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Neuro-computational Impact of Physical Training Overload on Economic Decision-Making

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► **To cite this version:**

Bastien Blain, Cyril Schmit, Anaël Aubry, Christophe Hausswirth, Yann Le Meur, et al.. Neuro-computational Impact of Physical Training Overload on Economic Decision-Making. *Current Biology - CB*, 2019, 29 (19), pp.3289-3297.e4. 10.1016/j.cub.2019.08.054 . hal-02339222

HAL Id: hal-02339222

<https://hal.sorbonne-universite.fr/hal-02339222>

Submitted on 30 Oct 2019

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1 **Title:**

2 **Linking endurance sport to intellectual work: the impact of physical training overload on choice**
3 **neural mechanisms**

4

5 **Short Title:**

6 **Executive fatigue induced by sport training**

7

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24

25 **Summary**

26 Overtraining syndrome is a form of burnout, defined in endurance athletes by unexplained
27 performance drop associated with intense fatigue sensation. Our working hypothesis is that the
28 form of fatigue resulting from physical training overload might share some neural
29 underpinnings with the form of fatigue observed after prolonged intellectual work, which was
30 previously shown to affect the executive control brain system. Indeed, executive control may
31 be required to prevent any impulsive behavior, including stopping physical effort when it hurts,
32 despite the long-term goal of improving performance through intense training. To test this
33 hypothesis, we induced a mild form of overtraining in a group of endurance athletes, which we
34 compared to a group of normally trained athletes on behavioral tasks performed during fMRI
35 scanning. At the behavioral level, training overload enhanced impulsivity in economic choice,
36 which was captured by a bias favoring immediate over delayed rewards in our computational
37 model. At the neural level, training overload resulted in diminished activation of the lateral
38 prefrontal cortex, a key region of the executive control system, during economic choice. Our
39 results therefore provide causal evidence for a functional link between enduring physical
40 exercise and exerting executive control. Besides, the concept of executive fatigue bridges the
41 functional consequences of excessive physical training and intellectual work into a single
42 neuro-computational mechanism, which might contribute to other clinical forms of burnout
43 syndromes.

44

45 **Keywords:** decision making, executive control, delay discounting, sport training, fatigue,
46 burnout, prefrontal cortex, fMRI, computational modeling

47

48 **INTRODUCTION**

49

50 A few decades ago, a marathon superstar at the peak of his career suddenly stopped running for
51 several years, citing mental and physical exhaustion, in the absence of apparent injury. This
52 extreme state of fatigue is at the heart of the so-called overtraining syndrome, a form of burnout
53 that strikes athletes in various types of endurance sport. Beyond subjective fatigue, the
54 overtraining syndrome is objectively characterized by a decrease in performance that persists
55 beyond substantial rest period ¹. It may also be accompanied by cardiac and endocrine
56 modifications, as well as symptoms shared with depression such as apathy, irritability,
57 restlessness, insomnia or loss of appetite ². As the underlying mechanisms remain unknown,
58 the overtraining syndrome represents a major issue for both athletes and coaches, and a potential
59 cause of doping practice.

60

61 Here, we suggest a neural mechanism that might underlie the effects of excessive physical
62 training. More specifically, our idea is that training overload induces fatigue in the executive
63 control brain system. Executive control is needed whenever routine motor or cognitive
64 processes must be monitored, interrupted and modified so as to better align the behavior to
65 long-term goals ^{3,4}. Maintaining physical effort for the sake of fitness, when aversive signals
66 such as aching muscles call for stopping, should therefore require executive control. This
67 assumption is difficult to test directly, as it would require monitoring executive control during
68 real-life endurance exercise. However, we reasoned that testing the signatures of a putative
69 fatigue in the executive control brain system might be feasible.

70

71 Indeed, we demonstrated in a previous fMRI study ⁵ that the executive control system is
72 susceptible to fatigue when engaged for a time as long as a workday. The demonstration

73 involved interleaving cognitive tasks meant to induce executive fatigue and choice tasks meant
74 to reveal executive fatigue. This procedure borrowed from sequential task paradigms that have
75 been widely used to assess resource depletion theories^{6,7}. Executive fatigue was revealed by
76 two markers recorded during inter-temporal decisions (choices between immediate and larger-
77 later monetary rewards). We observed: 1) at the neural level, a decreased excitability of the
78 lateral prefrontal cortex (LPFC) specifically during choice tasks, and 2) at the behavioral level,
79 an increased preference for immediate rewards in choice tasks.

80

81 Importantly, these markers were observed in the absence of any alteration in brain activity or
82 behavioral performance during cognitive tasks. This is consistent with the idea of an executive
83 fatigue, corresponding to an increase in the cost of mobilizing the executive control system, by
84 opposition to an executive dysfunction, as seen in patients with damage to the prefrontal cortex.
85 In other words, our notion of executive fatigue implies that executive control abilities are not
86 lost, but exerted with more parsimony. Thus, they are still mobilized in cognitive tasks where
87 performance has to be maintained, but not necessarily in choice tasks framed as mere expression
88 of subjective preference.

89

90 Here, we kept the label ‘executive fatigue’ for the collection of neural and behavioral signatures
91 previously observed following excessive cognitive work. If physical training overload also
92 leads to executive fatigue, then overtrained athletes should exhibit the same neural and
93 behavioral markers. The presence of these markers would provide evidence that physical
94 exercise over long periods might impact executive control and change temporal preferences.
95 This may be important for cognitive neuroscience in a context where failed replications have
96 casted serious doubt on whether control capacity can be reduced by its utilization at short time

97 scales ^{8,9}. For the general public, these signatures of executive fatigue would document the
98 neural adverse effects of pushing too far the demand on physical fitness.

99

100 We tested these predictions in a mild case of overtraining, called overreaching (OR), since
101 inducing a full-blown overtraining syndrome would be obviously unethical. This state can be
102 considered as a preliminary step, in the pathway to overtraining, which usually vanishes in a
103 week or two if training load is drastically reduced. OR is characterized regarding physical
104 exercise by a decreased maximal power output (MPO) and an increased rating of perceived
105 exertion (RPE), associated in everyday life with enhanced fatigue sensation but no depression-
106 like symptoms ^{10,11}.

107

108 To explore the effects of overreaching, we recruited 37 competitive male endurance athletes
109 (mean age around 35 years). Participants were assigned to either the control group with normal
110 training (n = 18) or to the group with training overload (n = 19), in a pseudo-random manner
111 that ensured matching of age and performance level. Their training program (Fig. 1) was
112 supervised during a total of nine weeks by the Insep (French institute for sport performance).
113 The overload concerned a period of three weeks (denoted phase III in Fig. 1) during which the
114 duration of each training session was increased by 40% on average. The general structure of
115 running, cycling and swimming sessions was maintained as usual. Physical performance was
116 monitored during cycling exercises performed on rest days (Pre, Post and Taper in Fig.1), and
117 subjective fatigue was assessed using a psychometric questionnaire ¹² every two days.

118 **RESULTS**

119

120 The effects of training overload on physical performance and effort sensation were assessed
121 during cycling tests that were conducted on the two days following phase III.

122 On day 1, participants completed on a cycle ergometer an exercise protocol designed to
123 determine their Post MPO, which was compared to the Pre MPO measured before the start of
124 training phase III. MPO corresponds to the maximal workload (in Watts) that participants could
125 sustain when physiological measures reached exhaustion criteria.

126 On day 2, participants came to the MRI center for two scanning sessions, separated by a 45-
127 min cycling trial, during which participants were instructed to give their best performance, i.e.,
128 to cover a maximal distance (see Fig. 2). The aim of including such an intense physical effort
129 was to disentangle the effects of acute (45-min) exercise from long-term (3-week) overload. It
130 also served to test for an interaction between exercise and overreaching, which would occur if
131 OR athletes were more fatigable (even by short exercises) than CTL athletes. Finally, it served
132 to measure perceived exertion, which was rated by participants every five minutes during the
133 cycling time trial, on a visual analog scale ¹³.

134

135 The behavioral and neural markers of executive fatigue were tested on day 2, during fMRI
136 scanning sessions (see Fig. 2). The behavioral marker was preference for immediate rewards,
137 relative to bigger-later rewards, in inter-temporal choices. Before scanning, participants
138 performed a calibration session where choice options were progressively adjusted, following a
139 bisection procedure, in order to find subject-specific indifference points. During scanning
140 sessions, inter-temporal choice task trials were tailored around subject-specific indifference
141 points, so their difficulty was matched across subjects. The neural marker was LPFC activity
142 during choice trials, compared to baseline. Choice trials were intermingled with executive task

143 trials (either N-back or N-switch), on which participants had been trained until passing a
144 threshold of 90% correct responses. There were two reasons for incorporating executive tasks.
145 The first reason was that we needed an independent contrast to isolate executive control regions,
146 which was provided by the difference between hard and easy versions of the tasks (change in
147 N). The second reason was that we intended to test the specificity of fatigue effects on choices,
148 which we observed in our previous study ⁵. Indeed, fatigue left unaffected brain activity
149 recorded during performance of executive tasks. The idea is that compensatory mechanisms
150 may be recruited to maintain performance, in tasks where there is an objective correct response
151 (N-back and N-switch), but not in tasks where the response is an expression of subjective
152 preference (inter-temporal choice).

153

154 **Overreaching effects on cycling exercise.** As predicted, MPO was significantly reduced by
155 training overload (Fig. 3A, left), but not by normal training (OR group: $\Delta\text{MPO} = -13.26 \pm 2.88$
156 W, $t_{18} = -4.61$, $p = 0.00022$; CTL group: $\Delta\text{MPO} = 3.60 \pm 2.74$ W, $t_{17} = 1.2$, $p = 0.25$), with a
157 significant difference in training effect (ΔMPO) between groups ($F_{1,32} = 16.3$, $p = 0.00031$).
158 Training overload also had the expected impact on perceived exertion (see Fig. 3A, right),
159 which was higher in OR relative to CTL participants (OR: $\text{RPE} = 15.59 \pm 0.16$; CTL: $\text{RPE} =$
160 14.74 ± 0.29 ; OR vs. CTL: $t_{34} = 2.56$, $P = 0.014$). Altogether, results from cycling exercises
161 confirmed that training overload was effective: it decreased physical performance while
162 increasing effort sensation.

163 Note that in the OR group, MPO measured after the last phase (Taper) was even higher than in
164 the Pre baseline ($\Delta\text{MPO} = 7.68 \pm 3.67$ W, $t_{18} = 2.15$, $p = 0.046$). Thus, athletes fully recovered
165 their physical capacity after training overload, showing that our manipulation was harmless in
166 the end.

167

168 **Overreaching effects on psychometric questionnaire.** The overreaching state induced by
169 training overload measures were corroborated by psychometric questionnaires (Brunel mood
170 scale) that participants filled every two days (Fig. 3B). Note that baseline fatigue level (at the
171 start of the training program) was matched between groups. The increase in subjective fatigue
172 between the beginning and the end of phase III was higher in OR relative to CTL participants
173 (OR: $\Delta\text{fatigue} = 3.78 \pm 0.98$; CTL: $\Delta\text{fatigue} = 0.21 \pm 0.74$; OR vs. CTL: $F_{1,30} = 6.89$, $P = 0.014$),
174 whereas there was no difference in the evolution of depression score ($F_{1,30} = 0.72$, $p = 0.4$).

175

176 **Overreaching effects on behavioral task performance.** Bayesian model selection indicated
177 that for both groups, the best account of choices made during calibration was provided by
178 exponential discounting of reward with delay, plus an additive parameter, termed immediacy
179 bias (IB), which captures the preference for immediate options, irrespective of reward and delay
180 (see Table 1).

181 When comparing between groups the proportion of impulsive choice made during the
182 calibration procedure, we observed a marginally significant difference, with a higher proportion
183 of impulsive choice following training overload (OR: $P_{im} = 0.46 \pm 0.026$; CTL: $= 0.38 \pm 0.031$;
184 difference: OR vs. CTL: $t_{35} = -1.99$, $p = 0.054$). Note that such model-free comparison is
185 limited because choices were progressively adjusted to indifference points through our adaptive
186 design. We thus compared fitted parameters (posterior means) between groups, and observed a
187 specific difference in the immediacy bias (Fig. 3C), which –in line with our key behavioral
188 prediction– was higher following training overload (OR: $IB = 0.4 \pm 0.21$; CTL: $IB = -0.34 \pm 0.16$;
189 OR vs. CTL: $t_{35} = -2.77$, $p = 0.0089$).

190 All the other parameters (Table 2), as well as the quality of fit (see Fig. 4, left), were similar in
191 the two groups. This suggests that training overload increased the attraction of immediate
192 rewards, but not the way option values were estimated and compared. In particular, the weight

193 assigned to delay (discount factor) and the stochasticity of choices (temperature parameter)
194 were not significantly affected by training overload.

195

196 However, such a difference in the immediacy bias between groups might come from a sampling
197 issue (the CTL group being by chance more patient than the global population, and/or the OR
198 group being more impulsive than the global population). To address this question, we included
199 as a reference a third independent control group of participants ($n = 106$), who were tested with
200 similar calibration procedures, for other purposes. Across all control participants, we conducted
201 permutation tests (1,000,000 iterations) to estimate the exact probability of observing by chance
202 a bias parameter of at least the same mean, with a sample of the same size, as that of the OR
203 group. This permutation procedure gave us a p-value of 0.025. We therefore conclude that the
204 observed bias parameter was unlikely to reflect a sampling issue, and more likely to represent
205 a true effect of training overload.

206

207 During scanning sessions, we observed no significant difference between groups in executive
208 task performance. We illustrate this absence of effect using correct response rate pooled across
209 tasks (Fig. 5A), but similar null results were obtained when analyzing tasks separately, or
210 comparing response time instead of accuracy, or focusing on switch cost. However, we
211 observed a trend for a remaining specific group difference in the immediacy bias (OR vs. CTL:
212 $F_{1,35} = 3.99$, $p = 0.054$), despite the adjustment of choice options following calibration (see Fig.
213 4). Regarding our secondary question, namely the effects of acute exercise, we found no
214 significant difference between scanning sessions, neither in executive task performance nor in
215 inter-temporal choices and no interaction between session and group (see table S1). Thus, 45
216 minutes of cycling, although athletes approached physical exhaustion, was insufficient to affect
217 executive control or to interact with the state of executive fatigue.

218 **Overreaching effects on neural activity.** To investigate the neural underpinnings of fatigue
219 effect on choice impulsivity, we isolated the executive control network using the conjunction
220 between choice-related activity (against baseline) and the difference in difficulty (hard minus
221 easy tasks), as was done in our previous study ⁵. The logic of this analysis was to locate brain
222 regions that are normally involved in both executive processing and inter-temporal choice (in
223 the control group). These regions would be candidate for mediating the impact of executive
224 fatigue on choice impulsivity, as they would be both responsive to executive demand and
225 recruited during inter-temporal decision-making. Thus, activity level extracted from these
226 regions served as a reference to assess the effects of training overload. As expected ^{5,14-20}, we
227 observed significant conjunction in a bilateral prefronto-parietal network (Fig. 5B; see Table
228 S2), including the middle frontal gyrus (MFG) and the inferior parietal lobule (IPL).

229

230 We focused on the left MFG cluster, as it perfectly overlapped with the unique brain region that
231 was found in the previous study ⁵ to both activate in the conjunction analysis and deactivate
232 during choices in relation with behavioral fatigue effects. Neural activity was extracted using a
233 general linear model that controlled for task factors such as delay, reward level, eventual choice
234 and response time (see methods). Choice-related activity (but not task-related activity) in the
235 independent left MFG cluster (defined from previous study) was significantly reduced
236 following training overload (OR: $\beta = 0.15 \pm 0.50$; CTL: $\beta = 1.86 \pm 0.43$; OR vs. CTL: $F_{1,35} = 6.36$,
237 $p = 0.016$). As seen with behavioral variables, there was no effect of acute exercise (no main
238 effect of session and no interaction; see Table S3) on neural activity. The difference between
239 group in choice-related left MFG activity was not observed in other clusters such as the left IPL
240 or the right MFG (see Fig. S1 and Table S4). Also, left MFG activation with the difficulty of
241 executive tasks was not different between groups (see Fig. 5C and Table S3). Moreover, the
242 interaction between task and group was significant, indicating that training overload mainly

243 impacted choice-related activity (CTL: $\Delta\beta = 1.35\pm 0.43$; OR: $\Delta\beta = -0.20\pm 0.48$; CTL vs. OR:
244 $F_{1,35} = 5.81$, $p = 0.021$).

245

246 Thus, training overload effects were predominant in the left MFG cluster and during the inter-
247 temporal choice task. The fact that left MFG activity was independent from reward and delay
248 levels (see Fig. S2) suggests that training overload did not affect temporal discounting. This is
249 consistent with the computational modeling analysis showing an effect on the immediacy bias
250 but not on the discount factor. We did not find any increase in choice neural activity in the OR
251 group compared to the CTL group, even at a very liberal threshold ($p < 0.05$ at the voxel level,
252 extent threshold of 4 voxels at the cluster level), even with a lower spatial smoothing that would
253 be more sensitive to activity in small subcortical regions such as the ventral striatum.

254

255 In addition, choice-related left MFG activity was correlated across participants with the
256 immediacy bias estimated during scanning sessions in the OR group ($r = -0.36$, $t_{17} = -4.32$, $p =$
257 0.0005). Although the coefficient should be interpreted with caution, due to the small sample
258 size^{21,22}, this significant correlation establishes a link between the neural and behavioral
259 markers of executive fatigue (Fig. S3). Note that the left MFG ROI was selected from the
260 previous study, by conjunction between executive- and choice-related activities, to avoid non-
261 independence issues. Moreover, this correlation is independent from the difference between
262 groups, as it is restricted to the OR group. It shows that athletes who exhibited lower activity in
263 left MFG during decision-making had a stronger bias in favor of immediate over delayed
264 rewards.

265

266

267 **DISCUSSION**

268 Our findings indicate that physical training overload reduces the excitability of left MFG and
269 the capacity to resist temptation of immediate reward in inter-temporal choice. These
270 conclusions rely on significant differences between overtrained and normally trained groups of
271 athletes, in both brain activity and behavioral performance, during choice tasks. There were
272 trends for interactions between groups and sessions, in the sense that overtrained athletes were
273 more fatigued after a one-hour cycling exercise, but these trends were not significant. The
274 association of neural and behavioral differences between groups was corroborated by an
275 independent correlation, observed within the overtrained group, between reduced left MFG
276 activity and enhanced immediacy bias. Although this correlation does establish a link between
277 neural and behavioral effects of overtraining, it does not imply that the neural effects were
278 mediating the behavioral effects. Unfortunately, we could not apply here the kind of mediation
279 analysis conducted in our previous study ⁵, because the consequences of overtraining were
280 assessed between participants, and because we did not get baseline impulsivity measurement
281 (prior to training). The absence of baseline measurement is a potential limitation to the
282 conclusions, but comparison to other datasets in healthy volunteers ensured that the difference
283 was due to overtrained athletes being more impulsive than the normal population.

284

285 The difference in choice impulsivity was best captured by the additive bias in the exponential
286 discounting model ²³. Interestingly, the two parameters of this ($\beta\delta$) model were previously
287 mapped onto opponent brain systems involved in the valuation of immediate versus delayed
288 reward. These opponent systems therefore had opposite influences on choice, with a more
289 ‘future-oriented’ system including the lateral prefrontal cortex and a more ‘present-oriented’
290 system including the ventral striatum. Interpreted in such a framework, increased choice
291 impulsivity in overtrained athletes would correspond to a less active ‘future-oriented’ system

292 (decrease in left MFG activity) rather than a more active ‘present-oriented’ system (no increase
293 in ventral striatum activity). Indeed, we did not observe any brain region that would have been
294 more active in overtrained athletes during economic choice.

295

296 We previously suggested the notion of executive fatigue as a label for the two choice-related
297 markers (increased impulsivity with decreased MFG activity) observed in the absence of any
298 change in behavioral performance or brain activity during cognitive tasks. As all neural and
299 behavioral markers were present in the overtrained group, we conclude and physical training
300 overload can also induce executive fatigue. This notion of executive fatigue is different from
301 physical fatigue, because it can be induced by purely intellectual work⁵. It is also different from
302 stress or sleep deprivation, which failed to influence inter-temporal choices in previous
303 experiments^{24,25}. Executive fatigue should also be distinguished from loss of motivation, since
304 it does not affect the arbitrage between reward and delay, as shown by computational modeling
305 of choice behavior, and because it impacts activity in a brain region (left MFG) that was not
306 sensitive to reward. Finally, executive fatigue does not imply that the choice process itself is
307 impaired, as would be reflected by a higher stochasticity, but rather that preference is shifted in
308 favor of immediate reward.

309

310 This new concept of executive fatigue should be contrasted to existing theories of ‘limited
311 willpower’ or ‘resource depletion’. These theories postulate that exerting self-control may
312 deplete a common limited resource and consequently affect performance in any subsequent task
313 that also involves self-control^{6,7}. However, the time scale typically envisaged in resource
314 depletion theories is that of minutes (e.g.,²⁶). Meta-analyses and multi-lab replication attempts
315 have seriously questioned that depletion effects can be obtained in sequential task paradigms at
316 such short time scale^{8,9}. Consistently, we observed here no effect of 45-min cycling on working

317 memory, task switching, choice impulsivity or brain activity. These results therefore suggest
318 that exerting executive control might indeed affect subsequent recruitment of executive control
319 but at a time scale that is much longer than usually considered (here, three weeks). We
320 nonetheless acknowledge that our participants were well-trained endurance athletes, who had
321 exceptional recovery capacity and highly competitive spirit. It remains possible that recreational
322 cyclists would have shown earlier fatigue effects, as suggested by a previous study investigating
323 interactions between acute exercise and cognitive abilities ²⁷.

324

325 Theories assuming that a resource is depleted by self-control have not identified what the
326 resource may be at the biological level ²⁸. Blood glucose has been proposed as a suitable
327 candidate resource, with some supporting evidence initially ^{6,29}. However, the beneficial effects
328 of glucose ingestion have been hard to replicate ^{30,31} and it was later suggested that they might
329 be more psychological than biological ^{32,33}. In our study, glucose is unlikely to have played a
330 role because participants had free access to food and drinks during both training and experiment
331 days. Instead, we suggest a specific neural basis for our concept of executive fatigue, with a
332 precise anatomical location, in the left MFG. It is remarkable that such different tasks as training
333 for triathlon and making inter-temporal choice precisely interfered in a single brain region.
334 Indeed, other regions of the parieto-prefrontal executive network recruited by inter-temporal
335 choices did not show any fatigue effect. It is the same MFG region that mediated the increase
336 in choice impulsivity induced by prolonged working memory and task-switching performance
337 ⁵, and the same MFG region on which transcranial magnetic stimulation (TMS) induced a
338 present bias in inter-temporal choice ^{16,34}. Our findings therefore concur to designate the left
339 MFG as the weak spot of the brain executive control system ^{15,20}, being susceptible to fatigue.

340

341 Yet our data are silent about why the MFG is harder to activate with fatigue. This may not
342 necessarily come from a local dysfunction of MFG neurons. Indeed, MFG activity could be
343 down-regulated by other brain systems for adaptive reasons, possibly because exerting
344 executive control would exhaust some energetic supply or accumulate some metabolic wastes.
345 It has been suggested for instance that stopping executive control might avoid the accumulation
346 of Amyloid- β peptide and allow its clearance during rest or sleep, such that neural cells remain
347 functional³⁵. More generally, executive fatigue might have origins in any of the numerous
348 physiological changes that have been reported following excessive sport exercise. One
349 interesting (but still debated) possibility is the release of inflammatory cytokines^{36,37}, which
350 are known to affect motivational processes^{38,39}. Yet the mechanisms through which peripheral
351 physiological changes would affect specific prefrontal cortex functions remain to be explored.

352

353 Alternatively, down-regulation could be adaptive at a functional rather than biological level,
354 for instance to avoid opportunity costs^{40,41}, i.e. to avoid losing the benefits of using executive
355 control resources for other purposes. Yet the latter hypothesis would imply that the opportunity
356 cost of executive control increases with time on task, which seems quite an arbitrary
357 assumption. Further studies are thus required to understand why the MFG is susceptible to
358 fatigue, whereas other brain regions such as the visual cortex can work all day long without any
359 behavioral consequence. In any case, the impact of fatigue can be construed as an increase in
360 the cost of recruiting the MFG, and thus exerting control. The implication is that control
361 resources can still be mobilized in a state of fatigue but for higher benefits. This would explain
362 why performance was maintained during executive control tasks, in which a precise financial
363 payoff was associated to every correct response. By contrast, the benefit of making a sound
364 decision in inter-temporal choice might have been too elusive to recruit executive control. Such
365 a view is consistent with suggestions that the effects of time-on-task on cognitive performance

366 and related brain activity are not robust ^{42,43}, and that the consequences of mental fatigue are
367 better conceived as shifts in cost-benefit arbitrages ^{44,45}.

368

369 The consequence of impulsive economic choice could itself be deemed adaptive, if immediate
370 rewards were instrumental to eliminate fatigue, as glucose is for reducing hunger. Yet in our
371 paradigm it remains unclear how a small amount of money could be used to improve
372 overreaching symptoms, so we consider as a bias the shift observed in favor of immediate
373 rewards. Another slightly different perspective could be that fatigue place subjects in a state of
374 need, pushing them to seek immediate rewards in order to restore their mood or some
375 overarching hedonic variable which they monitor on the long run. This hedonic regulation is
376 reminiscent of the spontaneous oscillations between pursuing ‘have to’ versus ‘want to’ goals
377 ⁴⁶ and may be the basis of the trade-off between work and leisure that is at the heart of labor
378 theory ⁴⁷.

379

380 In conclusion, our findings provide the first demonstration that physical training overload
381 induces some fatigue in the executive control brain system, associated with more impulsive
382 economic decisions. They suggest a neural mechanism that might explain not only why
383 overtrained athletes fail to overcome pain or fatigue signals, but also why they are at risk of
384 doping, which may help with immediate performance but compromise long-term achievements.
385 They could also account for the rise of fatigue syndromes observed in amateurs of extreme
386 sports such as ultra-trail, who may put in danger not only their heart and knees, but also their
387 brains. Finally, these findings could perhaps be extended to other types of work overload, and
388 therefore have applications not only for sport coaching but also for work management and
389 health care, since excessive work is one of the possible routes to burnout syndrome. We should
390 keep in mind, however, that our overtrained participants were (fortunately) not in a full-blown
391 burnout state. It remains possible, and even likely, that factors other than executive fatigue come

392 into play for a transition to long-term burnouts. Further research is needed to investigate those
393 putative factors.

394

395

396 **Acknowledgements**

397 The study was funded by the French anti-doping agency (AFLD). This work also benefited
398 from the program 'Investissements d'avenir' (ANR-10-IAIHU-06). BB received a PhD
399 fellowship from the Direction Générale de l'Armement. The funders had no role in study
400 design, data collection and analysis, decision to publish or preparation of the manuscript. We
401 wish to thank the staff of the Prisme facilities for behavioral testing and the Cenir facilities for
402 neuroimaging experiment.

403

404 **Author Contributions**

405 BB, CH, YLM and MP designed the experiment. CS, AA and YLM supervised the training
406 program. BB and CS collected the behavioral and fMRI data. BB and MP analyzed the data
407 and wrote the paper.

408

409 **Competing Interests statement**

410 Nothing to declare.

411 **Figure Legends**

412

413 **Fig. 1. Training procedures.**

414 Participants (37 male triathletes in total) were divided into two groups, following slightly different training
415 procedures. The loads assigned to the different training phases correspond to variations in daily exercise
416 duration (in proportion to subject-specific standard), while exercise intensity was kept constant. The
417 critical manipulation is the 40% increase in training load during the three weeks of phase III, in the
418 overreaching (OR) but not in the control (CTL) group. The other phases were identical in both groups,
419 with a two-week baseline phase of usual training at the beginning, and two tapering phases (recovery
420 periods) before and after the critical phase III. The maximal power output (MPO) was evaluated on rest
421 days before and after phase III, as well as after phase IV (as indicated by cyclist icons). The fMRI
422 experiment (indicated by brain icon) was conducted on the day following post-phase III MPO
423 measurement (see details in Fig. 2).

424

425 **Fig. 2. fMRI experiment procedures.**

426 Tasks are illustrated at different time scales from bottom to top. Participants performed two sessions of
427 behavioral tasks in the MRI scanner, before and after cycling (45-min time trial at maximal speed).
428 Sessions were divided into six 7-min runs, each including five blocks of executive tasks (N-back or N-
429 switch) intermingled with inter-temporal choices (IC). Executive tasks were 3-back (3-B) and 12-switch
430 (12-S) in the hard condition (for a total of 8 blocks, in red), versus 1-back (1-B) and 1-switch (1-S) in the
431 easy condition (for a total of 4 blocks, in blue). The first three runs of a session implemented one
432 executive task (N-back or N-switch), and the last three runs the other one. In each block a series of 16
433 to 32 different letters was presented on screen, each starting a new trial. The task to be performed was
434 instructed at the beginning of the block. In N-back tasks, participants indicated whether the current letter
435 was the same as the one presented N trials before (irrespective of case and color). In N-switch tasks,
436 participants categorized the current letter as either vowel versus consonant or upper versus lower case,
437 depending on its color. In this case, N designates the number of switches (color changes) during the
438 block. At the end of the block participants made three self-paced choices (with a 5s limit) between
439 immediate and delayed monetary rewards.

440

441 **Fig.3. Behavioral validation of overreaching effects**

442 (A) Results of cycling tests conducted after phase III (see Fig. 1). Graphs show the change in maximal
443 power output (MPO, left) measured during the incremental cycling test on day 1, and how ratings of
444 perceived exertion (RPE, right) vary during the cycling time trial on day 2 separately for the control (CTL,
445 green) and overreaching group (OR, purple) groups.

446 (B) Results of fatigue psychometric assessment. Graphs show the change in fatigue score (extracted
447 from Brunel mood scale) observed between the beginning and the end of phase III (see Fig.1).

448 (C) Results of temporal discounting calibration. Graphs show the posterior mean of immediacy bias, a
449 parameter integrated in the choice model to account for preference between present and future,
450 irrespective of rewards and delays. Plain and dotted lines as well as the shadowed area in between
451 illustrate mean and confidence intervals of the immediacy bias observed in a larger, independent cohort
452 of healthy volunteers (n=106). Error bars and shaded areas correspond to intersubject SEM. Black stars
453 denote p-values (* < 0.05, ** < 0.01, *** < 0.001).

454

455 **Fig. 4 Psychometric functions and model fits.**

456 Graphs show observed choice rate (dots with error bars) and modeled choice probability (lines with
457 shaded areas) for immediate rewards (IR), as a function of modeled relative values (difference between
458 subjective values of immediate and delayed rewards). Error bars and shaded areas represent
459 intersubjects SE. Overreaching (OR) and control (CTL) groups are shown in purple and green,
460 respectively. Left, middle and right panels correspond to calibration, first fMRI and second fMRI
461 sessions, respectively.

462

463 **Fig. 5. Neural underpinnings of overreaching effects.**

464 (A) Behavior observed during fMRI. Top graphs show the immediacy bias (posterior mean of model
465 parameter fitted on inter-temporal choices) and bottom graphs the executive performance (correct
466 response rate in hard versions divided by correct response rate in easy versions of executive tasks)
467 separately for the control (CTL, green) and overreaching group (OR, purple) groups (see also Table
468 S1). (B) Whole-brain fMRI activity. Statistical maps show the conjunction between choice-related activity
469 (against baseline) and effect of difficulty (hard versus easy version of executive tasks) in the control
470 group. Significant activation (voxel-wise threshold: $P < 0.001$ uncorrected, cluster-wise threshold: $P <$

471 0.05 FWE corrected) was observed in a dorsal parieto-prefrontal network including the middle frontal
472 gyrus (MFG), the pre-central gyrus (PCG) and the inferior parietal lobule (IPL). The MFG cluster
473 overlaps with the unique brain region (shown in red) from the same conjunction that was susceptible to
474 executive fatigue in a previous study ⁵. The sagittal section (bottom) corresponds to the blue line on the
475 glass brain (top); it shows functional activations overlaid on anatomical scans averaged across subjects.
476 The x, y, z coordinates refer to the MNI space (see also Table S2). (C) Neural activity extracted from
477 the MFG cluster. Graphs show regression estimates (β) extracted from the cluster shown in red, for
478 neural activity observed during inter-temporal choices with respect to baseline (top) and for neural
479 activity observed during hard versions of executive task relative to easy versions (bottom; see also Table
480 S3). Error bars and shaded areas correspond to intersubject SEM. Black stars denote a p-value < 0.05,
481 daggers denote a trend. S1 and S2 refer to fMRI sessions conducted before and after cycling exercise,
482 respectively.

483

484

485 **Tables**

486

$P(IR) = \frac{1}{1 + e^X}$		$X = \frac{1}{\beta} \left[\frac{DR}{1 + kD} - IR \right]$	$X = \frac{1}{\beta} [DRe^{-kD} - IR]$	$X = \frac{1}{\beta} \left[\frac{DR}{1 + kD} - IR \right] - bias$	$X = \frac{1}{\beta} [DRe^{-kD} - IR] - bias$
Calibration	EF	0.086 (0.013/0.022)	0.22 (0.12/0.21)	0.13 (0.032/0.15)	0.57 (0.83/0.41)
	EP	0	0.0037 (0/0.89)	0.00020(0/0.03)	0.99 (0.99/0.95)
fMRI sessions	EF	0.076 (0.12/0.014)	0.072 (0.014/0.013)	0.17 (0.014/0.29)	0.68(0.85/0.68)
	EP	0 (0.003/0)	0	0 (0/0.032)	1 (1/0.97)

487 **Table 1. Results of Bayesian model comparison.**

488 The four models combine two discounting functions (hyperbolic vs. exponential) and two possibilities for
 489 inclusion of an immediacy bias (present or absent) in the softmax choice function (see methods). IR and
 490 DR are immediate and delayed reward magnitudes, D is delay. β , k and *bias* are free parameters (choice
 491 stochasticity, discount factor and immediacy bias, respectively). The comparison was based on choices
 492 made by the two groups of participants taken together, separately for the calibration and fMRI sessions.
 493 EF is expected frequency and EP exceedance probability, provided for all participants and for each
 494 group separately (CTL/OR).

495

496

Parameter	CTL	OR	Difference	t-value	df	p-value
Immediacy bias	-0.34±0.16	0.40±0.21	-0.74	-2.77	35	0.0089
Discount factor	0.045±0.0083	0.040±0.0075	0.0050	0.45	35	0.66
Choice stochasticity	8.11±0.55	9.23±0.54	-1.12	-1.45	35	0.15
Balanced accuracy	0.70±0.019	0.70±0.011	0	-0.0003	35	0.99

497

498

Table 2. Comparison of model parameter estimates and quality of fit for choices made during calibration session.

499

500

Models were fitted on the calibration session, separately for the control (CTL) and overreaching (OR) groups. Parameters from top to bottom are denoted *bias*, *k* and β in the models (see Table 1). Balanced accuracy is the percentage of choices correctly predicted by the model, calculated separately for impulsive and patient choices before averaging. Note that balanced accuracy is low because options were adjusted to indifference points. Results are given as inter-subject means \pm standard errors. Groups were compared using two-sample two-tailed t-tests; df is degree of freedom.

506

507 **STAR METHODS**

508

509 **Participants**

510 The experimental design of the study was approved by the Ethical Committee of Hôpital de la
511 Pitié-Salpêtrière. Forty-two well-trained male triathletes ($[\dot{V}O_{2\max}] = 64.1 \pm 4.9 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$)
512 volunteered to participate in this study. They were paid a fix amount of 400€, plus one option
513 that was selected in a random trial of the choice task. All subjects had regularly competed in
514 triathlons for at least 3 years and were training a minimum of 10 hours per week. Their
515 performance level over the short (Olympic) distance triathlon (i.e., 1.5-km swimming / 40-km
516 cycling / 10-km running) ranged between 2 h and 2 h 20 min, which roughly corresponds to
517 national level of competition). Before participation, subjects underwent medical assessment by
518 a cardiologist to ensure normal electrocardiographic patterns and obtain a general medical
519 clearance. All subjects were free from chronic diseases and were not taking medication. After
520 comprehensive explanations about the study, all subjects gave their written informed consent
521 to participate.

522

523 Subjects were assigned to either the control group (CTL) or the overreaching group (OR) so as
524 to match performance level, habitual training volume, and past experience in endurance sports.
525 Five participants were excluded due to sleeping or excessive movements in the scanner or
526 failure to comply with instructions about behavioral tasks. In the end, our dataset included 18
527 CTL subjects (age = 36 ± 1.5) and 19 OR subjects (age = 35 ± 1.2).

528

529 To provide a reference point for the immediacy bias in the general population, we included
530 groups of participants with similar age, sex and education level, who were tested with the same
531 choice tasks in independent studies.

532

533 **Training procedures**

534 An overview of training procedure is shown in Fig 1. The training of each participant was
535 monitored for a period of nine weeks in total, which was divided into four distinct phases. The
536 two first phases (I and II) were similar in the OR and CTL groups. During the third phase (III),
537 the OR group completed a 3-week overload program designed to deliberately induce fatigue:
538 the duration of each training session was increased by 40% (e.g., a 1-hour run including 10
539 repetitions of 400 m at the maximal aerobic running speed was converted into an 85-min run
540 including 14 repetitions of 400 m at the maximal aerobic running speed). Participants
541 reproduced the same training program during each week of the overload period, which was kept
542 as usual, except for the increase in duration. The CTL group repeated its usual training program
543 during this third phase (III). Thereafter, all participants completed a 2-week taper period (IV),
544 where their normal training load (I) was decreased by 40%, following the guidelines for optimal
545 tapering in endurance sports ⁴⁸.

546

547 During training, fatigue and depression were monitored by asking participants to fill the Brunel
548 mood questionnaire ¹² every two days. We used a sub-selection of items to measure the change
549 in depression score (during the last two days, how often did you feel: “Miserable”, ”Unhappy”,
550 “Depressed”, “Unable to fall asleep”, “Insomniac”) and in fatigue score (“Collapsed”,
551 ”Energetic” (-), “Tired”, “Exhausted”, “Having heavy legs”) between the beginning and end of
552 each phase. Fatigue and depression scores were not different between groups at the beginning
553 of the training program.

554

555 During phase I, all subjects were familiarized (on separate days) with both the cognitive tasks
556 going to be performed during fMRI scanning, and the maximal power output (MPO) test
557 (described below). The MPO test was performed on three occasions: before phase III (Pre),

558 after phase III (Post) and after phase IV (Taper), on the same day of the week and at the same
559 time of the day. To ensure that performance variations across MPO tests were due to the global
560 training regimen and not to the training session performed the day before testing, the subjects
561 were required to abstain from training during a 24-h period before each MPO testing session.
562 The day after Post MPO test, all participants completed two 45-min fMRI sessions during which
563 they performed cognitive tasks. The two sessions were interspaced with a 45-min self-paced
564 cycling time trial.

565

566 **Cycling exercises**

567 All MPO tests were performed using an electronically-braked cycle ergometer (Excalibur Sport,
568 Lode®, Groningen, The Netherlands). The incremental exercise protocol started with a 6-min
569 warm-up at a workload of 100 W, and then increased by 25 W every 2 minutes until voluntary
570 exhaustion to estimate MPO. Subjects wore a facemask covering their mouth and nose to collect
571 all expired breath (Hans Rudolph, Kansas City, MO) and calculate $\dot{V}O_{2max}$ using a
572 metabolimeter (Quark, Cosmed®, Rome, Italy). Complete exhaustion was confirmed by
573 physiological criteria⁴⁹ – that is, a plateau in $\dot{V}O_{2max}$ despite an increase in PO. MPO was
574 calculated as $MPO = W_{last} + 25 (t/120)^{50}$, where W_{last} is the last completed workload and t the
575 number of seconds sustained in W_{last} . $\dot{V}O_{2max}$ was defined as the highest 30-sec average of
576 breath-by-breath values⁵¹.

577

578 The 45-min self-paced time trial (TT) was completed between the two fMRI sessions.
579 Participants were instructed to achieve their best performance. Before the TT, participants
580 respected a 15-min warm-up (10 minutes at a workload of 100 W and 5 minutes at 50% of the
581 Post MPO). Both warm-up and TT were performed on participants' own bike mounted on a
582 braked Cyclus2 ergometer (RBM GmbH, Leipzig, Germany). To mimic field conditions, the

583 triathletes were provided with distance, speed, PO, cadence information and *ad libitum* sport
584 drinks and water. Every five minutes during the TT, subjects' rating of perceived exertion
585 (RPE) was recorded using the 6-to-20 point Borg's scale¹³. This scale measures effort sensation,
586 with 6 corresponding to sitting in a chair, and 20 to the maximal effort ever experienced.

587

588 **fMRI experiment**

589 Participants came to the lab on the second day after the end of phase III. On this day, they
590 performed an inter-temporal choice calibration procedure to elicit their indifference curve.
591 Inter-temporal choices were real in the sense that the chosen option in one pseudo-randomly
592 selected trial was actually implemented (any trial could be drawn, except those where a delay
593 longer than one year had been selected). Subjects then performed two sessions of executive
594 tasks while fMRI data were acquired. Each session lasted for about 45 minutes (5 mins of setup,
595 10 mins of structural MRI acquisition before the first and after the last session, + 30 mins of
596 functional MRI during task performance). Sessions were divided into three consecutive runs of
597 N-switch blocks (two 12-switch runs separated by one 1-switch run) and three consecutive runs
598 of N-back blocks (two 3-back runs separated by one 1-back run). Each run comprised five
599 successive blocks. The task to be performed was indicated by a 5-s instruction screen presented
600 at the beginning of each block. The length of blocks was randomly varied between 16 and 32
601 trials (24 on average, duration = 43s) for N-switch tasks and between 18 and 26 trials (22 on
602 average, duration = 40s) for N-back tasks. The order of N-switch and N-back tasks was
603 counterbalanced across subjects. Every 50s on average (at the end of blocks), another 5-s
604 instruction screen indicated to participants that they would have to make three successive inter-
605 temporal choices, giving a total of 90 choices per session. The options proposed in inter-
606 temporal choices were tailored based on the results of the calibration session conducted just
607 before the fMRI experiment.

608

609 **Behavioral tasks**

610 For executive tasks, participants were instructed to reach the best possible performance level
611 (correct response rate) with the shortest possible response time. On the week before the
612 experiment as well as on the day of the experiment (before MRI sessions) they read the
613 instructions and were trained to perform all versions of executive tasks until they reached a
614 performance criterion (4 consecutive blocks above 90% of correct responses), or until they
615 reached a maximal duration of three hours.

616

617 In both the N-back and N-switch tasks, letters appeared successively at the center of the screen.
618 They could be vowels (e,a,i,o,u,y) or consonants (b,c,g,k,m,p), written with either upper or
619 lower case, and with either red or green color. On every trial, the letter was displayed for 900
620 ms, corresponding to the time window during which participants could give their response,
621 followed by a blank screen lasting for 400 ms.

622

623 For the N-back task, participants were instructed to indicate when the current letter was the
624 same as that presented N trials before. The ‘yes’ and ‘no’ responses were given by pressing left
625 or right arrow on the keyboard (key-response associations being counterbalanced across
626 participants). Difficulty was manipulated by changing N from 1 (easy version) to 3 (hard
627 version). The sequence of letters was pseudo-randomized so as to get one third of ‘yes’ and two
628 thirds of ‘no’ trials, among which half was made of traps (2- or 3-back repeats in the 1-back
629 version, and 1- or 2-back repeats in the 3-back version). Color and case were varied but had to
630 be ignored in this task.

631

632 For the N-switch task, color served as a contextual cue telling participants whether to perform
633 a vowel/consonant or an upper/lower case discrimination task. As an example, a subject had to
634 indicate consonant (left arrow) versus vowel (right arrow) when the letter was green, or upper
635 case (left arrow) versus lower case (right arrow) when it was red. Colors, discrimination tasks
636 and response keys were fully counterbalanced across participants. Letters were
637 pseudorandomly distributed over trials in order to balance the frequency of each task
638 (vowel/consonant or upper/lower case discrimination) and the side of correct response (left or
639 right). The difficulty was imposed by the frequency of switches (color changes) from one per
640 block in the easy version to 12 per block (40% of trials) in the hard version.

641

642 Just before the experiment, participants performed a calibration session with real choices. They
643 were told that one of the choices made either during the calibration or during test sessions would
644 be randomly drawn and implemented. This was actually done except that randomization was
645 biased in order to exclude delays longer than one year. The amount of money that they could
646 get varied between 1€ and 100€, which was quite significant relative to the fixed payoff (400€
647 for the entire experiment).

648

649 Choice task trials were intermingled with executive task trials (three per minute on average).
650 There were 90 choices per fMRI session, thus a total of 180 choices in the entire experiment.
651 Every trial, participants had a maximum of 5 s to state their preference between a small
652 immediate reward (with variable amount) and a delayed reward (with variable reward and
653 delay). The location (left or right) of the immediate and delayed options on the screen was
654 counterbalanced across trials. There were ten possible delays (3 days, 1 week, 2 weeks, 3 weeks,
655 1 month, 3 months, 6 months, 1 year, 5 years and 10 years) and three possible delayed rewards
656 (50€, 75€, 100€), which were presented in a randomized order. The immediate rewards were

657 derived from subject-specific indifference points, which describe how each of the delayed
658 reward is discounted with delay. These indifference points were obtained using a bisection
659 procedure (with 11 steps for each delayed reward and each delay) that was implemented in the
660 calibration session following on our previous study ⁵. In each session of the experiment, three
661 immediate rewards were presented for each of the ten delays and each of the 3 delayed rewards:
662 one around the indifferent point, one above and one below. The two options of a choice were
663 therefore close in (discounted) value, maximizing the sensitivity to potential fatigue effects, as
664 it was previously implemented for TMS studies ⁵². Between sessions, the amounts proposed as
665 immediate rewards were randomly varied by +/- 1€ to avoid repeating choices and hence
666 automatic responding. Note that delays and reward levels were different in the calibration
667 procedures used for the other datasets included as a reference point for the immediacy bias. The
668 immediacy bias is nevertheless comparable across datasets, because it is an additive parameter
669 (on top of reward and delay terms in the computation of subjective value).

670

671 **Behavioral data analysis**

672 Two main dependent variables were analyzed: first executive performance (correct choice rate
673 in hard relative to easy executive tasks, N-back and N-switch trials pooled together), second
674 the parameters of the best choice model (present bias, discount factor and choice temperature).
675 For each variable the main analyses tested the main effect of training overload (comparison
676 between groups), the main effect of acute physical exercise (comparison between sessions), as
677 well as the interaction between these two factors. Main effects and interactions were assessed
678 using two-way ANOVA, with session as a within-subject factor and group as a between-subject
679 factor. For comparisons involving only one factor (such as comparing between groups the
680 model parameters fitted on the calibration choices), we used two-tailed t-tests. We checked that
681 all significant results were maintained when we replaced t-tests by non-parametric tests

682 (Wilcoxon rank sum tests). For testing the effect of training overload on the immediacy bias,
683 we also computed the exact probability of obtaining at least the same mean, in a group of the
684 same size, from random sampling (1,000,000 iterations) within the cohort of control
685 participants (n=106).

686

687 **Computational modeling**

688 To fit impulsive choices (selection of immediate reward IR vs. delayed reward DR), we used a
689 standard softmax function of the relative value (RV) between the two options. This standard
690 model was compared to a variant including an additive immediacy bias that captures a
691 preference for the present independently from rewards and delays (eq 1 vs eq 2). In both cases,
692 RV was weighted by a temperature parameter β that adjusts the stochasticity of choices. To
693 calculate RV, we compared two classical delay discounting models, where rewards decrease
694 hyperbolically vs. exponentially with delay (see eq 3 vs. eq 4). In both cases, sensitivity to delay
695 (D) was captured by a discount parameter k . The four models were:

$$696 \quad P(IR) = \frac{1}{1+\exp(\frac{RV}{\beta})}, (eq\ 1); \quad P(IR) = \frac{1}{1+\exp(\frac{RV-bias}{\beta})}, (eq\ 2); \quad RV = \frac{DR}{1+kD} - IR, (eq\ 3);$$

$$697 \quad RV = DR \times \exp(-kD) - IR, (eq\ 4).$$

698 The four models (two softmax times two discounting functions) were fitted to choices made
699 during the calibration session (210 choices) and during each MRI session separately (90 choices
700 each) by the two groups of participants. Models were inverted by minimizing free energy, using
701 a variational Bayes approach under the Laplace approximation^{53,54}, as implemented in the VBA
702 Matlab toolbox⁵⁵, available at <http://mbb-team.github.io/VBA-toolbox/>). This algorithm not
703 only inverts nonlinear models to provide posterior distributions on fitted parameters, but also
704 estimates their evidence, which represents a trade-off between accuracy (goodness of fit) and
705 complexity (degrees of freedom). The log-evidences, estimated for each participant and model,
706 were submitted to a group-level random-effect analysis⁵⁶. This analysis was used to generate

707 exceedance probability, which measures the plausibility that a given model is more frequently
708 implemented by participants than any other model in the comparison set. For the calibration
709 session choices, priors were set between 0 and .1 for the discount rate parameter k , and between
710 0 and 10 for the choice stochasticity parameter β , with variance being adjusted so as to get a
711 flat prior. For the immediacy bias parameter, prior distribution was centered on 0, with a
712 variance equal to 1 (or 0 for the model without bias). For the MRI session choices, priors were
713 centered on the posterior means estimated on calibration choices. An illustration of best model
714 fit is provided in Fig. 4.

715

716 **MRI data acquisition**

717 T2*-weighted echo planar images (EPIs) were acquired with BOLD contrast on a 3.0 T
718 magnetic resonance scanner (Siemens Verio). A tilted-plane acquisition sequence was used to
719 optimize sensitivity to BOLD signal in the orbitofrontal cortex (44). To cover the whole brain
720 with sufficient temporal resolution (TR = 2.180s) we used the following parameters: 40 slices,
721 2.5 mm thickness, 1mm interslice gap. Structural T1-weighted images were coregistered to the
722 mean EPI, segmented and normalized to the standard T1 template and then averaged across
723 subjects for anatomical localization of group-level functional activation. EPI images were
724 analyzed using statistical parametric mapping (SPM8) environment (Wellcome Trust Center
725 for NeuroImaging, London, UK). Preprocessing consisted of spatial realignment,
726 normalization using the same transformation as anatomical images, and spatial smoothing using
727 a Gaussian kernel with a full width at a half-maximum of 8 mm.

728

729 **MRI data analysis**

730 In order to identify regions involved in both executive tasks and inter-temporal choices, we
731 regressed subject-level preprocessed fMRI time series against the following GLM. Two first

732 categorical regressors (one for each difficulty level) were included to model blocks of executive
733 task trials with boxcar functions. They were parametrically modulated by the block number
734 within a session (to capture any fatigue effect across blocks). A third categorical regressor was
735 included to model choice trial onsets with a stick function. It was modulated by four parametric
736 regressors including immediate reward (IR), delay, response time and eventual choice (1 for
737 patient and -1 for impulsive choice). These parametric regressors were meant to capture
738 specificities of each particular trial, whereas the categorical regressor captured common
739 processes involved in performing an inter-temporal choice. All regressors of interest were
740 convolved with a canonical hemodynamic response function (HRF). The GLM also included
741 subject-specific realignment parameters in order to correct for motion artifacts, adding six
742 regressors of non-interest.

743

744 Linear contrasts of regression estimates (betas) were computed at the subject level, and taken
745 to group-level random-effect analysis. Subject-level contrasts were categorical regressors
746 against implicit baseline, which captured easy task-related activity, hard task-related activity
747 and choice-related activity. A conjunction analysis (logical AND) was conducted at the group
748 level between the difficulty contrast (1 on hard and -1 on easy task-related regressors) and the
749 choice contrast (1 on choice-related regressors). Unless otherwise specified, activations maps
750 were thresholded at both the voxel level ($p < 0.001$, uncorrected) and the cluster level ($p < 0.05$
751 after family-wise error correction for multiple comparisons, corresponding to a minimum of
752 333 voxels).

753

754 The main region of interest (ROI), in the left MFG (red cluster in Fig. 5), was delineated from
755 a previous study⁵ to avoid non-independence issues. This ROI was defined as the intersection
756 between 1) clusters that showed significant conjunction between activation with task difficulty

757 and during choice, and 2) clusters in which choice-related activity showed significant
758 interaction between task difficulty and time on task (higher decrease in choice-related activity
759 in subjects performing hard tasks relative to subjects performing easy tasks). To test for the
760 specificity of overreaching effect on left MFG activity, we checked other ROI within the
761 executive control network involved in inter-temporal choice. These ROI were defined as 8mm
762 spheres (using MarsBar toolbox) centered on local maxima of choice-related activity in the
763 control group (maximizing the probability to observe a difference between groups). They
764 included the inferior parietal lobules bilaterally and the right MFG (see results in Fig. S1).
765 Regression estimates were extracted from all these ROIs and compared between groups and
766 sessions using two-tailed t-tests. The only significant effect was a difference between OR and
767 CTL groups in the left MFG. We also checked that activity in the left MFG cluster was not
768 affected by any parametric regressor of the GLM (block number, immediate reward, delay,
769 response time, choice type). In particular, left MFG activity was not related to reward or delay
770 (see Fig. S2), in keeping with the computational analysis showing that fatigue effect on choices
771 was independent from these factors. To establish a link between the behavioral and the neural
772 effects of executive fatigue, we tested across-subjects correlation between the fitted immediate
773 bias in inter-temporal choice and the choice-related activity in MFG, using robust regression
774 tool implemented in Matlab (see Fig. S3).

775 **References**

- 776 1. Meeusen, R. *et al.* Prevention, diagnosis, and treatment of the overtraining syndrome: joint consensus
777 statement of the European College of Sport Science and the American College of Sports Medicine. *Med.*
778 *Sci. Sports Exerc.* **45**, 186–205 (2013).
- 779 2. Armstrong, L. E. & Vanheest, J. L. The unknown mechanism of the overtraining syndrome. *Sports Med.* **32**,
780 185–209 (2002).
- 781 3. Miller, E. K. & Cohen, J. D. An integrative theory of prefrontal cortex function. *Annu. Rev. Neurosci.* **24**,
782 167–202 (2001).
- 783 4. Botvinick, M. & Braver, T. Motivation and Cognitive Control: From Behavior to Neural Mechanism. *Annu.*
784 *Rev. Psychol.* **66**, 83–113 (2015).
- 785 5. Blain, B., Hollard, G. & Pessiglione, M. Neural mechanisms underlying the impact of daylong cognitive
786 work on economic decisions. *Proc. Natl. Acad. Sci. U. S. A.* **113**, 6967–6972 (2016).
- 787 6. Muraven, M. & Baumeister, R. F. Self-regulation and depletion of limited resources: Does self-control
788 resemble a muscle? *Psychol. Bull.* **126**, 247 (2000).
- 789 7. Englert, C. The strength model of self-control in sport and exercise psychology. *Front. Psychol.* **7**, (2016).
- 790 8. Carter, E. C. & McCullough, M. E. Publication bias and the limited strength model of self-control: has the
791 evidence for ego depletion been overestimated? *Front. Psychol.* **5**, 823 (2014).
- 792 9. Hagger, M. S. *et al.* A multi-lab pre-registered replication of the ego-depletion effect. *Perspect. Psychol.*
793 *Sci.* **2** (2015).
- 794 10. Meur, Y. L. *et al.* A multidisciplinary approach to overreaching detection in endurance trained athletes. *J.*
795 *Appl. Physiol.* **114**, 411–420 (2013).
- 796 11. Lewis, N. A., Collins, D., Pedlar, C. R. & Rogers, J. P. Can clinicians and scientists explain and prevent
797 unexplained underperformance syndrome in elite athletes: an interdisciplinary perspective and 2016 update.
798 *BMJ Open Sport Exerc. Med.* **1**, e000063 (2015).
- 799 12. Lan, M. F., Lane, A. M., Roy, J. & Hanin, N. A. Validity of the Brunel Mood Scale for use With Malaysian
800 Athletes. *J. Sports Sci. Med.* **11**, 131–135 (2012).
- 801 13. Borg, G. A. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* **14**, 377–381 (1982).
- 802 14. McClure, S. M., Laibson, D. I., Loewenstein, G. & Cohen, J. D. Separate neural systems value immediate
803 and delayed monetary rewards. *Science* **306**, 503–507 (2004).

- 804 15. Kool, W., McGuire, J. T., Wang, G. J. & Botvinick, M. M. Neural and Behavioral Evidence for an Intrinsic
805 Cost of Self-Control. *PLOS ONE* **8**, e72626 (2013).
- 806 16. Hare, T. A., Hakimi, S. & Rangel, A. Activity in dlPFC and its effective connectivity to vmPFC are
807 associated with temporal discounting. *Front. Neurosci.* **8**, 50 (2014).
- 808 17. Wesley, M. J. & Bickel, W. K. Remember the future II: meta-analyses and functional overlap of working
809 memory and delay discounting. *Biol. Psychiatry* **75**, 435–448 (2014).
- 810 18. Jimura, K., Chushak, M. S., Westbrook, A. & Braver, T. S. Intertemporal Decision-Making Involves
811 Prefrontal Control Mechanisms Associated with Working Memory. *Cereb. Cortex* 1–12
812 doi:10.1093/cercor/bhx015
- 813 19. Koechlin, E., Ody, C. & Kouneiher, F. The architecture of cognitive control in the human prefrontal cortex.
814 *Science* **302**, 1181–1185 (2003).
- 815 20. McGuire, J. T. & Botvinick, M. M. Prefrontal cortex, cognitive control, and the registration of decision
816 costs. *Proc. Natl. Acad. Sci.* **107**, 7922–7926 (2010).
- 817 21. Cremers, H. R., Wager, T. D. & Yarkoni, T. The relation between statistical power and inference in fMRI.
818 *PLOS ONE* **12**, e0184923 (2017).
- 819 22. Friston, K. Sample size and the fallacies of classical inference. *NeuroImage* **81**, 503–504 (2013).
- 820 23. Laibson, D. Golden eggs and hyperbolic discounting. *Q. J. Econ.* **112**, 443–478 (1997).
- 821 24. Haushofer, J. *et al.* No Effects of Psychosocial Stress on Intertemporal Choice. *PLoS ONE* **8**, e78597
822 (2013).
- 823 25. Libedinsky, C. *et al.* Sleep deprivation alters effort discounting but not delay discounting of monetary
824 rewards. *Sleep* **36**, 899–904 (2013).
- 825 26. Baumeister, R. F., Bratslavsky, E., Muraven, M. & Tice, D. M. Ego depletion: is the active self a limited
826 resource? *J. Pers. Soc. Psychol.* **74**, 1252 (1998).
- 827 27. Chang, Y. K., Labban, J. D., Gapin, J. I. & Etnier, J. L. The effects of acute exercise on cognitive
828 performance: A meta-analysis. *Brain Res.* **1453**, 87–101 (2012).
- 829 28. Vadillo, M. A., Gold, N. & Osman, M. The Bitter Truth About Sugar and Willpower: The Limited
830 Evidential Value of the Glucose Model of Ego Depletion. *Psychol. Sci.* **27**, 1207–1214 (2016).
- 831 29. Gailliot, M. T. *et al.* Self-control relies on glucose as a limited energy source: willpower is more than a
832 metaphor. *J. Pers. Soc. Psychol.* **92**, 325 (2007).

- 833 30. Kurzban, R. Does the brain consume additional glucose during self-control tasks? *Evol. Psychol.* **8**,
834 147470491000800200 (2010).
- 835 31. Lange, F. & Eggert, F. Sweet delusion. Glucose drinks fail to counteract ego depletion. *Appetite* **75**, 54–63
836 (2014).
- 837 32. Job, V., Walton, G. M., Bernecker, K. & Dweck, C. S. Beliefs about willpower determine the impact of
838 glucose on self-control. *Proc. Natl. Acad. Sci.* **110**, 14837–14842 (2013).
- 839 33. Molden, D. C. *et al.* Motivational versus metabolic effects of carbohydrates on self-control. *Psychol. Sci.*
840 **23**, 1137–1144 (2012).
- 841 34. Figner, B. *et al.* Lateral prefrontal cortex and self-control in intertemporal choice. *Nat. Neurosci.* **13**, 538–
842 539 (2010).
- 843 35. Holroyd, C. B. The waste disposal problem of effortful control. *Motiv. Cogn. Control* 235–260 (2016).
- 844 36. Angeli, A., Minetto, M., Dovio, A. & Paccotti, P. The overtraining syndrome in athletes: a stress-related
845 disorder. *J. Endocrinol. Invest.* **27**, 603–612 (2004).
- 846 37. da Rocha, A. L. *et al.* The proinflammatory effects of chronic excessive exercise. *Cytokine* **119**, 57–61
847 (2019).
- 848 38. Harrison, N. A. *et al.* A Neurocomputational Account of How Inflammation Enhances Sensitivity to
849 Punishments Versus Rewards. *Biol. Psychiatry* **80**, 73–81 (2016).
- 850 39. Draper, A. *et al.* Effort but not Reward Sensitivity is Altered by Acute Sickness Induced by Experimental
851 Endotoxemia in Humans. *Neuropsychopharmacology* **43**, 1107–1118 (2018).
- 852 40. Kurzban, R., Duckworth, A., Kable, J. W. & Myers, J. An opportunity cost model of subjective effort and
853 task performance. *Behav. Brain Sci.* **36**, 661–679 (2013).
- 854 41. Boureau, Y.-L., Sokol-Hessner, P. & Daw, N. D. Deciding How To Decide: Self-Control and Meta-
855 Decision Making. *Trends Cogn. Sci.* **19**, 700–710 (2015).
- 856 42. Ackerman, P. L. *Cognitive fatigue: Multidisciplinary perspectives on current research and future
857 applications.* (American Psychological Association, 2011).
- 858 43. Hockey, R. *The psychology of fatigue: work, effort and control.* (Cambridge University Press, 2013).
- 859 44. Massar, S. A. A., Csathó, Á. & Van der Linden, D. Quantifying the Motivational Effects of Cognitive
860 Fatigue Through Effort-Based Decision Making. *Front. Psychol.* **9**, (2018).
- 861 45. Müller, T. & Apps, M. A. J. Motivational fatigue: A neurocognitive framework for the impact of effortful
862 exertion on subsequent motivation. *Neuropsychologia* **123**, 141–151 (2019).

- 863 46. Inzlicht, M., Bartholow, B. D. & Hirsh, J. B. Emotional foundations of cognitive control. *Trends Cogn. Sci.*
864 **19**, 126–132 (2015).
- 865 47. Kool, W. & Botvinick, M. A labor/leisure tradeoff in cognitive control. *J. Exp. Psychol. Gen.* **143**, 131
866 (2014).
- 867 48. Bosquet, L., Montpetit, J., Arvisais, D. & Mujika, I. Effects of tapering on performance: a meta-analysis.
868 *Med. Sci. Sports Exerc.* **39**, 1358 (2007).
- 869 49. Howley, E. T., Bassett, D. R. & Welch, H. G. Criteria for maximal oxygen uptake: review and commentary.
870 *Med. Sci. Sports Exerc.* **27**, 1292–1301 (1995).
- 871 50. Kuipers, H., Verstappen, F. T., Keizer, H. A., Geurten, P. & van Kranenburg, G. Variability of aerobic
872 performance in the laboratory and its physiologic correlates. *Int. J. Sports Med.* **6**, 197–201 (1985).
- 873 51. De Pauw, K. *et al.* Brain mapping after prolonged cycling and during recovery in the heat. *J. Appl. Physiol.*
874 **115**, 1324–1331 (2013).
- 875 52. Essex, B. G., Clinton, S. A., Wonderley, L. R. & Zald, D. H. The impact of the posterior parietal and
876 dorsolateral prefrontal cortices on the optimization of long-term versus immediate value. *J. Neurosci.* **32**,
877 15403–15413 (2012).
- 878 53. Friston, K., Mattout, J., Trujillo-Barreto, N., Ashburner, J. & Penny, W. Variational free energy and the
879 Laplace approximation. *NeuroImage* **34**, 220–234 (2007).
- 880 54. Daunizeau, J., Friston, K. J. & Kiebel, S. J. Variational Bayesian identification and prediction of stochastic
881 nonlinear dynamic causal models. *Phys. Nonlinear Phenom.* **238**, 2089–2118 (2009).
- 882 55. Daunizeau, J., Adam, V. & Rigoux, L. VBA: A Probabilistic Treatment of Nonlinear Models for
883 Neurobiological and Behavioural Data. *PLoS Comput. Biol.* **10**, e1003441 (2014).
- 884 56. Rigoux, L., Stephan, K. E., Friston, K. J. & Daunizeau, J. Bayesian model selection for group studies —
885 Revisited. *NeuroImage* **84**, 971–985 (2014).
- 886 57. Deichmann, R., Gottfried, J. A., Hutton, C. & Turner, R. Optimized EPI for fMRI studies of the
887 orbitofrontal cortex. *Neuroimage* **19**, 430–441 (2003).
- 888 58. Weiskopf, N., Hutton, C., Josephs, O., Turner, R. & Deichmann, R. Optimized EPI for fMRI studies of the
889 orbitofrontal cortex: compensation of susceptibility-induced gradients in the readout direction. *Magn.*
890 *Reson. Mater. Phys. Biol. Med.* **20**, 39–49 (2007).
- 891
- 892