

27 **Abstract**

28 Many occupations and sports require high levels of manual dexterity under thermal stress and
29 mental fatigue. Yet, multi-stressor studies remain scarce. We quantified the interactive effects
30 of thermal stress and mental fatigue on manual dexterity. Seven males (21.1 ± 1.3 y) underwent
31 6 separate 60-min trials characterised by a combination of 3 air temperatures (HOT: 37°C;
32 NEUTRAL: 21°C; COLD: 7°C) and 2 mental fatigue states (MF: mental fatigue induced by a
33 35-min cognitive battery; No-MF: no mental fatigue). Participants performed complex
34 (O'Connor test) and simple (Hand-Tool test) manual tasks pre- and post-trials to determine
35 stressors-induced performance changes. We monitored participants' rectal temperature and
36 hand skin temperature (T_{hand}) continuously and assessed reaction time (Hand-Click test) and
37 subjective mental fatigue (5-point scale). Thermal stress ($p < 0.0001$), but not mental fatigue
38 ($p = 0.290$), modulated T_{hand} (HEAT: $+3.3^\circ\text{C}$ [95%CI $+0.2, +6.5$]; COLD: -7.5°C [$-10.7, -$
39 4.4]). Mental fatigue ($p = 0.021$), but not thermal stress ($p = 0.646$), slowed reaction time
40 ($\sim 10\%$) and increased subjective fatigue. Thermal stress and mental fatigue had an interactive
41 effect on the complex manual task ($p = 0.040$), with COLD-No-MF decreasing performance
42 by -22% [$-39, -5$], while NEUTRAL-MF, COLD-MF, and HEAT-MF by -36% [$-53, -19$], $-$
43 34% [$-52, -17$], and -36% [$-53, -19$], respectively. Only mental fatigue decreased
44 performance in the simple manual task (-30% [$-43, -16$] across all thermal conditions;
45 $p = 0.002$). Cold stress-induced impairments in complex manipulation increase with mental
46 fatigue; yet combined stressors' effects are no greater than that of mental fatigue alone, which
47 also impairs simple manipulation. Mental fatigue poses a greater challenge to manual
48 dexterity than thermal stress.

49

50 **Introduction**

51 Many occupations such as those in the military and healthcare sectors, as well as competitive
52 sports, require high levels of manual dexterity to ensure optimal performance. However,
53 these occupations and sports are often performed under conditions of thermal stress and
54 mental fatigue, which pose a challenge for manual performance. A military doctor treating a
55 gunshot wound during a cold-weather operation, an ICU nurse intubating a patient after a
56 long shift and while wearing personal protective equipment, and a shooting athlete reloading
57 a rifle during a hot summer Olympics' final, are all examples of real-life scenarios where
58 optimal manual performance is essential, yet it may be impaired by the combined presence of
59 thermal and cognitive stressors.

60 Manual dexterity is described as the ability to make coordinated hand and finger movements
61 aimed at manipulating objects (21). This motor ability relies on neurophysiological (e.g.
62 reflex motor control of grip force) as well as neurocognitive mechanisms (e.g. visuo-motor
63 coordination, information processing and reaction time), and ranges from simpler to more
64 complex actions (e.g. from simply unscrewing a bolt using the thumb and index finger to
65 pinch-gripping a needle and placing it in a small hole) (21).

66 It is well established that thermal stress, and particularly cold stress, has a detrimental effect
67 on manual dexterity (9). For example, manual dexterity worsens when local hand and finger
68 temperatures decrease to $\sim 20^{\circ}\text{C}$ as a result of cold air exposure (20), with this effect
69 becoming more severe at hand skin temperatures of 15°C and below (9). Furthermore,
70 localised heating of the hand increases tapping speed; yet it also delays simple reaction time
71 (25). Local changes in hand and finger temperatures play a greater role in worsening manual
72 performance than changes in core temperature, with manipulative performance being hardly
73 influenced by decreases in core temperatures when the hand is kept warm (8; 12). Changes in
74 manual performance due to hand and fingers cooling are due to loss of cutaneous sensitivity
75 (35), secondary to conduction slowing in cold cutaneous nerve afferents (10; 41). Conduction
76 velocity in cutaneous nerve fibers decreases linearly when skin temperature drops from 36 to
77 23°C (10); a more pronounced slowing occurs at temperatures below 20°C (41), with
78 conduction blocks developing at skin temperatures $\sim 8^{\circ}\text{C}$ (35). Furthermore, cooling (but not
79 heating) of synovial fluid, reduces joint mobility, which can in turn contribute to thermal-
80 stress induced decrements in manual performance (22).

81 Beside thermal stress, cognitive stressors such as mental fatigue (i.e. a psychobiological state
82 induced by prolonged periods of demanding cognitive activity) (11; 23) can also be

83 detrimental to manual performance (3; 13) by increasing perceived exertion (32) and
84 hindering cognitive and perceptual skills (14), including reaction time (25).

85 While the independent effects of thermal (i.e. heat and cold stress) and cognitive stressors
86 (i.e. mental fatigue) on manual performance have been studied in isolation, there is a paucity
87 of data on their combined effects on the dexterous execution of both simple and more
88 complex manual tasks. This opens to the question of which stressor, i.e. thermal stress or
89 mental fatigue, poses a greater challenge to manual dexterity, and how their effects combine
90 under a multi-stressor scenario. There is some evidence that heat stress and mental fatigue
91 can interact synergistically in reducing cycling endurance capacity (36); yet, multi-stressors
92 studies remain scarce, particularly in the context of manual performance. Quantifying the
93 independent and interactive effects of multi-stressor scenarios on performance is
94 fundamentally important to better understand human integrative physiological responses (27).
95 Furthermore, this basic knowledge can support the development of applied interventions
96 aimed at mitigating the impact of the more detrimental stressor, to preserve performance
97 more effectively.

98 The interactions between stressors depend on the mechanisms by which each stressor exerts
99 its effects (5; 28). Stressors with largely independent mechanisms of action often induce
100 additive effects, while stressors that are mechanistically similar may induce synergistic or
101 antagonist effects (27). Both thermal stress and mental fatigue induce deterioration of
102 reaction time and hand motor coordination by either slowing peripheral conduction velocity
103 or engaging central cognitive resources. Accordingly, it would be reasonable to hypothesize
104 that those stressors may induce a synergistic deterioration of manual performance when
105 combined.

106 The aim of this study was to quantify the independent and interactive effects of thermal stress
107 and mental fatigue on manual performance. Our objectives were to assess manual dexterity
108 during simple and complex tasks following 60-min exposures to six combinations of three
109 environmental temperatures (i.e. 7, 21 and 37°C) and two mental fatigue states (i.e. with and
110 without mental fatigue) in healthy young adults. We hypothesized that thermal stress and
111 mental fatigue would interact synergistically in impairing manual dexterity, i.e. their
112 combined impact would be greater than the sum of their individual impacts.

113

114 **Methods**

115 *Ethical approval*

116 The testing procedure and the conditions were explained to each participant and they all gave
117 written informed consent for participation. The study was approved by the Loughborough
118 University Ethics Sub-Committee for Human Participants, and testing procedures were in
119 accordance with the tenets of the Declaration of Helsinki. All testing took place in
120 Loughborough (UK) between June and September 2017.

121

122 *Participants*

123 Given the experimental demands of the present study (i.e. each participant would partake in
124 six separate 60-min trials in hot, cold, and mentally fatigued conditions), and in line with
125 similar research (see e.g. 28; 36), we used a convenience sampling approach to recruit eight
126 non-smoking, recreationally active males (i.e. more than/or 3 exercise sessions per week)
127 with no neurological, cardiovascular nor sensory-related disorders (e.g. numbness over the
128 hands), and with normal or corrected-to-normal vision, were recruited from the student
129 population of Loughborough University to take part in this study.

130 Due to technical reasons, only 7 participants (age 20.6 ± 1.3 y; body fat 12.7 ± 2.1 %; height
131 180.3 ± 4.1 cm) completed all experimental trials. In the 24h prior to each trial, participants
132 were instructed to refrain from: 1) performing mental and physical training; 2) consuming
133 caffeine, alcohol or any other stimulant. All participants performed their trials at the same
134 time of the day. As we appreciated the limitations of a convenience sampling approach, we
135 performed a sensitivity analysis to determine the required effect size and F critical for a
136 statistically significant interaction between thermal stress and mental fatigue for the complex
137 manual task (i.e. ANOVA repeated measure, within-between interaction), given our sample
138 size of 7, an α of 0.05, a β of 0.95, a number of groups of 6, and a number of measurements
139 of 12. We determined those values to be 1.09 (effect size f) and 2.49 (F critical) and we
140 therefore used these parameters as a threshold for interpreting our findings. The power
141 analysis was performed in GPower 3.1.9.2.

142

143 *Experimental design*

144 We used a single-blind, repeated measure design, where participants were made aware of the
145 purpose of the study, but not of its hypotheses nor the characteristics of each experimental
146 trial (e.g. ambient temperature and induction of mental fatigue), to limit any expectation bias.
147 All participants took part in six different 60-min trials on separate days, which were
148 characterised by a different combination of three ambient temperatures (HEAT: 37.0 ± 0.4 °C;
149 NEUTRAL: 21.0 ± 0.4 °C; COLD: 7.0 ± 0.4 °C; relative humidity maintained at 40.0 ± 1.5 % RH

150 for all temperatures) and two mental fatigue states (MF: mental fatigue; No MF: no mental
151 fatigue) (Fig. 1). At the beginning (i.e. baseline) and at the end (i.e. post-test) of each trial
152 participants performed a complex manual task, i.e. O'Connor finger dexterity test (O'Connor
153 dexterity test, 2017), and a simpler manual task, i.e. modified Hand-Tool Dexterity test
154 (Hand-Tool Dexterity test, 2017). We introduced both simpler and more complex manual
155 dexterity tasks to provide a more comprehensive assessment of the potential interactive
156 effects of our chosen stressors, as well as for their relevance to occupational settings (e.g. a
157 soldier controlling a drone or reloading a gun). The mode of execution of both tests
158 administered falls within a general assessment of manual dexterity, which depending on the
159 task may require more complex vs. simpler motor actions.

160 During all trials, participants rested in a seated position in a climatic chamber, while wearing
161 a standardised clothing ensemble consisting of T-shirt, running shorts, socks and running
162 shoes. We monitored participants' whole-body thermal state [i.e. rectal temperature (T_{rec}),
163 hand skin temperature (T_{hand}), and upper body mean skin temperature ($T_{upper\ body}$)] and
164 cognitive state (i.e. reaction time and subjective mental fatigue), in order to quantify the
165 impact of each stressor on participants' physiological and cognitive responses. All trials were
166 performed in a counter-balance order to avoid any order effect.

167 By comparing participants' change in manual performance between pre- and post-test in each
168 trial with the pre-to-post change in performance in the NEUTRAL-No MF trial (i.e. namely
169 the control condition), this design allowed for the quantification of the independent effect of
170 each individual stressor (i.e. HEAT-No MF; COLD-No MF; NEUTRAL-MF), as well as of
171 their interaction (i.e. HEAT-MF; COLD-MF), on both simple and complex manual tasks.

172 It should be noted that magnitude of heat stress (i.e. 60 min of passive exposure in moderate
173 heat & humidity) was known to likely be insufficient to impair psychomotor function and
174 hence manual dexterity; yet the question of more relevance during the HEAT trials was
175 whether addition of mental fatigue would elicit impairments in dexterity.

176

177 *Thermal stress*

178 To induce hot and cold thermal stress, we passively exposed participants to a hot, a thermo-
179 neutral, and a cold climate, characterised by an ambient temperature of 37, 21 and 7°C,
180 respectively, with a constant relative humidity of 40%. We chose these ambient temperatures
181 for several reasons. First and foremost, we wanted to ensure that the heat and cold exposures
182 selected for the 60-min trials would be sufficient to induce large changes in hand skin
183 temperature (e.g. reducing hand temperature to ~20°C), which was confirmed during pilot

184 studies. Second, we wanted to replicate average ambient temperatures likely to be
185 experienced in an occupational setting relevant for the purpose of this study such as a military
186 operation in Afghanistan. We confirmed that the average temperature during the coldest part
187 of the year in Helmand province in Afghanistan is $\sim 7^{\circ}\text{C}$ ($\sim 40\%$ RH), whereas the average
188 temperature during the hottest part of the year in the same province is $\sim 37^{\circ}\text{C}$ ($\sim 40\%$ RH)
189 (World Weather Online.com).

190

191 *Mental fatigue*

192 In order to generate prolonged periods of demanding cognitive activity (Desmond et al. 2001;
193 Job et al. 2001) that would be sufficient to induce a state of mental fatigue at the end of the
194 mental fatigue trials, participants underwent a 35-min cognitive test battery, consisting of 5
195 separate tasks, each lasting 7 min. The first three tasks were arithmetic calculations (based on
196 the Key stage 2 of the UK national curriculum (17), followed by The Stroop Colour and
197 Word Test (37), and the McKinsey problem solving test (34). All tests were written tests,
198 performed using a sheet of paper and a pencil provided to participants. To avoid a learning
199 effect between trials, while maintaining the same level of cognitive demands, each participant
200 performed three different versions of the same five tasks (e.g. different papers from Key stage
201 2) during each of the three mental fatigue trials they took part in. The tests were performed
202 under time pressure, and verbal encouragement was given to complete them within the time
203 allocated. The combination of time pressure and cognitive demand provided by these tests
204 was deemed appropriate to induce a state of mental fatigue, which was later confirmed by
205 both objective (i.e. reaction time) and subjective measures (i.e. self-reports of mental fatigue
206 via a Likert scale). During the no-mental fatigue trials, participants watched non-stimulating
207 videos.

208

209 *Experimental protocol*

210 Participants arrived at the laboratory on testing days, they changed into shorts and short
211 sleeve t-shirt and underwent preliminary measurements and preparation. They then
212 underwent a full familiarization with testing procedures, including the manipulative tasks (i.e.
213 several mock trials were allowed until participants confirmed confidence in the task), and the
214 assessments of mental fatigue (i.e. reaction time and Likert scale).

215 Following the familiarisation, participants self-inserted a rectal probe 13 cm passed the anal
216 sphincter (BlueTemp temperature probe, UK) to record T_{rec} as an index of core temperature.
217 A skin thermistor (Grant, UK) was taped to the centre of the hairy portion of the dominant

218 hand with hypoallergenic medical tape (3M, UK) to record local T_{hand} . Similarly, six
219 additional skin thermistors were taped to the centre of the forehead, the chest, the abdomen,
220 the scapula, the tricep and forearm, to record local skin temperatures for the calculation of a
221 simple mean of upper body skin temperature ($T_{upper\ body}$). T_{rec} , T_{hand} , and $T_{upper\ body}$ were
222 recorded at 2Hz via a dedicated data acquisition system (USB- Temp, MCCdaq, USA) and
223 custom-written software (DASYLab, MCCdaq, USA), and then averaged every 5 min for the
224 duration of the 60-min trials. At this point, participants moved into the climatic chamber,
225 which had been previously regulated to the air temperature and humidity required for the
226 specific 60-min trial. Participants took 5 min to enter the chamber and assume a seated
227 position on a small desk, where testing equipment was placed by accompanying the
228 investigator. The following 55 min consisted of: a. baseline fatigue assessment and
229 manipulation tasks (10 min); b. cognitive test battery or watching non-stimulating videos (35
230 min); c. post-test fatigue assessment and manipulation tasks (10 min).

231 Once seated in the chamber, participants first performed 3 consecutive reaction time tests,
232 consisting of having to tap a box on a computer screen with their dominant index finger as
233 fast as they could when this turned from red to green (click test; Humanbenchmark.com,
234 2017). Reaction time was recorded in milliseconds and the average of 3 attempts was
235 calculated. Second, participants had to report on a 5-point Likert scale [1: Not mentally
236 fatigued; 2: Slight mental fatigue; 3: Mentally drained; 4: Mentally fatigued; 5: Mentally
237 exhausted; note: this was modified from the 12-point mental fatigue scale (24; 18)] their
238 current mental fatigue state. Third, participants performed the pre-test manual tasks. The
239 O'Connor dexterity test consisted in having to place as many pins as possible in each hole of
240 the O'Connor board in 3 min (note: participants were instructed to place three pins per hole).
241 Upon completion of the O'Connor dexterity test, participants performed a modified version
242 of the Hand-Tool Dexterity test. This test consisted of having to unscrews and screw as many
243 horizontal hex nuts as possible in 3 min. Nuts were screwed on 23 horizontal bolts mounted
244 on a wooden board. The number of pins and nuts were used as performance indicators for
245 complex and simple manual tasks, respectively. At this point, and depending on the trial,
246 participants underwent either the cognitive test battery or watched non-stimulating videos.
247 Upon completion of this period, participants underwent again the objective and subjective
248 assessment of mental fatigue, as well as the two manipulative tasks. Once those tasks were
249 completed, participants exited the climatic chamber and were de-instrumented.

250

251 *Statistical analysis*

252 To assess the independent and interactive effects of thermal stress and mental fatigue on
253 physiological and perceptual responses, and on manual performance, we first calculated the
254 difference (i.e. Δ) between baseline and post-test assessments for each parameter and for each
255 individual participant. While units of measures were maintained for physiological and
256 perceptual parameters in baseline vs. post-trial differences (e.g. changes in T_{hand} were
257 expressed as $\Delta^{\circ}\text{C}$), participants' manual performance was calculated as a percentage
258 difference between baseline and post-test in each trial.

259 First, we analysed differences in baseline (i.e. pre-test) T_{rec} , T_{hand} , $T_{\text{upper body}}$, reaction time,
260 subjective fatigue, fine and gross manipulative performance, by means of 1-way repeated
261 measures ANOVAs (i.e. 6 levels, one for each experimental trial). Second, we analysed
262 ΔT_{rec} , ΔT_{hand} , $\Delta T_{\text{upper body}}$, Δ reaction time, Δ subjective fatigue, Δ performance in fine and gross
263 manipulation (%), for the independent and interactive effect of thermal stress (3 levels:
264 NEUTRAL vs. HEAT vs. COLD) and mental fatigue (2 levels: MF vs. No-MF), by means of
265 2-way repeated measure ANOVAs.

266 Post-hoc analyses were conducted with Tukey's multiple comparison tests. Regarding the
267 manual tasks, we compared participants' performance in each experimental trial including
268 either thermal stress, mental fatigue or both, with the performance in the NEUTRAL-No MF
269 (i.e. control) trial.

270 Data are reported as means, standard deviation (SD), and 95% Confidence Intervals (CI).
271 Observed power was computed using $\alpha=0.05$. Statistical analysis was performed using
272 GraphPad Prism (version 8.0; GraphPad Software, La Jolla, CA, USA).

273

274 **Results**

275 *Body temperatures*

276 Baseline (i.e. pre-test) T_{rec} , T_{hand} , $T_{\text{upper body}}$ did not differ amongst the six trials (Tab.1).

277 First, we found that neither thermal stress ($F_{(2,12)}=1.051$; $p=0.380$; explained variance 4.5%),
278 nor mental fatigue ($F_{(1,6)}=1.386$; $p=0.284$; explained variance 4.1%) had a significant effect
279 on ΔT_{rec} (Fig. 2A).

280 Second, we found that thermal stress ($F_{(2,12)}=44.96$; $p<0.0001$; explained variance 75.6%),
281 but not mental fatigue ($F_{(1,6)}=1.344$; $p=0.290$; explained variance 0.3%), had a significant
282 effect on ΔT_{hand} . No interactions occurred between thermal stress and mental fatigue ($F_{(2,$
283 $12)}=0.20$; $p=0.820$; explained variance 0.2%). When collapsed over mental fatigue trials and
284 compared to the NEUTRAL trial, ΔT_{hand} was -7.5°C ([95%CI: $-10.7, -4.4$]; $p<0.0001$) in the
285 COLD, while it was $+3.3^{\circ}\text{C}$ ([95%CI: $+0.2, +6.5$]; $p<0.0001$) in the HEAT (Fig. 2B). When

286 expressed in absolute terms, post-test T_{hand} corresponded to $22.7 \pm 2.5^{\circ}\text{C}$ during COLD trials,
287 and $34.7 \pm 1.1^{\circ}\text{C}$ during HEAT trials.

288 Third, we found that thermal stress ($F_{(2,12)}=116.6$; $p<0.0001$; explained variance 85.1%), but
289 not mental fatigue ($F_{(1,6)}=0.281$; $p=0.615$; explained variance 0.1%), had a significant effect
290 on $\Delta T_{\text{upper body}}$. No interactions occurred between thermal stress and mental fatigue ($F_{(2,$
291 $12)}=0.08$; $p=0.917$; explained variance 0.1%). When collapsed over mental fatigue trials and
292 compared to the NEUTRAL trial, $\Delta T_{\text{upper body}}$ was -4.4°C ([95%CI: $-5.6, -3.2$]; $p<0.0001$) in
293 the COLD, while it was $+2.2^{\circ}\text{C}$ ([95%CI: $+1.0, +3.4$]; $p<0.0001$) in the HEAT (Fig. 2C).

294 Table 2 reports post-trial data for T_{rec} , T_{hand} , and $T_{\text{upper body}}$.

295 All in all, these results indicated that our thermal stress conditions were effective in inducing
296 large changes in local skin temperature of the hand and in upper body skin temperature,
297 independently of the presence of mental fatigue.

298

299 *Objective and subjective measures of mental fatigue*

300 Baseline (i.e. pre-test) reaction time and subjective fatigue did not differ amongst the six
301 trials (Tab.1).

302 First, we found that mental fatigue ($F_{(1,6)}=9.44$; $p=0.021$; explained variance 21.4%), but not
303 thermal stress ($F_{(2,12)}=0.45$; $p=0.646$; explained variance 2.6%), had a significant effect on
304 Δ reaction time (Fig. 3A). No interactions occurred between thermal stress and mental fatigue
305 ($F_{(2, 12)}=1.38$; $p=0.288$; explained variance 4.1%). When collapsed over thermal stress trials,
306 the difference in Δ reaction time between No-MF and MF trials was $+33$ ms ([95%CI: $+7,$
307 $+59$]; $p<0.0001$). Given that baseline reaction times were on average 352 ms (see Tab. 1), this
308 difference corresponded to $\sim 10\%$ increase in reaction time because of the cognitive test
309 battery administered during MF trials.

310 Second, we found that mental fatigue ($F_{(1,6)}=1405$; $p<0.0001$; explained variance 86.9%), but
311 not thermal stress ($F_{(2,12)}=0.84$; $p=0.452$; explained variance 0.8%), had a significant effect on
312 Δ subjective fatigue (Fig. 3B). No interactions occurred between thermal stress and mental
313 fatigue ($F_{(2, 12)}=1$; $p=0.396$; explained variance 0.8%). When collapsed over thermal stress
314 trials, the difference in Δ subjective fatigue between No-MF and MF trials was $+2.5$ scale
315 points ([95%CI: $+2.3, +2.7$]; $p<0.0001$). Given that all participants reported a mental fatigue
316 of “1 – Not Mentally fatigued” at the beginning of all trials (see Tab. 1), this difference
317 indicated that participant reported being between “3 – Mentally drained” and “4 – Mentally
318 fatigued” at the end of MF trials. Table 2 reports post-trial data for reaction time and
319 subjective fatigue.

320 All in all, these results indicated that our mental fatigue conditions were effective in inducing
321 a state of mental fatigue, which was confirmed by both objective (i.e. reaction time) and
322 subjective measures (i.e. self-reports), and which was independent of thermal stress.

323

324 *Manual performance*

325 Baseline performance in the complex and simple tasks did not differ amongst the six trials
326 (Tab.1).

327 First, we found that mental fatigue ($F_{(1,6)}=54.4$; $p=0.0003$; explained variance 48.7%), but not
328 thermal stress ($F_{(2,12)}=2.88$; $p=0.094$; explained variance 6.6%), had a significant effect on
329 Δ complex manual performance. Also, we found a significant interaction between thermal
330 stress and mental fatigue ($F_{(2, 12)}=4.24$; $p=0.040$; explained variance 8.9%). When compared
331 to NEUTRAL-No MF, manual performance in the complex task decreased by: -22%
332 ([95%CI -39, -5]; $p=0.012$) in the COLD-No MF; by -16% ([95%CI -33, +1]; $p=0.075$) in the
333 HEAT-No MF; by -36% ([95%CI -53, -19]; $p=0.0002$) in the NEUTRAL-MF; by -34%
334 ([95%CI -52, -17]; $p=0.0003$) in the COLD-MF; and by -36% ([95%CI -53, -19]; $p=0.0002$)
335 in the HEAT-MF (Fig. 4). These results indicated that mental fatigue alone induced greater
336 detriments on dexterity in the complex task (i.e. 36% performance drop) than cold stress
337 alone (i.e. 22% performance drop), and that when interacting with either cold or heat stress,
338 mental fatigue decreased manual performance by an extent equal (i.e. ~35% combined
339 performance drop) to what observed when fatigue acted alone.

340 Second, we found that mental fatigue ($F_{(1,6)}=28.9$; $p=0.002$; explained variance 36.1%), but
341 not thermal stress ($F_{(2,12)}=0.81$; $p=0.468$; explained variance 3.9%), had a significant effect on
342 Δ simple manual performance. No interactions occurred between thermal stress and mental
343 fatigue ($F_{(2, 12)}=0.78$; $p=0.476$; explained variance 2.2%). When collapsed over thermal stress
344 trials, the difference in Δ simple manual performance between No-MF and MF trials was -
345 30% ([95%CI: -43, -16]; $p=0.002$). Table 2 reports post-trial data for the complex and simple
346 tasks.

347 All in all, these results indicated that mental fatigue was the main inducer of the observed
348 detriments in dexterity during the simple manual task (i.e. 30% performance drop), and that
349 these detriments were independent of thermal stress.

350

351 **Discussion**

352 The aim of this study was to determine the independent and interactive effects of thermal
353 stress and mental fatigue on manual dexterity. In assessing changes in manual performance

354 during complex and simple tasks following on single and combined exposures to heat, cold,
355 and mental fatigue, we hypothesized that thermal stress and mental fatigue would interact
356 synergistically in reducing manual dexterity in healthy young adults.

357 With regards to the complex manual task, and contrary to our hypothesis, we found that,
358 while thermal stress and mental fatigue interacted in reducing manual dexterity (i.e. ~35%
359 performance decrement), their mode of interaction was not synergistic. In fact, stressors
360 interaction followed a pattern whereby mental fatigue increased the individual impact of cold
361 (i.e. 22% performance decrement) and heat (i.e. 15% performance decrement), yet by an
362 extent no greater than that induced by mental fatigue alone (i.e. 36% performance
363 decrement). With regards to the simple manual task, we found that mental fatigue was the
364 main inducer of the observed detriments in dexterity (i.e. 30% performance drop), with these
365 detriments being independent of thermal stress.

366

367 *Independent effects of thermal stress*

368 When considering the effects of thermal stress, our findings are in line with previous single-
369 stressor studies. Our observed ~22% performance decrement in dexterity during the complex
370 task resulting from hand skin temperature dropping to an absolute value ~23°C ($\Delta -7.5^\circ\text{C}$), is
371 in line with previous results that have demonstrated an increase in hand numbness and a
372 decrease in finger dexterity at finger skin temperature between 22 and 14°C (9; 38). It is
373 important to note that we measured hand skin temperature at the centre of the back of the
374 hand. Given the large capacity for fast vaso-constriction (and -dilation) of the glabrous
375 portion of the fingers (39), one would expect that our recorded drops (and rises) in hand skin
376 temperature provide an underestimation of the actual extent of finger skin cooling (and
377 heating) occurring during our experiments. It is well-known that whole-body exposures to
378 cold increase proximal-to-distal differences in skin temperature, and that drops in local skin
379 temperature are more pronounced as one moves from to central body parts to fingers and toes
380 (e.g. as confirmed in our study when comparing ΔT_{hand} vs. $\Delta T_{\text{sk-upper body}}$) (39). Hence, it
381 appears likely that fingers' skin temperature may have dropped well below our recorded hand
382 temperature of ~23°C and within the 22 to 14°C range previously shown to be associated
383 with decreased hand dexterity (9; 38). Mechanistically, changes in manual performance due
384 to hand and fingers cooling arise from loss of cutaneous sensitivity (35), secondary to
385 conduction slowing in cold cutaneous nerve afferents (10; 41). Given that conduction
386 velocity in cutaneous nerve fibers decreases linearly when skin temperature drops from 36 to
387 23°C (10), it could be hypothesised that our observed decrements in fine manipulation were

388 likely due to loss of cutaneous sensitivity. However, we did not measure peripheral
389 conduction velocities in the current study, and so this hypothesis remains speculative. Beside
390 cold-induced conduction slowing, cold-induced changes in joint mobility may have also
391 played a role in decreasing manual dexterity during the complex task in the current study.
392 Cold causes joints' synovial fluid to become viscous, which in turn reduces movements speed
393 and efficiency by increasing hand stiffness (6; 21; 22), all of which could have contributed to
394 our observed cold-induced decrements in dexterity.

395 Finally, we did not observe any clear effect of thermal stress on dexterity during the simpler
396 manual task. This is not entirely surprising when considering that the cutaneous sensory
397 feedback that was likely impaired by thermal (and particularly cold) stress in the current
398 study is generally more important for finer and more complex sensorimotor actions, such as
399 those required when participants had to pinch-grip, move and accurately place each pin in
400 their respective small hole in the O'Connor test board (15b, 21, 36b). In fact, increases in
401 local tissue temperature can improve simpler, gross motor function (particularly during whole
402 body exercise) and these effects underlies the classic benefits of pre-exercise warm up on
403 subsequent motor performance (15).

404

405 *Independent effects of mental fatigue*

406 Regarding mental fatigue, it appears clear from our findings that this stressor had a prominent
407 role in reducing manual performance. Specifically, mental fatigue explained ~49% and ~36%
408 of observed variance during complex and simple manual tasks whereas thermal stress
409 explained only 6% and 4% of the variance, respectively.

410 Albeit lasting only 35 min, our cognitive test battery appeared effective in inducing both a
411 subjective state of mental fatigue, as well as an objective ~10% reduction in reaction time
412 during a task requiring visuo-motor coordination of the hand analogous to what required by
413 the manipulative tasks we administered (see Fig.3). The increase in both objective and
414 subjective measures of mental fatigue indicated that our cognitive test battery elicited a
415 significant level of cognitive load and perceived strain over the course of the MF trials.

416 Current theories on the effects of mental fatigue on physical performance suggest that this
417 psychobiological state may limit exercise tolerance via higher perceived exertion (32).
418 Furthermore, and in the context of short duration tasks presenting a certain level of cognitive
419 demand such as manual dexterity tasks, mental fatigue may hinder hand function (3; 13) due
420 to its detrimental impact on cognitive and perceptual skills (14), including reaction time (26).
421 Mental fatigue has been previously demonstrated to negatively influence attention, action

422 monitoring and cognitive control (2). Accordingly, we believe that our observed effects of
423 mental fatigue on manual performance are likely due to the induction of a significant
424 cognitive load, which may have been detrimental to neuropsychological parameters such as
425 attention, action monitoring, and reaction time, all of which are important for efficient
426 manual handling.

427 Although we did not record rates of perceived exertion, it could also be speculated that,
428 similarly to what is reported for submaximal whole-body exercise such as cycling (32), a
429 state of mental fatigue could have increased the perceived effort required by our manual
430 tasks, in turn leading to greater motor fatigue and worse overall performance given the same
431 task. It is important to note that mental fatigue seems to be similarly detrimental to both local
432 and whole-body exercise (40). For example, Bray et al. showed that cognitive effort induced
433 by a short-duration protocol negatively affected voluntary submaximal and maximal
434 contractions during a handgrip test (3; 4). These authors reported greater proportional EMG
435 amplitude scores in the hand flexor muscles during the handgrip tasks in the participants who
436 performed the cognitive tasks. Bray et al.'s observations indicated that cognitive strain
437 contributed to peripheral fatigue (e.g. accumulation of metabolites) by inhibiting descending
438 neural activation of muscle motor units required to support the submaximal contraction (3; 4).
439 Given that grip strength plays an important role in efficient manual handling, it cannot be
440 excluded that similar mental fatigue-induced changes in descending neural input to hand and
441 fingers muscles may have contributed to our observed decrements in dexterity under mental
442 fatigue states.

443

444 *Combined effects of thermal stress and mental fatigue*

445 Thermal stress and mental fatigue combine in many occupational and sporting settings (6),
446 and the potential for additive or synergistic interactions between these stressors may result in
447 magnifying hazards to individuals exposed to real world, multi stressors scenarios (27).
448 Within the constraints of our experiment (i.e. 60-min thermal stress exposure and 35-min
449 cognitive load), our findings indicated that, even when combined with thermal stress, mental
450 fatigue caused the greatest challenge to manual tasks. Importantly, and contrary to our initial
451 hypothesis, we found that, while thermal stress and mental fatigue interacted in reducing
452 dexterity during the complex task (i.e. ~35% performance decrement), their mode of
453 interaction was not synergistic. In fact, stressors interaction followed a pattern whereby
454 mental fatigue increased the individual impact of cold (i.e. ~22% performance decrement)
455 and heat (i.e. ~15% performance decrement), yet by an extent no greater than that induced by

456 mental fatigue alone (i.e. ~36% performance decrement). This observation indicated a mode
457 of interaction between thermal stress and mental fatigue which followed the recently
458 proposed “most severe strain takes precedence” principle (27), whereby the more severe
459 strain “mental fatigue” takes precedence over the less severe strain “thermal stress”.
460 According to this multi-stressor principle, the mode of interaction between stressors is
461 influenced by the impact magnitude of each individual stressor (e.g. thermal stress and
462 mental fatigue) (29). That is, the greater the effect of one stressor (e.g. mental fatigue), the
463 greater the probability that the detrimental effects of this stressor will take precedence over
464 the effects of the second stressor (e.g. thermal stress). This model fits well with our
465 observation that the interactive effects of thermal stress and mental fatigue were neither
466 additive nor synergistic, but that in fact their interactive-impact magnitude was equivalent to
467 the individual impact of the “most severe stressor” mental fatigue.

468 A state of mental fatigue in our participants is likely to have contributed to a less efficient
469 information’s processing, secondary to a reduced allocation of attentional resources to task-
470 relevant cognitive processes (26). Mental fatigue may affect all stages of information
471 processing that receive modulatory top-down input, from stimulus processing to response
472 execution, and this notion is supported by studies that examined the effects of mental fatigue
473 on preparatory processes in different cognitive tasks (1; 31). It could be therefore argued that
474 in our study, mental fatigue may have negatively affected the efficiency of stimulus
475 information processing relevant for initiating hand motor responses (26). The (likely)
476 “central effect” of mental fatigue appeared to be more severe than the (likely) “peripheral
477 effects” of thermal (cold) stress on hand sensorimotor function, and this differential impact
478 could explain why mental fatigue took precedence over thermal stress in limiting the
479 manipulative performance of our participants.

480 Mental fatigue has been recently reported to interact synergistically with heat stress during
481 cycling performance in the heat (36). Hence our findings may at first appear to contrast with
482 those of Otani et al. (36). However, it should be noted that in the study of Otani et al. (36)
483 both mental fatigue and heat stress induced independent severe strains, particularly as the
484 heat stress exposure resulted in a significant rise in core temperature prior to the cycling tests
485 in the heat. The severe mental and heat strain induced by the protocol of Otani et al. (36)
486 could have therefore produced the hyper-additive effects they observed. Our trials in the heat
487 did not induce any changes in core temperature, but in fact it only raised skin temperature.
488 Furthermore, it is likely that we did not observe a synergistic effect between heat and mental
489 fatigue because of the different performance task we adopted, and the differential effects that

490 heat has on local vs. whole-body motor tasks and exercise. In contrast with the effects of a
491 high core temperature on endurance whole body performance, local increases in tissue and
492 muscle temperatures can indeed be beneficial to perform short-duration dynamic work such
493 as the dexterity tasks we administered (21). Accordingly, we believe that our findings and
494 those of Otani et al. (36) can be interpreted as two examples of how variations in the impact
495 magnitude of a stressor may modulate its role in a multi-stressor interaction (27).

496

497 **Limitations**

498 We recognise some limitations to this study. First, our sample size is rather modest, although
499 it appeared sufficient to demonstrate the effects of our chosen stressors, likely due to their
500 large effect sizes (i.e. stressors induced performance decrements in the range of 20 to 30%).
501 Second, we did not implement performance tests that would clearly delineate central from
502 peripheral effects of our stressors (i.e. simple- vs. choice-reaction time tasks using the same
503 peripheral motor demands). Third, our experimental model did not involve a scenario where
504 core temperature is shifted along with skin temperature. While evidence indicates that local
505 changes in hand and finger temperatures play a greater role in worsening manual
506 performance than changes in core temperature, we appreciate that increases in core
507 temperature due to a combination of activity-induced metabolic heat and exposure to hot
508 environments may have implications for manual dexterity and may be relevant to some
509 occupational settings. Building on our findings, future studies should therefore consider
510 mechanistic approaches to isolate peripheral from central effects in the interaction of thermal
511 stress and mental fatigue, and how those may be modulated by changes in core temperature.

512

513 **Perspectives and significance**

514 From a fundamental standpoint, our study provides further support to the fact that human
515 integrative responses to multi-stressor scenarios follow a “worst-stressor-takes-precedence”
516 principle. From an applied point of view, our study supports the development of strategies
517 that primarily target the mitigation of mental fatigue to sustain manual performance in those
518 real world occupational (e.g. military, healthcare) and sport scenarios, which sees workers
519 and athletes being exposed to a combination of mental fatigue (e.g. induced by cognitive
520 stress or long shift work) and thermal stress (e.g. induced by exposure to extreme climates of
521 by wearing personal protective equipment).

522

523 **Conclusions**

524 We conclude that, within the constraints of our experiment (i.e. a combination of 60-min
525 passive exposures to air temperatures of 7 or 37°C with 35-min of cognitive load), mental
526 fatigue posed the greatest challenge to manual dexterity in healthy young adults, even when
527 combined with heat and cold stress. Our findings highlight the important role that mental
528 fatigue can play in decreasing physical performance, both in isolation as well as when
529 interacting with other environmental stressors known to deteriorate manual dexterity such as
530 cold stress.

531

532 **Acknowledgements**

533 The authors thank Prof. George Havenith for the use of the climatic chambers at the
534 Environmental Ergonomics Research Centre (Loughborough University, UK).

535

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642 **Table and figure captions**

643

644 **Table 1.** Baseline (i.e. pre-test) T_{rec} , T_{hand} , $T_{\text{sk-upper body}}$, reaction time and subjective fatigue,
645 and fine and gross manipulative performance (i.e. number of pins correctly placed and
646 number of bolts screwed and unscrewed in 3 min), for the 7 participants, for of each of the 6
647 experimental trials. Data are reported as means and standard deviations. p-values for the
648 independent effect of trial (1-way ANOVA) are also reported.

649

650 **Table 2.** Post-test T_{rec} , T_{hand} , $T_{\text{sk-upper body}}$, reaction time and subjective fatigue, and fine and
651 gross manipulative performance (i.e. number of pins correctly placed and number of bolts
652 screwed and unscrewed in 3 min), for the 7 participants, for of each of the 6 experimental
653 trials. Data are reported as means and standard deviations.

654

655 **Figure 1.** Experimental design outlining the six separate trials undertaken by each
656 participant. By comparing participants' change in manipulative performance between pre-
657 and post-test in each trial with the pre-to-post change in performance in the NEUTRAL-No
658 MF trial (i.e. namely the control condition), this design allowed for the quantification of the
659 independent effect of each individual stressor (i.e. HEAT-No MF; COLD-No MF;
660 NEUTRAL-MF), as well as of their interaction (i.e. HEAT-MF; COLD-MF), on both fine
661 and gross manipulation.

662

663 **Figure 2.** Mean (N=7) difference and 95% CI for the ΔT_{rec} (A), ΔT_{hand} (B), and $\Delta T_{\text{upper body}}$
664 (C). Data were collapsed over mental fatigue trials and compared to the NEUTRAL trial to
665 visualise the independent effect of HEAT and COLD stress on body temperatures. *
666 corresponds to $p < 0.05$ for 2-way ANOVA post-hoc analyses.

667

668 **Figure 3.** Mean (N=7) difference and 95% CI for the reaction time (A) and subjective fatigue
669 (B). Data were collapsed over thermal stress trials to visualise the independent effect of
670 mental fatigue on objective and subjective measures. * corresponds to $p < 0.05$ for 2-way
671 ANOVA main effect.

672

673 **Figure 4.** Mean difference (N=7) and 95% in manual performance for the complex task. Data
674 for the 5 experimental conditions (i.e. COLD-MF, HEAT-MF, NEUTRAL-MF, COLD-No
675 MF, HEAT-No MF) were compared to the NEUTRAL-No MF trial (i.e. namely the control

676 condition) to visualise the independent and interactive effects of HEAT and COLD, and of
677 MENTAL FATIGUE, on manual performance. * corresponds to $p < 0.05$ for 2-way ANOVA
678 post-hoc analyses.

	NEUTRAL-No MF	NEUTRAL-MF	COLD-No MF	COLD-MF	HEAT-No MF	HEAT-MF	
T_{rec} (°C)	37.32 ±0.21	37.11 ±0.17	37.24 ±0.18	37.29 ±0.32	37.19 ±0.27	37.26 ±0.26	(p=0.560)
T_{hand} (°C)	31.34 ±2.65	30.15 ±1.72	29.67 ±2.87	29.45 ±2.07	30.52 ±2.81	30.29 ±3.01	(p=0.584)

T _{upper body} (°C)	31.81 ±0.80	31.26 ±0.81	31.62 ±0.99	31.53 ±0.27	31.75 ±1.25	32.02 ±1.46	(p=0.580)
Reaction time (ms)	352 ±38	357 ±40	347 ±32	348 ±52	353 ±52	357 ±27	(p=0.886)
Subjective fatigue (1-5)	1.0 ±0.0	1.0 ±0.0	1.0 ±0.0	1.0 ±0.0	1.0 ±0.0	1.0 ±0.0	(p=1.000)
Fine manual task (N pins)	43.3 ±6.2	49.4 ±4.6	48.4 ±8.8	48.9 ±5.1	43.4 ±6.7	49.3 ±7.7	(p=0.200)
Gross manual task (N bolts)	42.3 ±9.8	49 ±9.6	42.3 ±10.4	49.7 ±4.3	45.7 ±8.0	51 ±4.0	(p=0.199)

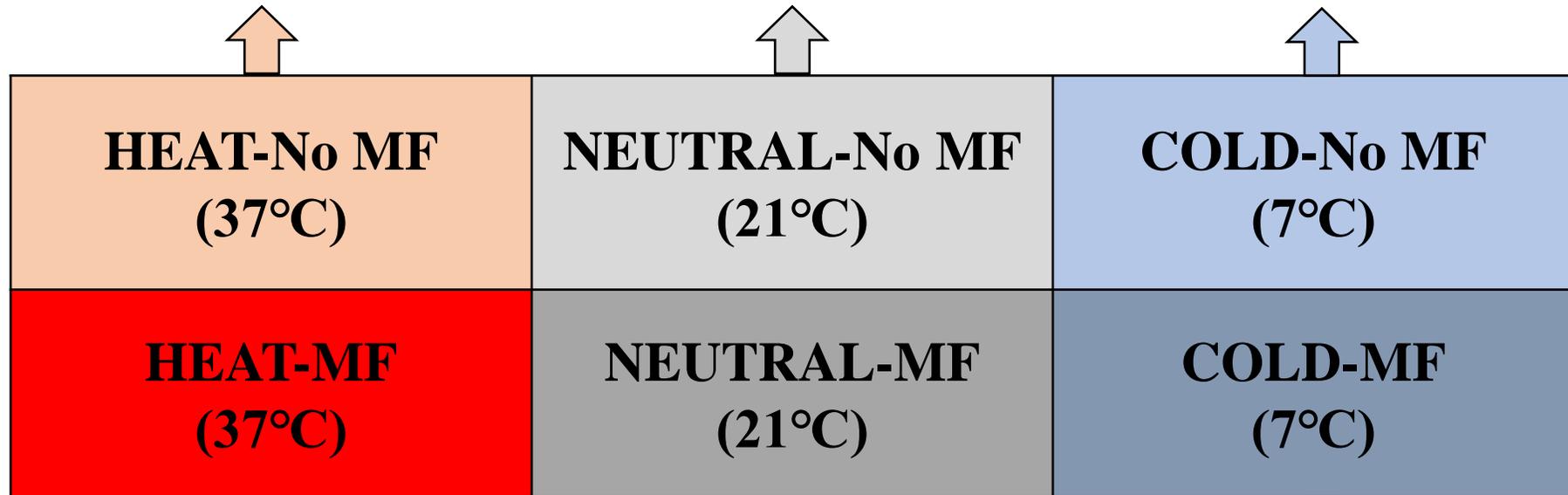
	NEUTRAL-No MF	NEUTRAL-MF	COLD-No MF	COLD-MF	HEAT-No MF	HEAT-MF
T_{rec} (°C)	37.12 ±0.22	36.96 ±0.16	37.15 ±0.22	37.25 ±0.36	37 ±0.18	37.23 ±0.26
T_{hand} (°C)	32.08 ±1.72	30.78 ±0.99	23.48 ±3.19	21.93 ±1.50	34.76 ±1.42	34.65 ±0.92

T _{upper body} (°C)	32.29 ±0.75	31.7 ±0.60	27.71 ±2.49	27.52 ±1.48	34.65 ±0.43	34.46 ±0.81
Reaction time (ms)	359 ±37	377 ±34	350 ±38	400 ±48	360 ±66	400 ±42
Subjective fatigue (1-5)	1.1 ±0.4	3.6 ±0.8	1.0 ±0.0	3.8 ±0.7	1.0 ±0.0	3.4 ±0.5
Fine manual task (N pins)	48.1 ±4.4	37.6 ±2.6	44.1 ±10.1	38.1 ±7.5	41.9 ±5.1	37.6 ±5.1
Gross manual task (N bolts)	46.7 ±5.6	39.6 ±4.0	41.1 ±7.8	40.1 ±8.6	53.3 ±6.3	42.6 ±7.6

Independent effect of HEAT

Control condition

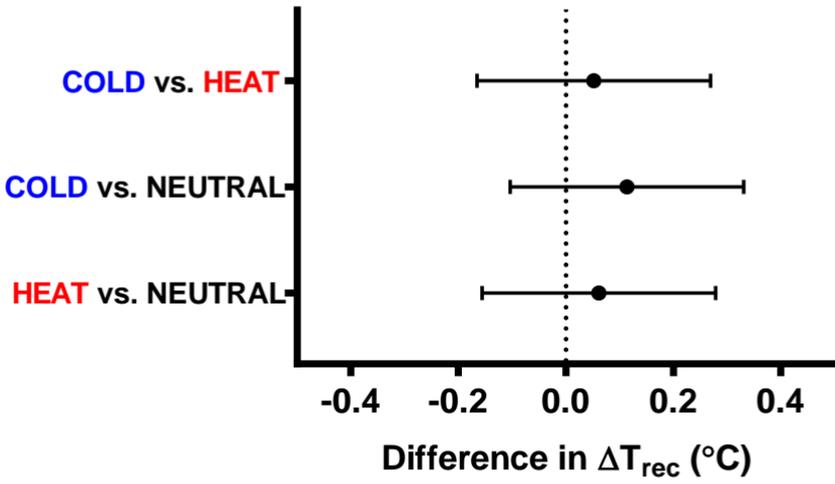
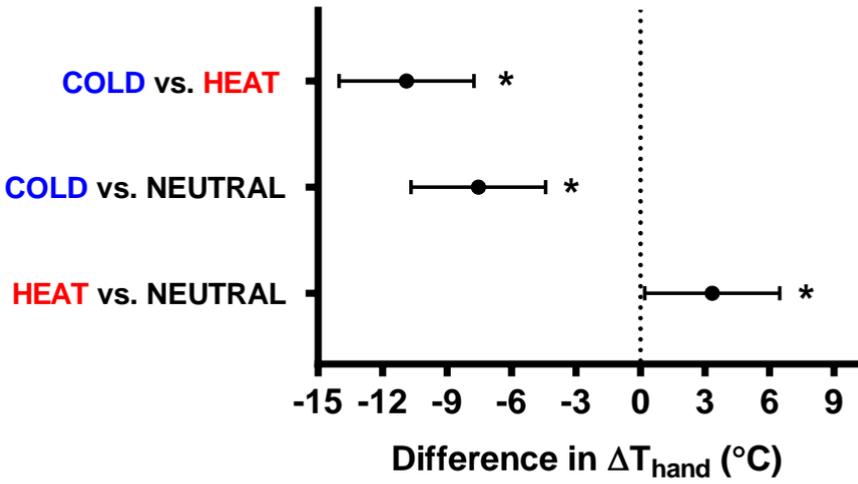
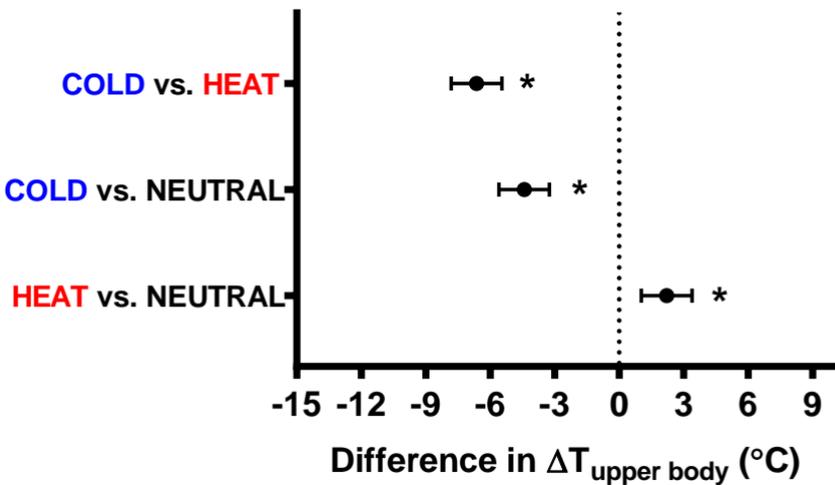
Independent effect of COLD



Interaction
HEAT + Mental Fatigue

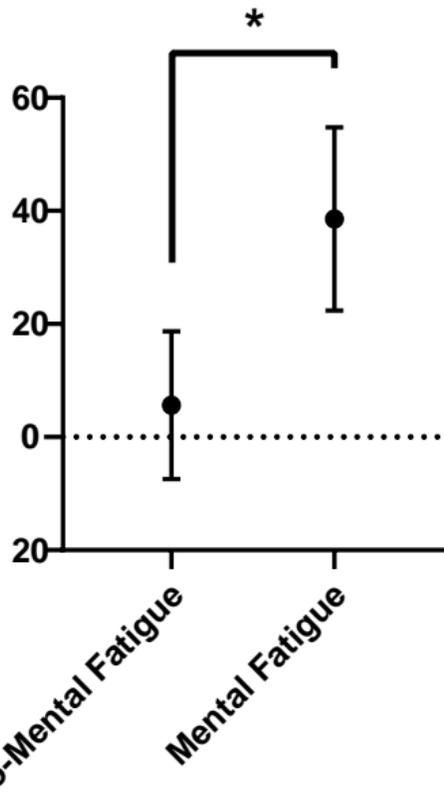
Independent effect of
Mental Fatigue

Interaction
COLD + Mental Fatigue

A**B****C**

A

Difference pre vs. post trials (ms)

**B**

Difference pre vs. post trials (scale points)

