threshold was defined as the lowest intensity at which a single electrical stimulus was detected 100% of the time. To determine this threshold, a staircase method was used, based on previous studies (van den Broeke and Mouraux, 2014a, 2014b). The procedure was as follows: stimulation began at an intensity of 1 mA; then, the intensity was successively reduced by steps of 0.05 mA until the participant could not detect the stimulation anymore. At this point, the intensity of stimulation was increased by steps of 0.01 mA until they were detected. The procedure was repeated until an intensity was found at which the participants detected the stimulation 3 times in a row. This value was defined as the EDT.

2.4.4. High Frequency Stimulation protocol

In rugby and endurance phases, HFS of the skin was delivered similarly to the participants and consisted of 5 trains of 100 Hz electrical stimulation. Each train

lasted 1 second and trains were separated by a 9-second break (Klein et al., 2004). The entire protocol lasted 50 seconds. After each train, participants were asked to rate the intensity of the pain elicited using a 10-cm visual analog scale (VAS), anchored from “No pain" to "Maximum imaginable pain."

The stimulation intensity was set at 5 mA for all participants. This value was chosen because it represents approximately 20 times the mean EDT and can elicit reliable sensitization to mechanical pinprick stimulation (Cayrol et al., 2020).

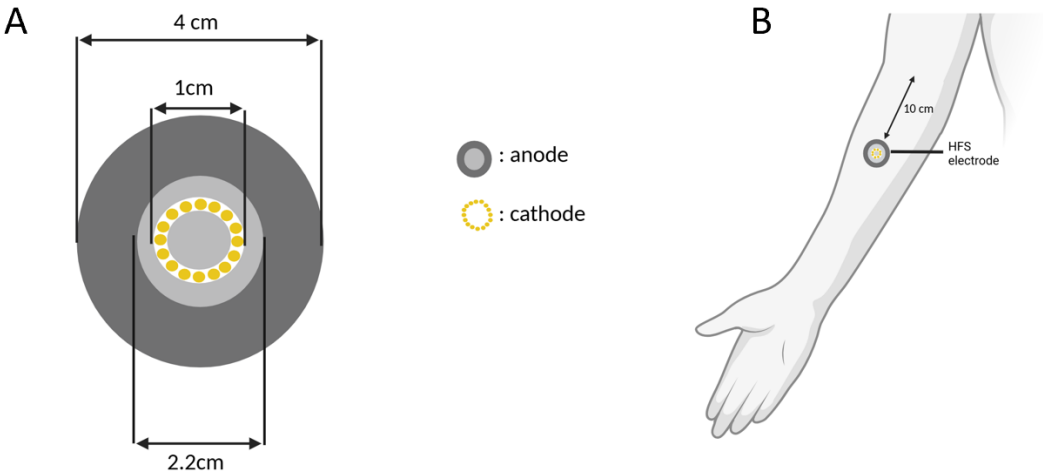

Figure 2. Experimental set-up. 2.A. description of the electrode used to deliver high frequency stimulation (HFS) and EDT. The electrode consisted of 16 blunt stainless-steel pins (cathode), surrounded by a concentric stainless-steel anode with an internal diameter of 2.2 cm and an external diameter of 4 cm. The electrode is specifically designed to recruit small nerve fibres present in the superficial layers of the skin **2.B.** The electrode was placed on the midline of the volar forearm, 10 cm from the cubital fossa.

2.4.5. Evaluation of sensitivity to mechanical pinprick stimulation

MPS was assessed, in rugby and endurance phases, with a pinprick stimulator consisting of a holding cylinder containing a freely sliding weight exerting a force of 128 mN applied onto the skin through a blunt needle tip with a diameter of 0.25 mm (MRC Systems, city, Germany). Each stimulus was applied and removed slowly (approx. 1 s) to ensure consistent application of the planned force (van den Broeke et al., 2015) Pinprick stimuli were used as the sensitization induced by HFS is preferential for mechanical stimulation (Leone et al., 2024). After each stimulation, participants were asked to report whether the sensation was painful or not (MPS pain) and to rate the intensity of their perception on a 10-cm VAS

anchored from “No sensation” to “Most intense imaginable sensation” (MPS VAS).

2.4.6. Assessment of the secondary hyperalgesia area

Assessment of the area of secondary hyperalgesia differed between rugby phase and endurance phase because the method used during endurance phase is more precise.

Rugby phase

The SHA area was assessed along 2 axes: medial-lateral and distal-proximal (Figure 3.A.). Mechanical pinprick stimuli were repeatedly applied at 1-cm intervals, moving from the wrist toward the center and from the cubital fossa to the center for the distal-proximal axis. For the medial-lateral axis, participants rotated their forearm (i.e., prono-supination) to ensure the pinprick application remained perpendicular to the skin. Participants verbally indicated when they felt a noticeable increase in the sensation elicited by the pinprick stimulus. To confirm the location, the experimenter moved 1 cm back and retested the point where the sensation was increased. Upon confirmation, the point was marked, and the distance from the center of the conditioned site was measured.

Endurance phase

The area of SHA was assessed along 4 axes: distal-proximal, medial-lateral distomedial-to-proximolateral, and distolateral-to-proximomedial (Figure 3.B.). Mechanical pinprick stimuli were repeatedly applied at 0.5-cm intervals, moving from the wrist toward the center and from the cubital fossa to the center for the distal-proximal axis. For disto-medial to proximo-lateral, and disto-lateral to proximo-medial axes the same procedure was followed. Participants verbally indicated when they felt a noticeable increase in the sensation elicited by the pinprick stimulus. To confirm the location, the experimenter returned to the starting point and retested, the point where the sensation was increased. Upon confirmation, the point was marked. At the end of the procedure, the distances between each marked point and the point corresponding to the center of the HFS electrode were measured for each of the 8 directions. A cubic interpolation was performed to estimate the intermediate values between the measured points. This technique

produced a continuous curve linking the 4 or 8 points, then the surface area was computed to provide an estimate of the SHA area (function interpclose, pchip interpolation in MATLAB).

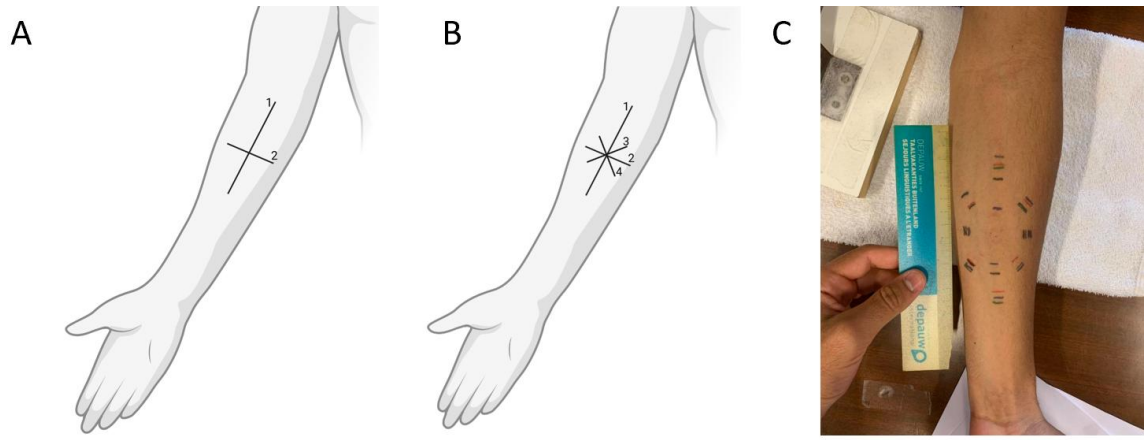

Figure 3. **Directions along which was tested the secondary hyperalgesia area. 3.A.** Directions along which was tested the secondary hyperalgesia area during rugby phase (1 = proximal-distal, 2 = medial-lateral). **3.B.** Directions along which was tested the secondary hyperalgesia area during endurance phase (1 = proximal-distal, 2 = medial-lateral, 3 = disto-lateral- to- proximo-medial, 4 = disto- medial -to- proximo-lateral). **3.C.** Example picture of a participant of the ATH group from endurance phase.

2.5. Statistical analyses

Statistical analyses were conducted with the SPSS software (SPSS, version 29.0.2.0 (20), IBM Corp., Armonk, NY, USA). The significance threshold was set at $p < 0.05$. Data was reported as mean ± standard deviation (M±SD) unless specified otherwise. Normality of data was verified using histograms, QQ plots, and Shapiro-Wilk tests.

Baseline characteristics and questionnaires scores were compared between groups with a one-way ANOVA or a Kruskal-Wallis test, based on normality assessment. In case of significant main or interaction effects, post-hoc paired comparisons with Bonferroni correction of p-values were conducted.

Concerning the pain elicited by mechanical pinprick stimuli, the responses to each of the three stimuli was scored 0 if not painful or 1 if painful yielding a score between 0-3 for each participant and each time point. The painfulness of the stimulation was then coded as 0 for scores 0 and 1 (i.e., 0/3 or 1/3 stimulation

perceived as painful) and 1 for scores 2/3 and 3/3. Finally, percentage of painful stimulations were computed by dividing the sum of the transformed responses (0 or 1) by the total number of stimulations delivered, pooled for each timepoint, group, and forearm. No inferential statistics were conducted as general linear models including a random intercept on the participant were not estimable.

Two types of analyses were conducted to compare MPS and SHA between groups. First, analyses were conducted separately for each sport (i.e., within the rugby group and separately in the endurance group). Second, comparisons between sports were conducted (rugby vs endurance). Between sports comparisons only included data acquired before and 30 min after HFS as other timepoints differed between phases. This delay has been shown to be sufficient to observe SHA post-HFS (Lebrun et al., 2025). In addition, there was no SED group in the rugby phase, hence data collected from the SED group in the endurance phase were not taken into account for all between-sport analyses.

2.5.1. Within-sport analyses

Rugby phase

MPS VAS. The impact of the within-subject factor "time" (T0, T1, T2, T3) and the between-subject factor "group" (ATH, INT) on the difference in MPS VAS between stimulated and control forearm (MPS VAS_{stim} - MPS VAS_{cont}) was assessed with a repeated-measures ANOVA (RM-ANOVA). To confirm that potential group differences were related to a change in sensitization of the stimulated forearm, two additional RM-ANOVA were performed, examining separately the impact of the "time" and "group" factors on the MPS VAS at the HFS and control forearm.

SHA. The impact of the factor “time” (T1, T2, T3) and “group” (ATH, INT) was examined on the square root of SHA with a RM-ANOVA.

Endurance phase

MPS VAS. The impact of the within-subject factor "time" (T0, T1, T2, T3, T4) and the between-subject factor "group" (ATH, INT, SED) on the difference in MPS VAS between stimulated and control forearm (MPS VAS_{stim} - MPS VAS_{cont}) was assessed with a repeated-measures ANOVA (RM-ANOVA). To confirm that potential group

differences were related to a change in sensitization of the stimulated forearm, two additional RM-ANOVA were performed, examining separately the impact of the "time" and "group" factors on the MPS VAS at the HFS and control forearm.

SHA. The impact of the factor "time" (T1, T2, T3, T4), "group" (ATH, INT, SED), and the between subject factor "examiner pair" (TG/MB, AN/PL) was examined on the square root of SHA area with a RM-ANOVA. The factor "examiner pair" was added upon visual examination of the data, where a potential examiner bias was observed (Annex 1).

2.5.2. Between-sports analysis.

MPS VAS. The impact of the factors "sport" (rugby, endurance) and "level" (ATH, INT) was assessed on the difference between forearms (HFS, control) in difference between MPS VAS pre HFS (T0) and 30 min post HFS (i.e., T2 in rugby phase, T3 in endurance phase) [(MPS VAS 30min - MPS VAS T0)$_{stim}$ - (MPS VAS 30min - MPS VAS T0)$_{cont}$] with linear mixed model with a random intercept on the participant (LMM-RI). The difference between forearm at T0 [(MPS VAS T0)$_{stim}$ - (MPS VAS T0)$_{cont}$] was also included as a continuous co-variate to control for potential baseline differences.

SHA. The impact of the factor "sport" (rugby, endurance) and "level" (ATH, INT) was assessed on the square root of the SHA area measured 30 min post HFS (i.e., T2 in rugby phase, T3 in endurance phase) using one-way ANOVA. A square root transformation was applied to ensure linearity of the SHA values.

For all RM-ANOVA, the assumption of sphericity was tested using Mauchly's test. When the data violated the sphericity assumption, Greenhouse-Geisser corrections were applied to correct the F-values. Assumptions related to LMM-RI (i.e., normality and homoscedasticity of the residuals, normality of random effects) were examined with normal QQ plots and histograms. In case of violation, transformation of the data (log, square root) was considered. Significant interaction effects were examined using pairwise comparisons of marginal means with Bonferroni correction of p-values. In the absence of significant interaction, a similar procedure was conducted on main effects.

3. Results

3.1. Participants data

Rugby phase

In total, 24 subjects were recruited and analysed (12 athletes and 12 intermediate). Table 2 summarizes the sociodemographic characteristics of the participants and the questionnaires scores in each group. No significant between-group difference was found, except for the score of the IPAQ for vigorous PA ($H_{(1)}$ = 5.643, p = 0.018).

	Athlete (N = 12)	Intermediate (N = 12)	p-value
Age (years)	25.9 ± 3.9	24.8 ± 3.4	0.48
Weight (Kg)	67.9 ± 9.6	67.5 ± 8.5	0.92
Height (cm)	169.0 ± 6.5	165.2 ± 4.3	0.09
IPAQ total vigorous (MET-min/week)	4556 ± 1590	2673 ± 2285	0.017
IPAQ total PA (MET-min/week)	7014 ± 1878	5265 ± 3265	0.12
AUDIT (/40)	6.0 ± 3.6	8.3 ± 3.3	0.12
KSS (/10)	4.3 ± 1.8	3.9 ± 1.4	0.54
STAI STATE (/80)	32.4 ± 5.4	28.2 ± 5.7	0.07
STAI TRAIT (/80)	39.8 ± 7.3	42.2 ± 10.4	0.52

Table 2. Sociodemographic characteristics of the subjects and questionnaires results in rugby phase. Abbreviations. IPAQ, International Physical Activity Questionnaire; AUDIT, Alcohol Use Disorders Identification Test; STAI, State-Trait Anxiety Inventory; KSS, Karolinska Sleepiness Scale; PA, physical activity.

Endurance phase

Two participants from the SED group stopped the procedure due to excessive pain during HFS protocol and were removed from further analyses. One participant from the ATH group was excluded from the SHA analyses because the measurement was

not correctly done. Table 3 summarizes the sociodemographic characteristics of the participants and the questionnaires scores in each group. Alcohol consumption, tested by the AUDIT questionnaire, was significantly different between groups ($H_{(2)}$ = 11.109, p = 0.004): participants in the ATH group had significantly lower AUDIT scores (3.85 ± 3.80) compared to those in the INT group (diff = 3.55; $t_{(57)}$ = 15.200, p = 0.013) and the SED group (diff = 5.37; $t_{(57)}$ = 15.817, p = 0.011). IPAQ for moderate physical activity score was significantly larger in the ATH group (1795 ± 1500 MET-min/week) as compared to the SED group (diff = 1338 MET-min/week; $H_{(2)}$ = 19.814, p = 0.001) and significantly larger in the INT group (1192 ± 1120 MET-min/week) as compared to the SED group (diff = 735 MET-min/week; $H_{(2)}$ = 13.939, p = 0.033; Figure 4). Regarding the IPAQ for total physical activity, post-hoc comparisons showed that the INT group scores (3866 ± 2343 MET-min/week) were significantly larger than the SED group scores (diff = 2045 MET-min/week; $H_{(2)}$ = 14.961, p = 0.019; Figure 4) and that the ATH group scores (6690 ± 4510 MET-min/week) were significantly larger than the SED group scores (diff = 4869 MET-min/week; $H_{(2)}$ = 24.511, p = <0.001). Concerning the IPAQ for vigorous physical activity, post-hoc comparisons showed that the ATH group scores (2594 ± 2333 MET-min/week) were significantly larger than the SED group scores (diff = 2176 MET-min/week; $H_{(2)}$ = 23.922, p = <0.001; Figure 4).

	Athlete (N = 20)	Intermediate (N = 20)	Sedentary (N = 18)	p-value
Age (years)	25.1 ± 9.6	24.9 ± 9.6	25.0 ± 10.1	0.885
Weight (Kg)	65.4 ± 12.4	75.2 ± 23.9	69.6 ± 15.6	0.516
Height (cm)	174.5 ± 9.5	175.2 ± 9.3	174.7 ± 10.1	0.97
IPAQ total vigorous (MET-min/week)	2594 ± 2333	1108 ± 1002	418 ± 640	<0.001
IPAQ total moderate (MET-min/week)	1795 ± 1500	1192 ± 1120	457.5 ± 608	0.001
IPAQ total PA (MET-min/week)	6690 ± 4510	3866 ± 2343	1821 ± 1410	<0.001
AUDIT (/40)	3.9 ± 3.8	7.4 ± 3.5	9.2 ± 7.2	0.004
KSS (/10)	2.6 ± 1.4	3 ± 1.8	3.3 ± 1.1	0.075
STAI STATE (/80)	46.8 ± 4.7	48.4 ± 2.5	48.2 ± 4.8	0.43
STAI TRAIT (/80)	47.0 ± 4.8	47.6 ± 3.6	47.7 ± 5.4	0.873
BIOPAIN Q1 (/100)	17.8 ± 19.1	19.3 ± 22.3	23.6 ± 19.4	0.328
BIOPAIN Q2 (/100)	30.4 ± 17.8	40.5 ± 23.9	41.6 ± 22.6	0.209

Table 3. Sociodemographic characteristics of the subjects and questionnaires results in endurance phase. P-value are the results of the ANOVA or the Kruskal-Wallis depending on the distribution of the data. Abbreviations. IPAQ, International Physical Activity Questionnaire; AUDIT, Alcohol Use Disorders Identification Test; STAI, State-Trait Anxiety Inventory; KSS, Karolinska Sleepiness Scale; PA, physical activity; BIOPAIN, Questionnaire assessing anxiety and pain expectations related to experimental pain.

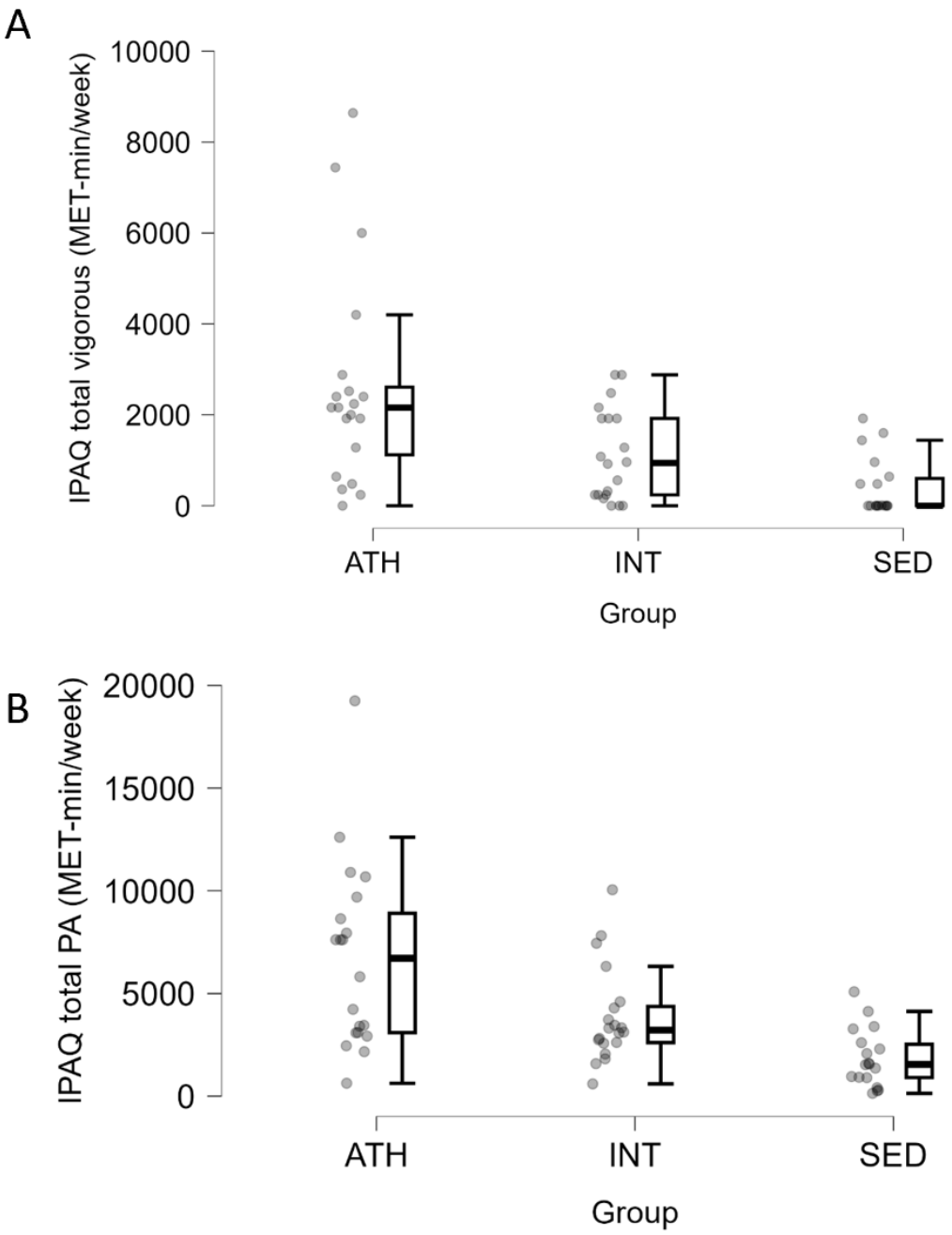

Figure 4. Boxplots and dot plot of the IPAQ scores across the 3 groups of endurance phase. Boxplots of total vigorous physical activity (IPAQ total vigorous in A) and total physical activity (IPAQ total PA in B) across the different groups. Abbreviations: ATH, athlete; INT, intermediate; SED, sedentary; IPAQ, International Physical Activity Questionnaire; MET, metabolic equivalent.

3.2. Electrical detection threshold

The mean EDT, calculated only in endurance phase, was 0.28 ± 0.17 mA for the ATH group, 0.20 ± 0.09 mA for the INT group and 0.25± 0.13 mA for the SED

group. The 3 groups were not significantly different from each other ($H_{(2)}$= 1.5570, p = 0.4590).

3.3. Intensity of perception of HFS

Rugby phase

The perceived intensity of HFS was 75.99 ± 18.26 mm for the ATH group and 77.17 ± 12.38 mm for the INT group. There was no significant difference in the mean intensity of the 5 trains for the HFS perception between the groups ($F_{(1,23)}$ = 0.034; p = 0.854).

Endurance phase

The pain ratings obtained during HFS stimulation were not significantly different between groups ($H_{(2)}$ = 0,248; p = 0,884). The mean value of the ratings in the ATH group was 71.76 ± 20.40 mm; 73.53 ± 17.08 mm in the INT group; and 75.74 ± 15.01 mm in the SED group.

3.4. Pain elicited by mechanical pinprick stimuli

Rugby phase

Across all timepoints, 14.1% of responses were considered painful. Before HFS, no stimuli were rated as painful. After HFS, a difference emerged between arms: no stimuli were perceived as painful on the control forearm, compared to 28.1% on the HFS-stimulated forearm. Within groups, 6.3% of ATH vs. 21.9% INT individuals reported pain. These proportions remained constant at all timepoints post-HFS. Figure 5.A represents these percentages.

Endurance phase

Across all timepoints, 17.6% of responses were considered painful. Before HFS, only 1.7% of stimuli were rated as painful. After HFS, a difference emerged between arms: only 1.0% of stimuli were perceived as painful on the control forearm, compared to 34.1% on the HFS-stimulated forearm. Within groups, 21.7% of SED, 18% of ATH, and 13.5% of INT individuals reported pain. Over time, the

proportion of painful responses remained relatively stable after HFS, with values ranging from 19.8% at T1 to 23.3% at T4. Figure 5.B represents these percentage.

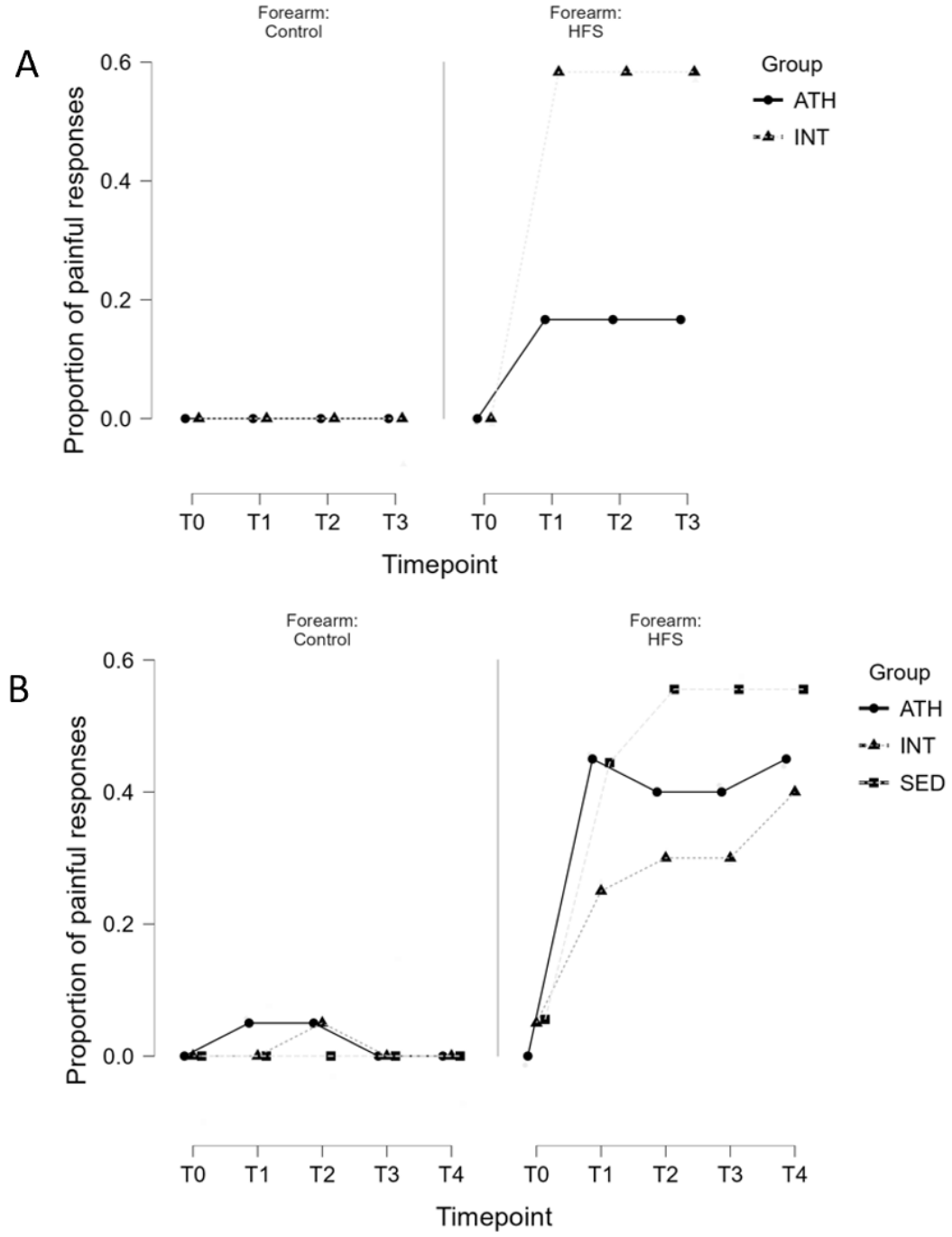

Figure 5. Percentage of mechanical pinprick stimuli perceived as "painful" by group, forearm and timepoint. 5.A, ATH and INT groups of rugby phase (T0, before HFS; T1, 25 min post HFS; T2, 30 min post HFS; T3, 35 min post HFS). **5.B,** ATH, INT and SED groups of endurance phase (T0, before HFS; T1, 10 min post HFS; T2, 20 min post HFS; T3, 30 min post HFS; T4, 50 min post HFS). Error bars represent 95% CI. Abbreviations: ATH, athlete; INT, intermediate; SED, sedentary; HFS, High frequency stimulation.

3.5. Within-sport analysis

3.5.1. Mechanical pinprick sensitivity

Rugby phase

Table 4 summarizes the intensity of the pinprick stimulation between HFS arm and control arm. The RM-ANOVA revealed a significant main effect of "time" ($F_{(1.520,33.432)}$ = 25.858, p < .001; Figure 6.A.), and no significant interaction between "time" and "group" ($F_{(1.520,33.432)}$ = 1.920, p = .170) on the difference in MPS between stimulated and control forearm. Pairwise comparisons revealed that MPS was significantly higher after HFS compared to before (T1 vs T0: $t_{(23)}$ = 6.889, p < .001; T2 vs T0: $t_{(23)}$ = 6.187, p < .001; T3 vs T0: $t_{(23)}$ = 4.924, p < .001).

To confirm that these results were due to an increase in pinprick sensitivity at the HFS arm (and not a decreased perceived sensation at the control arm), a RM-ANOVA was realized separately on the ratings obtained from the control and HFS arm.

On the HFS arm (Figure 6.B.), a significant main effect of "time" was found ($F_{(1.735,38.168)}$ = 14,262, p < .001) but no significant interaction between "time" and "group" ($F_{(1.735,38.168)}$ = 2.929, p = .072). Pairwise comparisons revealed that MPS was significantly higher after than before HFS (T0 vs T1: $t_{(23)}$ = 5.325, p < .001; T0 vs T2: $t_{(23)}$ = 4.358, p = .001; T0 vs T3 $t_{(23)}$ = 3.611, p = .005). Other timepoints were not significantly different (all p > 0.431).

On the control arm (Figure 6.C.), a significant main effect of "time" was revealed ($F_{(1.689,37.652)}$ = 11.358, p < .001) but no significant interaction between "time" and "group" ($F_{(5.044,138.723)}$ = 1.119, p = .329). Pairwise comparisons showed that MPS was significantly lower after than before HFS (T0 vs T1: $t_{(23)}$ = 3.103, p = .031; T0 vs T2: $t_{(23)}$ = 3.765, p < .005; T0 vs T3: $t_{(23)}$ = 3.848, p < .006). Other timepoints were not different (all p > .085).

	T0 (mm)	T1 (mm)	T2 (mm)	T3 (mm)
ATH (N=12)	1.56 ± 8.02	18.67 ± 8.10	21.11 ± 23.97	16.56 ± 10.77
INT (N=12)	3.51 ± 8.01	25.16 ± 20.33	27.05 ± 23.98	32.06 ± 30.13

Table 4. Intensity of the pinprick stimulation measured by a VAS. Abbreviations: ATH, athlete; INT, intermediate. T0, before HFS; T1, 25 min post HFS ; T2, 30 min post HFS ; T3, 35 min post HFS.

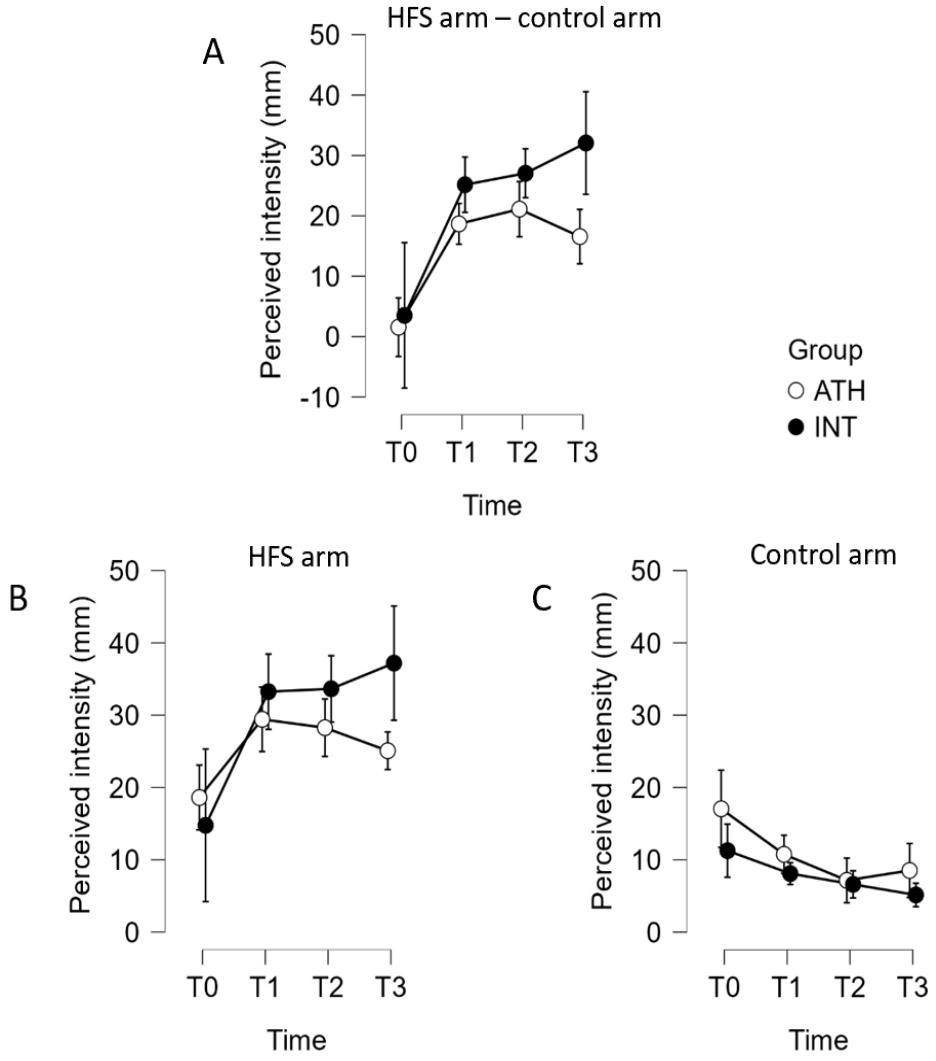

Figure 6. Evolution of the mean value of the perceived intensity to pinprick stimulations across groups and time. 6.A, evolution of the perceived intensity to pinprick stimulations (calculated as HFS arm – control arm). **6.B**, evolution of the perceived intensity to pinprick stimulations on the HFS arm. **6.C**, evolution of the perceived intensity to pinprick stimulations on the control arm. Error bars represent 95% CI. Abbreviations: ATH, athlete; INT, intermediate; T0, before HFS; T1, 25 min post HFS; T2, 30 min post HFS; T3, 35 min post HFS.

Endurance phase

Table 5 summarizes the intensity of the pinprick stimulation applied on the HFS and control arm. The RM-ANOVA revealed a significant main effect of "time" ($F_{(2.741,52)} = 55.699$, $p < .001$; Figure 7.A.), and no significant interaction between "time" and "group" ($F_{(5.483,106)} = 0.161$, $p = .982$) on the difference in MPS between stimulated and control forearm. Pairwise comparisons revealed that MPS was significantly higher after HFS compared to before (T1 vs T0: $t_{(57)} = 89.910$, $p < .001$; T2 vs T0: $t_{(57)} = 95.993$, $p < .001$; T3 vs T0: $t_{(57)} = 104.372$, $p < .001$; T4 vs T0: $t_{(57)} = 96.370$, $p < .001$).

	T0 (mm)	T1 (mm)	T2 (mm)	T3 (mm)	T4 (mm)
ATH (N=20)	0.92 ± 8.91	21.53 ± 16.10	23.18 ± 12.54	24.05 ± 17.49	28.42 ± 17.47
INT (N=20)	0.90 ± 9.88	21.53 ± 17.27	24.82 ± 18.30	25.78 ± 18.82	26.47 ± 21.06
SED (N=18)	1.17 ± 8.72	19.19 ± 13.25	22.33 ± 19.57	23.24 ± 19.57	25.20 ± 19.14

Table 5. Intensity of pinprick stimuli measured by a VAS. Abbreviations: ATH, athlete; INT, intermediate; SED, sedentary. T0, before HFS; T1, 10 min post HFS; T2, 20 min post HFS; T3, 30 min post HFS; T4, 50 min post HFS.

To confirm that these results were due to an increase in pinprick sensitivity at the HFS arm (and not a decreased perceived sensation at the control arm), further analyses were conducted. A RM-ANOVA was realized on the control and the HFS arm.

On the HFS arm (Figure 7.B.), a significant main effect of "time" was found ($F_{(2.723,149.772)} = 28.333$, $p < .001$) but no significant interaction between "time" and "group" ($F_{(5.446,149.772)} = 0.190$, $p = .973$). Pairwise comparisons revealed that MPS was significantly higher after than before HFS (T0 vs T1: $t_{(57)} = 65.439$, $p < .001$; T0 vs T2: $t_{(57)} = 45.838$, $p < .001$; T0 vs T3: $t_{(57)} = 39.160$, $p < .001$; T0 vs T4: $t_{(57)} = 46.481$, $p < .001$). Other timepoints were not significantly different (all $p > 0.755$).

On the control arm (Figure 7.C.), a significant main effect of "time" was revealed ($F_{(2.522,138.723)} = 25.705$, $p < .001$) but no significant interaction between "time" and

"group" ($F_{(5.044, 138.723)}$ = 0.207, p = .960). Pairwise comparisons showed that MPS was significantly lower after than before HFS (T0 vs T1: $t_{(57)}$ = 9.082, p = .004; T0 vs T2: $t_{(57)}$ = 37.883, p < .001; T0 vs T3: $t_{(57)}$ = 36.417, p < .001; T0 vs T4: $t_{(57)}$ = 46.011, p < .001). Other timepoints were not different except T1 vs T2 ($t_{(57)}$ = 15.281, p < .001).

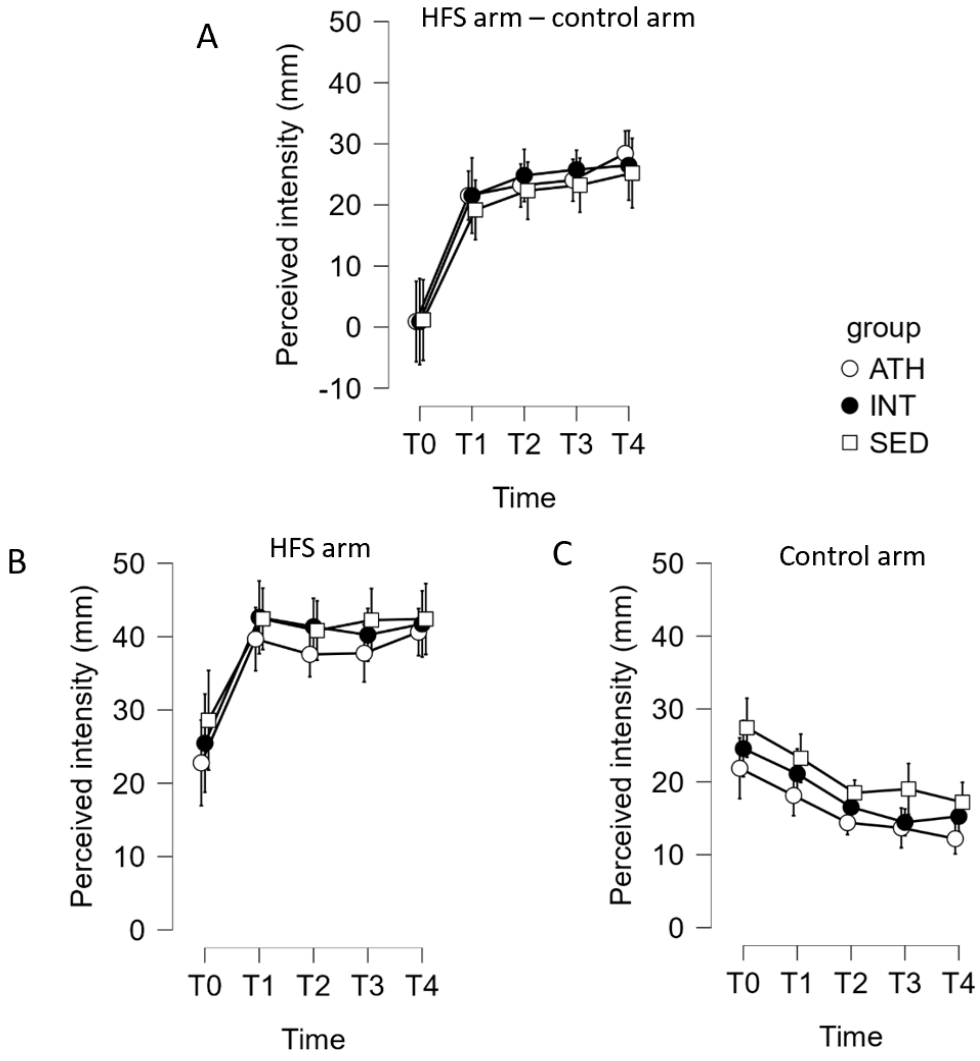

Figure 7. Evolution of the mean value of the perceived intensity to pinprick stimulations across groups and time. **7.A**, evolution of the perceived intensity to pinprick stimulations (calculated as HFS arm – control arm). **7.B**, evolution of the perceived intensity to pinprick stimulations on the HFS arm. **7.C**, evolution of the perceived intensity to pinprick stimulations on the control arm. Error bars represent 95% CI. Abbreviations: ATH, athlete; INT, intermediate, SED, sedentary; T0, before HFS; T1, 10 min post HFS; T2, 20 min post HFS; T3, 30 min post HFS; T4, 50 min post HFS.

3.5.2. Secondary hyperalgesia area

Rugby phase

The RM-ANOVA revealed a significant effect of "time" ($F_{(1.317,28.977)} = 28.561$, $p < .001$) and group ($F_{(1,22)} = 17.134$, $p < .001$). However, no "group" x "time" interaction was found ($F_{(1.317,28.977)} = 2.530$, $p < .115$). Post-hoc comparisons showed that SHA significantly decreased over time (T1 vs T2: $t_{(23)} = 5.287$, $p < .001$; T1 vs T3: $t_{(23)} = 5.544$, $p < .001$; T2 vs T3: $t_{(23)} = 3.718$, $p < .001$). The evolution of SHA is summarized in Table 6 across each timepoint and between sports and levels in Figure 8.A.

	T1 (cm)	T2 (cm)	T3 (cm)
ATH (N=12)	4.21 ± 1.72	2.86 ± 1.34	2.18 ± 1.48
INT (N=12)	6.11 ± 1.48	5.53 ± 1.43	4.96 ± 1.90

Table 6. Square root of SHA at each timepoint. Abbreviations: ATH, athlete; INT, intermediate. T0, before HFS; T1, 25 min post HFS; T2, 30 min post HFS; T3, 35 min post HFS.

Endurance phase

The RM-ANOVA revealed a significant effect of "time" ($F_{(3,49)} = 9.677$, $p < .001$), indicating that SHA varied across time points. A significant effect of "examiner pair" was also found ($F_{(1,51)} = 11.184$, $p = .002$). However, no significant main effect of "group" ($F_{(2,51)} = 1.836$, $p = .170$) and no "group" x "time" interaction were found ($F_{(4.661,153)} = 0.781$, $p = .554$). Post-hoc comparisons showed that SHA significantly increased over time until T2 and then remained stable (T1 vs T2: $t_{(56)} = 21.368$, $p < 0.001$; T1 vs T3: $t_{(56)} = 30.685$, $p < 0.001$; T1 vs T4: $t_{(56)} = 15.564$, $p < 0.001$). Table 7 summarizes the mean ± SD of SHA at each timepoint and Figure 8.B. represents the evolution of SHA between the group across the different timepoints.

	T1 (cm)	T2 (cm)	T3 (cm)	T4 (cm)
ATH (N=19)	4.76 ± 2.92	5.65 ± 3.55	5.68 ± 3.26	5.60 ± 3.49
INT (N=20)	5.80 ± 2.41	6.66 ± 2.75	6.95 ± 2.65	6.55 ± 3.39
SED (N=18)	6.49 ± 2.82	6.91 ± 3.47	7.18 ± 3.70	7.41 ± 3.53

Table 7. Square root of SHA at each timepoint. Abbreviations: ATH, athlete; INT, intermediate, SED, sedentary. T0, before HFS; T1, 10 min post HFS; T2, 20 min post HFS; T3, 30 min post HFS; T4, 50 min post HFS.

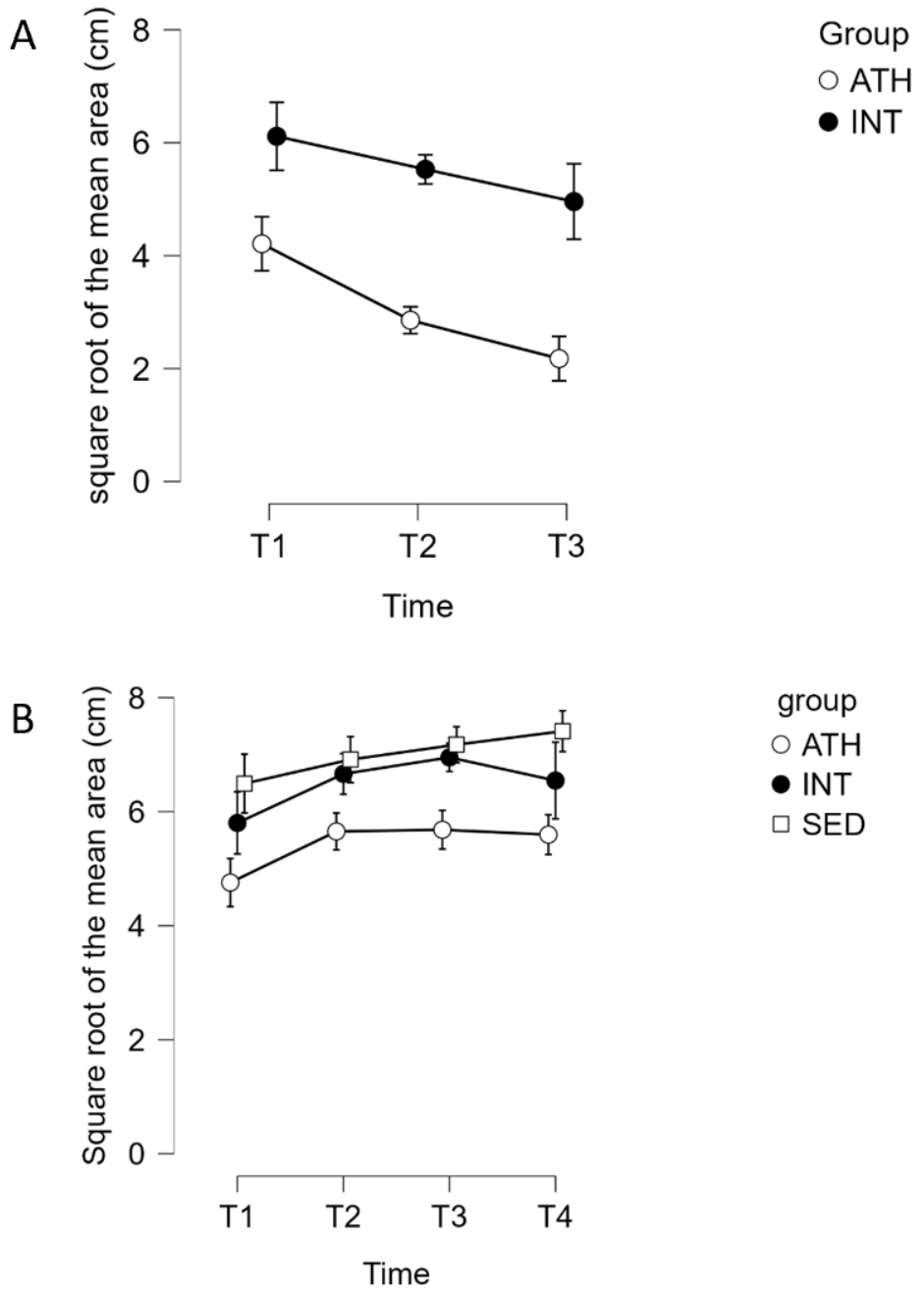

Figure 8. Evolution of the secondary hyperalgesia area between groups at each time point. 8.A, evolution of SHA across the 2 groups of rugby phase (T1, 25 min post HFS; T2, 30 min post HFS; T3, 35 min post HFS). **8.B**, evolution of SHA across the 3 groups of endurance phase (T1, 10 min post HFS; T2, 20 min post HFS; T3, 30 min post HFS; T4, 50 min post HFS). Error bars represent 95% CI. Abbreviations: ATH, athlete; INT, intermediate; SED, sedentary.

3.6. Between-sport analysis

3.6.1. Mechanical pinprick sensitivity

The LMM-RI showed no significant main effect of "sport" ($F_{(1,67.84)} = 0.032$, $p = 0.859$), "level" ($F_{(1,67.84)} = 0.687$, $p = 0.410$) and their interaction ($F_{(1,67.84)} = 0.429$, $p = 0.515$). The baseline difference between the 2 forearms was 0.96 ± 11.83 mm (estimate = -0.885; SE = 0.09; $t_{(80)} = -9.810$; $p = 0.293$). Figure 9. represents each participant's values by level and sport.

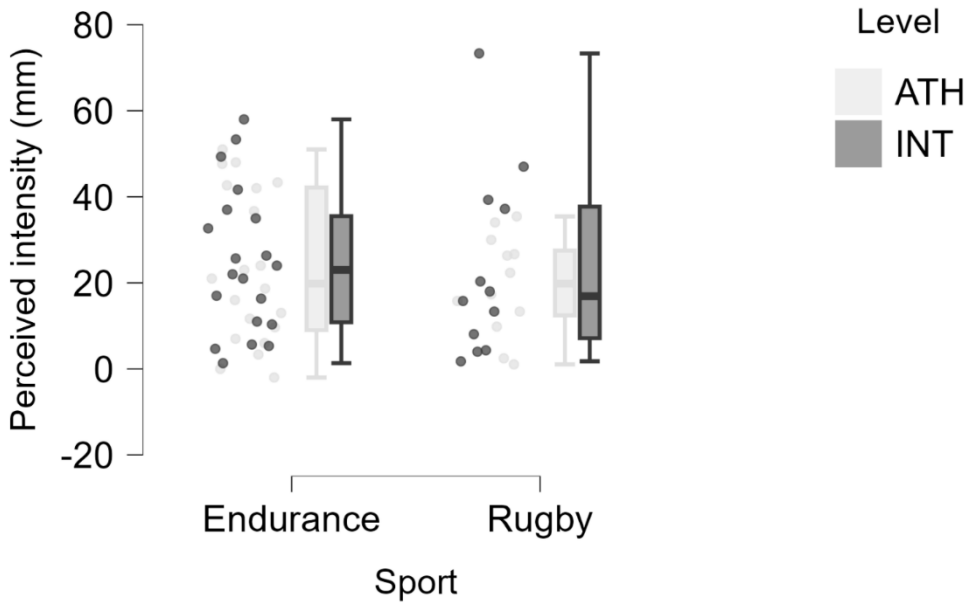

Figure 9. Dot plot of MPS by level and sport. Difference in mechanical pinprick sensitivity (MPS, VAS in mm) between forearms (HFS, control) calculated as the change from baseline to 30 min post-HFS stimulation. Groups are divided by sport type (rugby, endurance) and physical activity level (ATH, INT). Each point represents the mean perceived intensity of a participant. Abbreviations: ATH, athlete; INT, intermediate.

3.6.2. Secondary hyperalgesia area

The square root of SHA for the rugby group 30 min post-HFS was 4.19 ± 1.93 cm. For the endurance group 30 min post-HFS, it was 6.33 ± 2.99 cm. The square root of SHA of all the ATH combined was 4.59 ± 3.00 cm, and 6.42 ± 2.35 cm for the INT subjects. Figure 10. represents the mean value of the square root of SHA by sport and group.

The ANOVA revealed a significant main effect of "level" ($F_{(1,57)} = 8.723$, $p = .005$). Also, a significant main effect of "sport" was found ($F_{(1,57)} = 11.838$, $p = .001$). The "group" × "sport" interaction was not significant ($F = 1.174$, $p = .283$).

Regardless of group, endurance ATH had significantly larger SHA than rugby ATH ($t_{(62)} = 10.781$; $p = .002$). Also, INT participants exhibited significantly larger SHA than ATH participants, irrespective of sport ($t_{(62)} = 9.275$; $p = .003$).

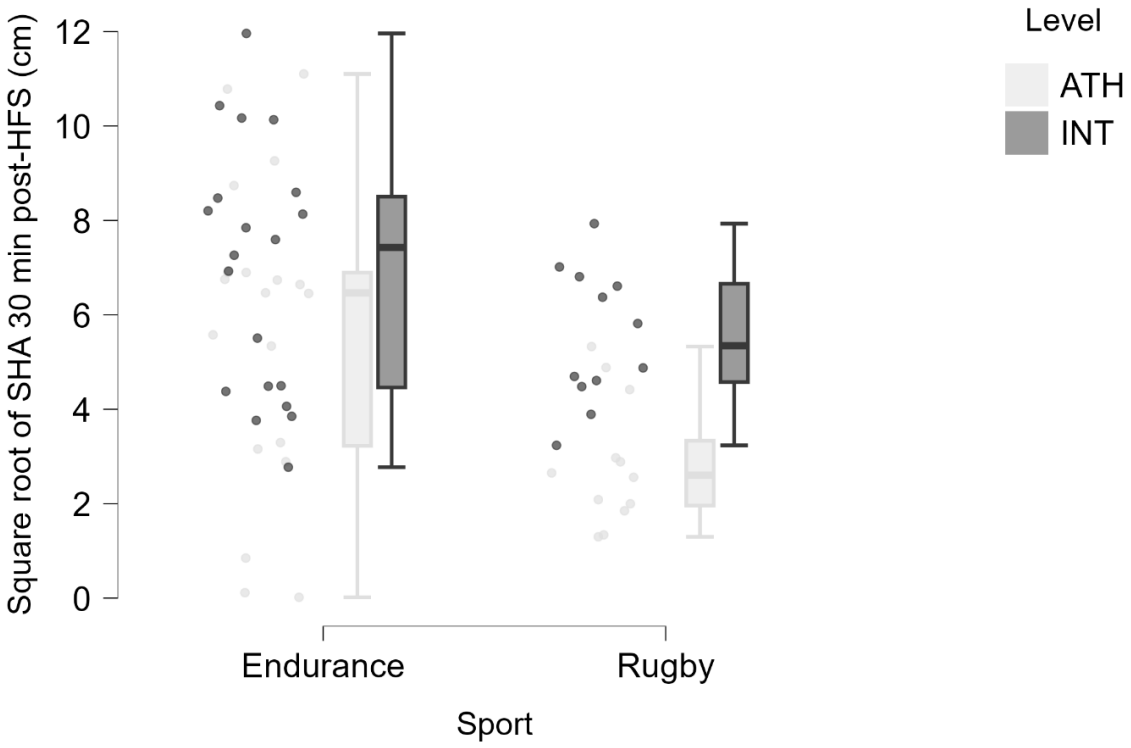

Figure 10. Dot plot of the square root of SHA by sport and level. Square root of secondary hyperalgesia area measured 30 min post-HFS by sport type (rugby, endurance) and physical activity level (ATH, INT). Each point represents a participant. Abbreviations: ATH, athlete; INT, intermediate; SHA, secondary hyperalgesia area; HFS, high frequency stimulation.

4. Discussion

4.1. General interpretation of the results

The aim of this study was to evaluate the effects of physical activity on secondary hyperalgesia (SH) by comparing two types of sports: endurance sports and rugby, in relation to the level of physical activity. Our results highlight a significant influence of sport type on the development of SH. The rugby group exhibited a

significantly smaller area of secondary hyperalgesia (SHA) compared to the endurance group.

We also found that the level of physical activity itself plays a role in the manifestation of SH. Specifically, regardless of the type of sport, the elite group demonstrated a significantly smaller SHA compared to the intermediate group. However, this finding must be interpreted cautiously due to the limitations discussed below.

No interaction was observed between sport type and physical activity level on SHA, suggesting that the influence of activity level on SHA is consistent across sport types.

4.2. Effect of sport on SHA

As we hypothesised rugby group showed significantly reduced SHA area compared to endurance group. This finding suggests that rugby players, who are regularly exposed to acute painful stimuli through physical contact, may develop physiological mechanisms that lead to chronic adaptations and greater resistance to central sensitization (CS). In addition to the inherent implications of the sport, which we will discuss below, rugby involves frequent contact, often painful. Rugby players can face an average of 800 impacts per match (Lokteff et al., 2020). Several studies indicate that repeated stimulation can effectively and progressively increase pain threshold and pain tolerance across multiple types of stimuli (e.g., heat and pressure) (Neisser et al., 1959; Greenspan et al., 1994; Taylor et al., 1993). A longitudinal experimental study demonstrated that habituation to pain may be centrally mediated through the involvement of antinociceptive systems (Bingel et al., 2007). In their study Bingel et al., administered a daily painful stimulation over 8 days to 20 participants, reporting substantially decreased pain ratings associated with reduced responses to nociceptive stimuli in the thalamus, anterior insula, SII and putamen (Bingel et al., 2007). These regions are known for their involvement in pain perception coding (Bornhovd et al., 2002; Bingel et al., 2002). During the 8 days, in parallel to these decreased responses, the rostral area of the anterior cingulate cortex (rACC) (located in the subgenual region, adjacent to the pregenual anterior cingulate cortex) displayed increasing responses over time. A study of

Faymonville demonstrated that the rACC is closely linked to the analgesia involved in hypnosis (Faymonville et al., 2000). Other findings indicate that the rACC, in association with the brainstem, is involved in opioid analgesia (Petrovic et al., 2002; Salomon et al., 2004; Kuper et al., 2005). The endogenous opioid system is based on pain and stress inhibitory neurotransmitters that bind to μ-opioid receptors (similar to morphine) (Zubieta et al., 2005; Matthes et al., 1996). Furthermore, some studies show that, in the absence of opioid responses (e.g., when using naloxone as an antagonist), no habituation phenomenon occurs (Fechir et al., 2012; Janicki et al., 1979). The use of naloxone is also associated with a reduction in the rACC analgesic effect (Eippert et al., 2009). We suggest that rugby player may develop habituation to contact and, thus, develop better pain modulation. However, in the study of Bingel et al. (2007) even if the pain thresholds of the ‘‘non-stimulated’’ hand also increased over time (suggesting a systemic effect), the main effect remained local. Based on this observation, further studies should assess habituation effects across different body regions, comparing endurance athletes and rugby players. Although the habituation effect is specific, a study of Jepma et al. (2014) showed that painful stimuli applied on different skin areas increased pain perception over time. This effect peaked after the first eight out of 24 stimulations and then appeared to decrease, being replaced by a global habituation effect.

4.3. Effect of level of practice on SHA

Concerning SHA our results show three effects. There is an effect of time, showing that SHA significantly decreases over time, which is consistent with another study using HFS (Klein et al.,2004). There is an effect of group which we discussed above. To a lesser extent, there is an effect of level. It is known that an acute bout of exercise reduces pain sensitivity and increases pain thresholds in animals and humans by promoting analgesia (Belavy et al., 2020; Lima et al., 2017; Naugle et al., 2012). Although exercise induced hypoalgesia (EIH) is an acute and short-term phenomenon. Naugle et al. observed in 2014 and 2017 that pain-free individuals reported more regular physical activity than others. Two systematic reviews and meta-analysis, both from 2020, found that regular exercise training may be effective for reducing pain sensitivity in both chronically painful individuals and pain-free individuals (Belavy et al., 2020; Vaegter et al., 2020; Ohlman et al., 2018). This

seems to show that the EIH could also persist over time leading to chronic adaptation. Among these mechanisms, we can mention descending inhibitory pathways originating cortically and that regulate the transmission of nociceptive signals (Latremoliere et al., 2009). At the level of the brainstem, specifically the rostral ventromedial medulla (RVM) is a key structure as it is capable of inducing analgesia in second-order neurons located in the spinal cord by both facilitating and inhibiting nociceptive signals (Sluka et al., 2018). These supraspinal centers could activate endogenous pain modulation pathways, which in turn could limit the spread of SHA (Vo & Drummond, 2013, 2014a, 2014b; Rempe et al., 2014). The NMDA (N-methyl-D-aspartate) are ionotropic glutamate receptors, located in the membranes of neurons in the central nervous system. They are, among other things, involved in the amplification of nociceptive information, such as central sensitization (Woolf et al., 1991; Ma et al., 2002). This receptor when phosphorylated, enhances channel conductance and increases the insertion of NMDA receptors into the synapse (Chen et al., 2006; Da Silva et al., 2010; Lima et al., 2017). According to the study of Sluka, NMDA receptors might be more phosphorylated in sedentary people compared to physically active individuals. A narrative review highlighted the link between central sensitization and prolonged increase in the excitability of nociceptive neurons in the CNS (Woolf 2011). This could partly explain the smaller areas of SHA observed in athletes.

In addition, the alcohol consumption tested by the AUDIT questionnaire showed a significant difference between the ATH group and the INT group. In the rugby phase and in the endurance phase respectively, the ATH group exhibited an average score of 6 and 3.9 which represents a non-risky consumption, whereas the INT group exhibits an average score of 8.3 and 7.4, which represents a risky consumption according to the test. In 2001, a cross-sectional study involving 1776 individuals concluded that a high consumption of alcohol is linked with a high concentration of C-reactive protein, interleukin 6 (IL-6) and tumour necrosis factor α (TNF α), which are known to be markers of inflammation and neuro-inflammation (Imhof et al. 2001; McGill et al., 2016). On the contrary, a moderate consumption of alcohol is linked to lower levels of inflammatory and neuro-inflammatory markers (Pai et al., 2005; Daniela et al., 2022). Moreover, neuro-inflammation contributes to CS because of pro-inflammatory cytokines in the CNS and Peripheral Nervous System (PNS)

, which modulate neuronal activity and alter neurotransmission, resulting in increased excitability and sensitivity of sensory neurons (Ji et al., 2018; Zhang et al., 2007; Zhen et al., 2007). These mechanisms could partly explain smaller areas of SHA observed in athletes.

4.4. Results on MPS

In contrast, MPS measurements did not reveal a significant difference between the sport groups either at baseline or after high-frequency stimulation (HFS). Although MPS increased significantly and continuously post HFS for all participants, confirming HFS as an effective method for inducing central sensitization, no differences were found between the rugby and endurance groups. However, 18% of athletes in the endurance group reported pain, compared to only 6.3% in the rugby group who perceived MPS as painful. These central mechanisms include strengthening descending inhibitory pathways, reducing neuronal hyperexcitability, modulating neurogenic inflammation, and improving emotional regulation.

4.5. Potential reporting biases

Furthermore, as the data rely on declarative measures, they are inherently susceptible to social desirability biases (Myers et al., 2003; Gijsbers et al., 2005). For instance, some participants, especially males or contact sport athletes, may consciously or unconsciously feel inclined to conform to gendered stereotypes that associate high pain tolerance with athletic or masculine ideals. Similarly, it is possible that the participants were influenced by stereotypes suggesting that women are perceived as more fragile and less pain tolerant. Self-reported measures can also be influenced by the gender or age of the experimenter relative to the participant (Kàllai et al. 2004).

4.6. Limitations

This study presents several methodological limitations that should be acknowledged. First, group composition may introduce a gender bias: the contact

sports group is exclusively female, whereas the endurance group includes both males and females. This disparity could influence results, particularly in pain-related measures, even though no significant differences in gender distribution were found within the endurance group.

Similarly, the absence of significant findings regarding physical activity level, even if a trend was noted within the endurance group, could suggest that the influence of physical activity on central sensitization is specific to contact sports, such as rugby, rather than endurance sports.

Last and not the least, an inter-rater bias needs to be underlined, given that three teams of examiner took turns on this work.

5. Conclusion

The purpose of this research was to assess how physical activity impacts central sensitization through a comparison of two sports: rugby and endurance sports; based on the athletes' level of practice. Findings indicate that the choice of sport significantly affects central sensitization. Individuals in the rugby category displayed a clearly reduced area of secondary hyperalgesia (SHA) compared to those in the endurance group. These observations imply that consistent practice in contact sports, characterized by regular pain exposure, may improve pain processing, consequently restricting the expansion of hyperalgesia. This central desensitization reflects an adaptation of the central nervous system, rendering athletes more resilient to pain.

Additionally, the level of practice appears to be an influential factor. Elite athletes demonstrated a smaller SHA compared to intermediate athletes. However, this variation was not statistically significant when considering only the endurance sport participants. This could suggest that the impact of practice level on central sensitization is specific to contact sports.

No significant interaction was found between the type of sport and the level of practice, indicating that their influences on SHA operate separately. Regarding mechanical pinprick sensitivity (MPS), every subject exhibited an elevation

following high-frequency stimulation, verifying the effective provocation of central sensitization. Nevertheless, no significant difference was noted among the groups.

In conclusion, the very nature of this study, which is an observational study, is such that we can't establish a causal link but only a correlation link between the analysed variables. For example, our results may be influenced by the fact that individuals with a high level of central sensitization tend to avoid contact sports, thereby introducing bias into our observations. To better interpret the observed differences between types of sports practice, further studies are needed. These studies should delve deeper into the comprehension of central sensitisation mechanisms.

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7. Annex

Annex 1

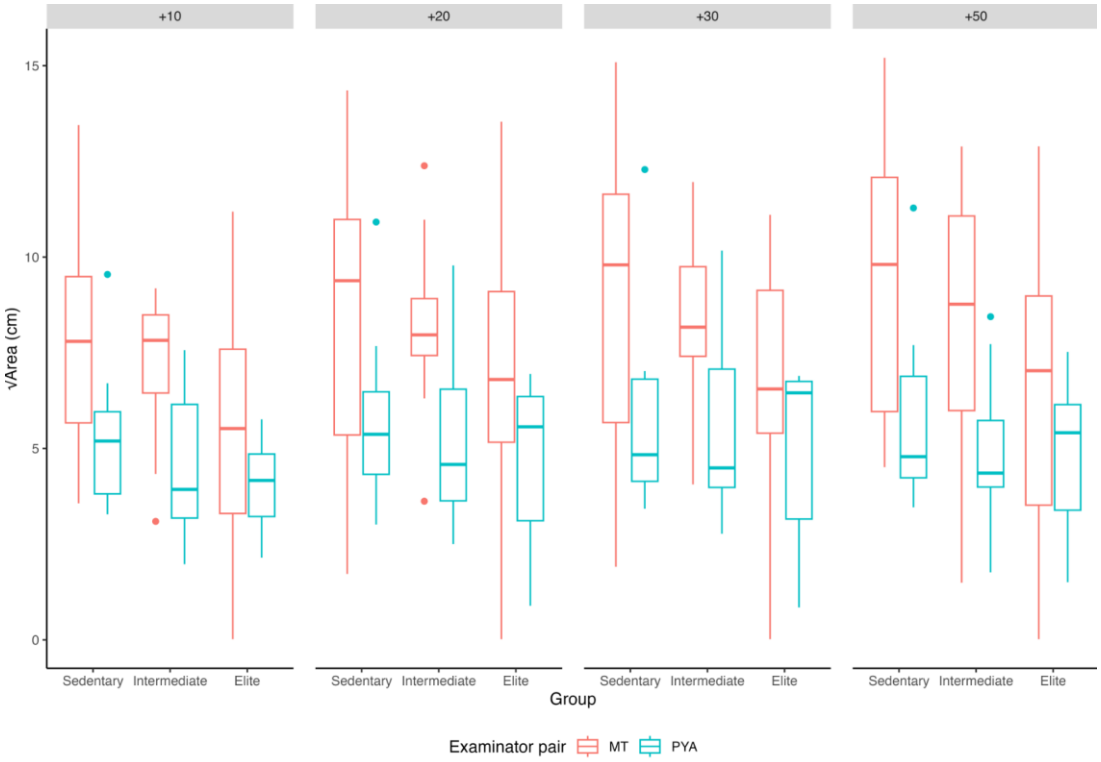

Figure 10. Boxplots representing the variation in SHA (√Area, in cm) across time points (+10, +20, +30, and +50 min) following HFS stimulation. The data are grouped by PA level (Sedentary, Intermediate, and Elite) and by examinator pairs. The boxes indicate the interquartile range (IQR), with the horizontal line representing the median. The whiskers extend to 1.5 times the IQR, and individual dots denote outliers.

This study aims to determine whether SH develops similarly in rugby players and endurance athletes in relation to the level of practice, if contact sports are associated with specific adaptations modulating CS (e.g., exposure to repeated nociceptive stimuli) that are not related to adaptations specifically induced by physical training.
84 participants allocated in 2 groups were recruited for this study: A rugby group composed of 24 females rugby players allocated in 2 groups (12 amateurs players and 12 athletes) and an endurance group composed of 60 subjects of both sexes allocated in 3 groups (20 athletes, 20 intermediate and 20 sedentary subjects).
A high frequency stimulation (HFS) protocol was executed on one of the volar forearms in order to induce central sensitization (CS), which was assessed through secondary hyperalgesia (SH). Mechanical pinprick sensitivity (MPS) and secondary hyperalgesia area (SHA) were assessed 10, 20, 30 and 50 minutes post-HFS in endurance group and 25, 30 and 35 minutes post-HFS in rugby group. In both groups, MPS was also assessed before HFS and on both forearms for each timepoint.
Rugby players exhibited a smaller SHA than endurance athletes, and elite athletes—regardless of sport—showed a reduced SHA compared to intermediates. MPS increased in all participants after HFS, with no significant group differences.

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