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1 Training level reveals a dynamic dialogue between stress and
2 memory systems in birds

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25 **Abstract**

26 Chronic stress profoundly affects forms of declarative memory, such as spatial memory, while it may
27 spare non-declarative memory, such as cue-based memory. It is known, however, that the effects of
28 chronic stress on memory systems may vary according to the level of training of an individual was
29 submitted. Here, we investigated, in birds, how chronic stress impact spatial and cue-based memories
30 according to training level. For that, control and chronically stressed Japanese quail were trained in a
31 task that could be solved using spatial and cue-based memory and tested for their memory
32 performance after 5 and 15 training days (initial training and overtraining, respectively) and following
33 an emotional challenge (exposure to an open field). Our results showed that, compared to control
34 quail, chronic stress impacted negatively spatial memory performances in stressed birds after initial
35 training, but these differences were lowered after overtraining. Control birds seemed to shift from
36 spatial to cue-based memory to solve the task across overtraining. However, an emotional challenge
37 before testing reinstated the negative impact of chronic stress on spatial memory performances
38 between the groups, revealing that chronic stress/overtraining did not eliminate the spatial memory
39 and differences caused by stressors can reemerge depending on the individual's immediate
40 psychological state. Contrary to spatial memory, cue-based memory was not affected in chronically
41 stressed birds compared to control birds in any test occasion, confirming its resistance against the
42 negative effects of chronic stress. Altogether these findings reveal a dynamic dialogue between stress,
43 training level, and memory systems in birds.

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45 Keywords: bird cognition; chronic stress; spatial memory; cue-based memory; overtraining; Japanese
46 quail.

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56 **1. Introduction**

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58 It has long been recognized that chronic stress strongly modulates learning and memory
59 performance [1–3]. However, the relationship between chronic stress and memory are still
60 controversial: some studies reported an improving effect of chronic stress on memory performance [4–
61 6], whereas others reported a negative effect [6–8]. Overall, chronic stress generally provokes memory
62 impairment for complex tasks and improves simple tasks [3]. These discrepancies support the fact that
63 memory is not a single unit. Different parts of the brain are responsible for different memory systems
64 that process different types of information and are differently affected by stress [9].

65 Two memory systems have had a considerable amount of scientific interest in the last decades
66 as they present strong parallels between humans and animals. The first one is spatial memory, a form
67 of declarative memory based on the hippocampus and used mainly to establish a relationship between
68 different cues from the environment, which allow the creation of a cognitive mental map [10,11]. As
69 the cues from the environment are treated in relation to each other, the spatial memory is considered to
70 be more complex than the cue-based memory, a non-declarative form of memory that results from a
71 simple association between a salient cue and the target and is based on the striatum [9,12,13]. From
72 the first week of life, chicks can already be trained to use both their spatial and cue-based memory.
73 When the environmental information allows the use of both memory systems, chicks were seen to rely
74 on their cue-based memory [14]. We recently showed that, in quail, individual differences in
75 behavioral traits, such as fearfulness and stress-coping, alters the way birds use these different
76 systems. Indeed, fearful and easily stressed quail use their spatial memory preferentially, while less
77 fearful/stressed individuals prefer to rely on their cue-based memory [15]. The same occurs for the
78 relationship between individual exploratory level and memory systems in free-range chickens: less
79 exploratory chickens, known to be easily startled, have better spatial memory than more exploratory
80 chickens [16–18].

81 Besides intrinsic factors, external insults, such as hippocampal lesions or chronic stress, may
82 also influence which memory system an individual will preferentially use. Hippocampal lesioned and
83 chronic stressed quail present similar patterns of behavior when different memory systems are
84 requested: while these animals present important impairments on spatial memory, they have their cue-
85 based memory spared and, in some cases, even improved [13,19].

86 Beyond chronic stress, the training level can also influence the use of multiple memory
87 systems [9,20–23]. The majority of the knowledge on this area comes, however, from studies on
88 rodents. Indeed, rats trained to learn the location of a reward in a maze preferentially use their spatial
89 memory after a few days of training and shift to a cue-based dominant response with overtraining [24].
90 Training and stress levels may also interact: the initial differences in memory performance due to

91 stress may disappear with overtraining [3]. Other studies suggest training itself may be a source of
92 stress and reduce hippocampal neurogenesis [25,26], which could explain the shift between memory
93 systems. While much is known on chronic stress effects on declarative spatial or non-declarative cue-
94 based memory performance, the influence of the level of training and its interaction with chronic stress
95 influence remains poorly understood. Furthermore, the understanding of these interactions and their
96 applicability to other taxa, such as birds, is still limited and merits further investigation.

97 Using the Japanese quail (*Coturnix coturnix*) as the animal model, in this work, we
98 investigated whether and how chronic stress could differentially impact spatial and cue-based
99 memories according to the level of training. In previous work, we developed reliable protocols to
100 study the effects of chronic stress on different quail behavior and cognitive abilities. In quail, chronic
101 stress is known to increase individuals' emotional reactivity (to both novel objects and humans, for
102 example) and disrupt feeding patterns [27–29]. These negative effects may be long lasting, during up
103 to seven weeks after the termination of the stress procedure [30]. While our results suggested that
104 chronic stress strongly impair quail spatial memory, with lesser impacts on cue-based memory [19],
105 we did not take into consideration the possible effects of training level and their interactions with
106 chronic stress. In order to fill this knowledge gap, here, control and chronically stressed Japanese quail
107 were trained in a dual spatial/cued task, which could be solved using the spatial or cue-based
108 memories and tested for their performances on each type of memory after five and fifteen training
109 days. Additionally, as an animal's immediate psychological state may interact with chronic stress and
110 impact the relative use of different memory systems and memory performance [19,31–33], a series of
111 tests were conducted after an emotional challenge that consisted of exposing quail to an unfamiliar
112 environment (open field). Finally, birds were submitted to a test to assess whether they learn to find
113 the target cup by a simple association between the target cup's color and the reward or by detecting the
114 difference of colors between the target cup and the remaining cups. Based on the literature, we
115 expected chronically stressed quail to show lower performance in the spatial memory test than control
116 ones after initial training (five days of training). These differences were expected to lower or disappear
117 after overtraining (fifteen days of training) and reinstated after the emotional challenge. Concerning
118 the cue-based memory, we expected no differences between chronically stressed and control quail.
119 Since this is a simple form of memory, we expected the emotional challenge would not disrupt it.

120

121 **2. Methods**

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123 **2.1. Animals**

124

125 All Japanese quail were bred and maintained at the Pôle d'Expérimentation Avicole de Tours
126 (UE PEAT, INRAE, 2018. Experimental Poultry Facility, DOI: 10.15454/1.5572326250887292E12)

127 where the experiment took place. These quail had a controlled and known genetic background, being
128 selected over 60 generations to have intermediate, control-like levels of fear/anxiety responses
129 (intermediate durations of tonic immobility) [34,35].

130 One-day old chicks were placed on communal floor pens. When chicks reached 21 days old,
131 they were sexed by feather dimorphism, and males were transferred to a single home cage (41×51×25
132 cm), under a 12:12h light-dark schedule (light was on at 0800h). Artificial turf was available on the
133 cage floor, allowing animals to dust bathe. The ambient temperature was kept at approximately
134 $20\pm 2^{\circ}\text{C}$. Food and water were provided *ad libitum*.

135 Animal care and experimental treatments followed the French Ministry of Agriculture
136 guidelines and European regulations on animal experimentation (86/609/EEC). They also followed
137 local animal regulations (C37-175-1) of the French Ministry of Agriculture under the EEC directive
138 and under ethics committee approval (agreements N° 1789 and 1848, Val de Loire).

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140 **2.2. Chronic stress procedure**

141

142 To stress quail chronically, we followed the same procedures as described in [19]. When quail
143 reached 21 days old, they were transferred to individual cages. They were then divided into two
144 treatment groups: a control and a chronic stress group. Quail from the chronic stress group were
145 submitted to chronic unpredictable stress (CUS) for three weeks consisting of multiple negative
146 stimulations or stressors (from five to six) per day. Each stressor occurred at unpredictable times each
147 day/night to improve the unpredictability of the stressor delivery and decrease habituation to the stress
148 procedure. This CUS procedure has been fully described and was shown to induce a state of chronic
149 stress in quail [19,27,28,30,36,37]. Stressors were delivered directly in the quail's home cage: 30 min
150 of confinement of the bird in the corner of its home cage, 30 min of food frustration by placing
151 transparent devices on the feeder just before light on, 2×15 min of soft home cage shaking, interspaced
152 by 15 min, unpredictable sounds (100 dB) with or without biological significance for quail. Outside
153 disturbances were also delivered, such as a passage of a plastic stick on the home cage rods (twice a
154 day for 2 min), sprayings of air or water on feathers (2 sprays interspaced by 2 min), and 2-min of
155 waving a plastic flag in front of the home cage. Birds were also moved outside their homecage and
156 individually transferred into a new environment for 30 min.

157 The control group was left undisturbed and underwent similar routine husbandry procedures as
158 CUS birds. The experimenters regularly visited the control quail room to ensure they have spent the
159 same amount of time with control and chronically stressed birds. Systematically, when stressors
160 prevented CUS birds from feeding, an opaque device was also placed on the feeder of control birds to
161 prevent them from feeding for an equivalent amount of time.

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2.3. Learning and memory task

The following procedures and the arena used for the task were previously used and validated by our group in chickens and quail [13,15,17,19].

At the end of the CUS procedure, 17 control and 20 chronically stressed birds were submitted to a training procedure followed by a series of memory tests (Figure 1). The CUS procedure was stopped before the start of the training for two main reasons: the first one was to dissociate the effects of chronic stress from those of a possible acute, immediate stress that could occur if animals were stressed just before the training/testing sessions. The second reason is that, since the behavioral and cognitive effects of CUS in quails can be seen long after the procedure stopped [28,30,34], the stopping of CUS allowed us to test for the long-term consequences and implications of the procedure in animals' learning and memory.

After preliminary phases dedicated to familiarizing birds to the food reward (mealworms), the cups and the arena, control and chronically stressed birds were submitted to a dual spatial/cued task during five days that consisted of learning to find food (mealworm) hidden in a single cup (target cup) in an arena that contained eight opaque cups. On each trial, birds were introduced in the arena by a different starting point among three possibilities. The location of the target cup was constant among trials and days of training, allowing animals to solve the task using spatial memory. Moreover, the target cup was black, whereas other non-target cups were white. Thus, birds could also solve this task using their cue-based memory, based on the color of the cup.

The day after the fifth day of training, birds were submitted to a spatial test followed by a displacement test. During the spatial test, all cups were white, and the task could only be solved by remembering the spatial location of the target cup during the training phase. During the displacement test, performed 30 min later, the black target cup was displaced to a new position (different from the position used during training). Thus, both spatial and cue-based memories could provide a solution to the test. Quail could go back either to the spatial location of the target cup during the training phase (spatial memory) or go directly to the displaced black cup (cue-based memory) [16,17,19].

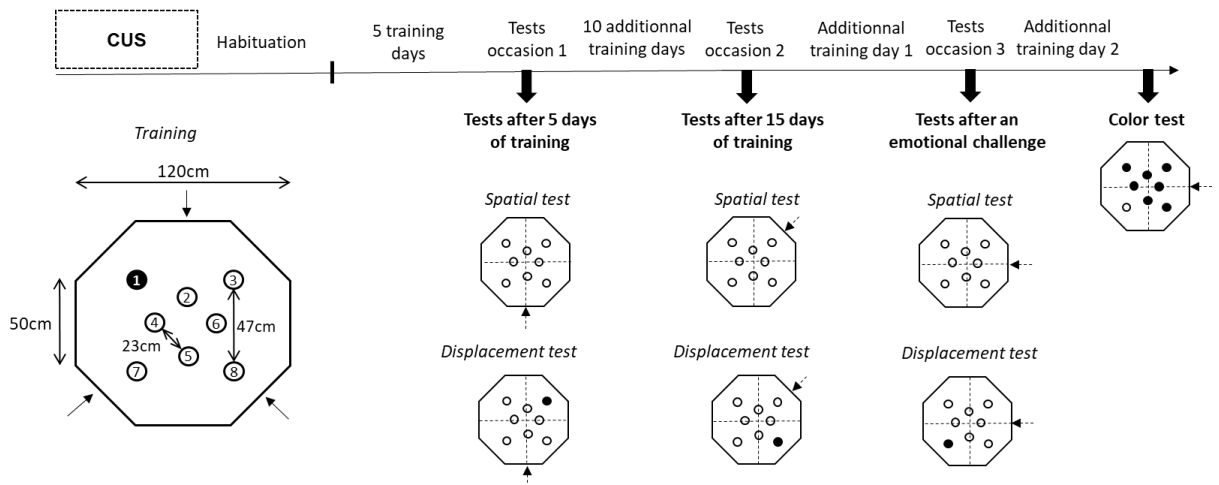
After this first test occasion, birds were trained for ten additional days in the dual spatial/cued task before being submitted to the second test occasion of spatial and displacement tests. Following the second test occasion, birds were trained for an additional day (recall training) in the dual spatial/cued task to avoid that lack of food during the second test occasion reduced bird motivation in subsequent tests. After this first recall training day, all birds were challenged by exposure to an open field test and were submitted to the third occasion of spatial and displacement tests.

On the following day, quail were submitted to a second additional training day (recall training) to keep birds motivated. The day after, birds were submitted to a new test, called the "color test", to assess whether birds found the target cup by a simple association between its color (black) and the

201 reward or by learning a more general rule that the target cup was of a different color compared to the
 202 remaining cups.

203 During all the memory tests, behaviors of quail were recorded by a camera placed above the
 204 apparatus and computerized by a tracking video system (Ethovision XT; Noldus IT, The Netherlands).

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209 **Figure 1: Schedule of the experiment and schematic representation of the apparatus used**
 210 **for training and testing.** At three-weeks-old, quail were submitted to chronic unpredictable stress
 211 (CUS) for three weeks. At the end of the CUS procedure, stressed and control birds were trained in a
 212 dual spatial/cued learning task and submitted to spatial and displacement memory tests after 5 and 15
 213 days of training. After an additional training day, quail were submitted to an emotional challenge
 214 (exposure to an open field) followed by a new series of tests. After the last training day, birds were
 215 submitted to the color test. Quail could enter the arena from three different starting points (dark
 216 arrows), three starting points during training, and one during testing. The dotted lines represent the
 217 division of apparatus into four different quadrants.

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219 2.4. The dual spatial/cued task

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221 2.4.1. Mealworms familiarization

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223 One week before the beginning of training, a brown ceramic cup (6x7cm) was placed in each
 224 quail's home cage. For seven days, three times per day (spaced about 3h), 3 or 4 mealworms were
 225 deposited in the cup to familiarize birds with the cups and mealworms.

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2.4.2. *Habituation*

After familiarization, birds were submitted to the habituation phase. Birds were food-deprived one hour before each habituation session. During five days, once a day, each quail was introduced into the center of a beige octagonal arena (120cm long; 50cm high) surrounded by a blue curtain (1.90m high) and lighted by a bulb at the ceiling (18 Lux). Eight black cues were disposed of in the arena, four on the walls and four on the curtain. Eight ceramic cups similar to those used for the familiarization were placed in the arena and contained mealworms. Four cups were wrapped with white paper, whereas black paper wrapped another four cups. In each habituation session, exploration of the arena and the cups was allowed until the bird found and ate all mealworms or after a maximum time of 600 s. Between each quail and day of habituation, the position of black and white cups was randomly moved. The number of cups visited was recorded on each day to estimate the level of exploration and habituation of the birds (Figure 1).

2.4.3. *Training*

On each day of training, birds were submitted to 2 training trials per day (1 hour between each trial). On each trial, birds were introduced in the arena by a different starting point among three possibilities (Figure 1). Only one cup was rewarded and contained three mealworms (target cup). The target cup was always black and at a fixed position on each trial, whereas the seven other cups were non-rewarded and white. When the bird reached the target cup and ate the mealworms, the trial was ended, or after a maximum time of 300 s. If the bird did not find the target cup, the experimenter gently guided it and allowed it to eat the mealworms. The bird returned to its home cage between each trial. The latency to find and eat the food in the rewarded black cup was recorded on each trial.

2.4.4. *The spatial test*

This test was used to assess the impact of chronic stress on spatial memory. Each bird was allowed to freely explore the arena and the 8 cups for 1 minute. All cups were empty and, more importantly, of similar color (white). The number of cups visited (number of errors) before reaching the target cup was scored. Moreover, the arena was virtually divided into four equal quadrants, and the time spent in each quadrant (spatial quadrant and three other quadrants) during the test was measured using the tracking video system (Figure 1).

The spatial test was conducted after 5 and 15 days of training (initial training and overtraining, henceforth) and after an emotional challenge by exposing birds to an open field (emotional challenge, henceforth).

266 2.4.5. *The displacement test*

267

268 The displacement test was used to assess the impact of chronic stress on the use of spatial and
269 cue-based memory systems. It was systematically conducted 30 min after the spatial test. During this
270 test, similarly to the training phase, the arena was equipped with one black cup and seven white cups,
271 but all cups were empty of food. The black cup was displaced to a new position (Figure 1). The new
272 position was changed for each test conducted after initial training, overtraining, and emotional
273 challenge. All birds were allowed to explore the arena and the cups for 1 min freely. The number of
274 errors before reaching the spatial and displaced cup was scored. Similar to the spatial test, the arena
275 was virtually divided into four equal quadrants (spatial quadrant, displaced cup quadrant, and two
276 other quadrants), and the time spent in each quadrant during the test was measured using the tracking
277 video system. The time spent on the two other quadrants was averaged.

278

279 2.4.6. *Tests after an emotional challenge*

280

281 The third occasion of both tests (spatial and displacement tests) was conducted after an
282 emotional challenge. This emotional challenge consisted of exposing the birds to an open field test,
283 which is known to provoke anxiety-like quail behaviors [19,38,39]. Each quail was individually placed
284 in the center of a square arena (80 × 80 × 80 cm) of white wood with a beige linoleum floor. The arena
285 was placed into a new experimental room, surrounded by a green curtain and strongly lighted (50 lux).
286 Each quail was allowed to explore the arena for 5 min before being withdrawn from the arena. Thirty
287 minutes after the open field test, quail were submitted to a spatial test followed by a displacement test.

288

289 2.4.7. *The color test*

290

291 This test aimed to assess whether birds learn to find the target cup by a simple association
292 between its color (black) and the reward or by detecting the difference of colors between the target cup
293 and the remaining cups (Figure 1). Each bird was allowed to freely explore the arena and the eight
294 cups for 1 minute. All cups were empty and black, except for one white cup and not located in the
295 spatial position used for training. The number of visits before reaching the white cup was scored.
296 Moreover, the number of visits before reaching the black cup located in the spatial location used
297 during training was scored and compared to those to reach the white cup and other black cups. As for
298 previous tests, the time spent in the four equal quadrants (white cup quadrant, spatial black cup
299 quadrant, and two other black cup quadrants) of the arena was measured. This test was performed after
300 a second recall training day conducted the day after the third test occasion.

301

302

2.5. Statistical analysis

Data from habituation (number of cups visited) and from training (latency to reach the target cup) were analyzed by parametric analyses of variance (ANOVA repeated measures) with stress group (control and chronically stressed quail) as between-subject factors and days (mean values for both training trials within days) as within-subject factors.

For spatial, displacement, and color tests, the number of errors (or visits) before reaching the target cup(s) and the time spent in the different quadrant of the arena were analyzed by ANOVA with groups (control and stressed) as between-subject factors and test occasions (test after initial training, test after overtraining and test after the emotional challenge) as within-subject factors. Additional within-subject factors (e.g., quadrants or cups considered) were also included, dependent on the variables under consideration. Exploratory analyses showed that when the time spent on quadrants was averaged (the three “other quadrants” during the spatial test and the two “other quadrants” during the displacement and color tests), the results were similar than when quadrants were analyzed separately. To facilitate data comprehension and visualization, we therefore kept and included only the averaged time in other quadrants in our analyses. When main effects or interactions were significant, analyses were followed by multiple comparisons corrected by Tukey HSD.

When an individual did not find a target cup and visited less than 4 cups, it was attributed a number of 8 errors and an equivalent time of 15 sec in each quadrant. All statistical analyses were performed using IBM SPSS 21 and R version 3.6.1. Statistical significance was set at $p < 0.05$.

3. RESULTS

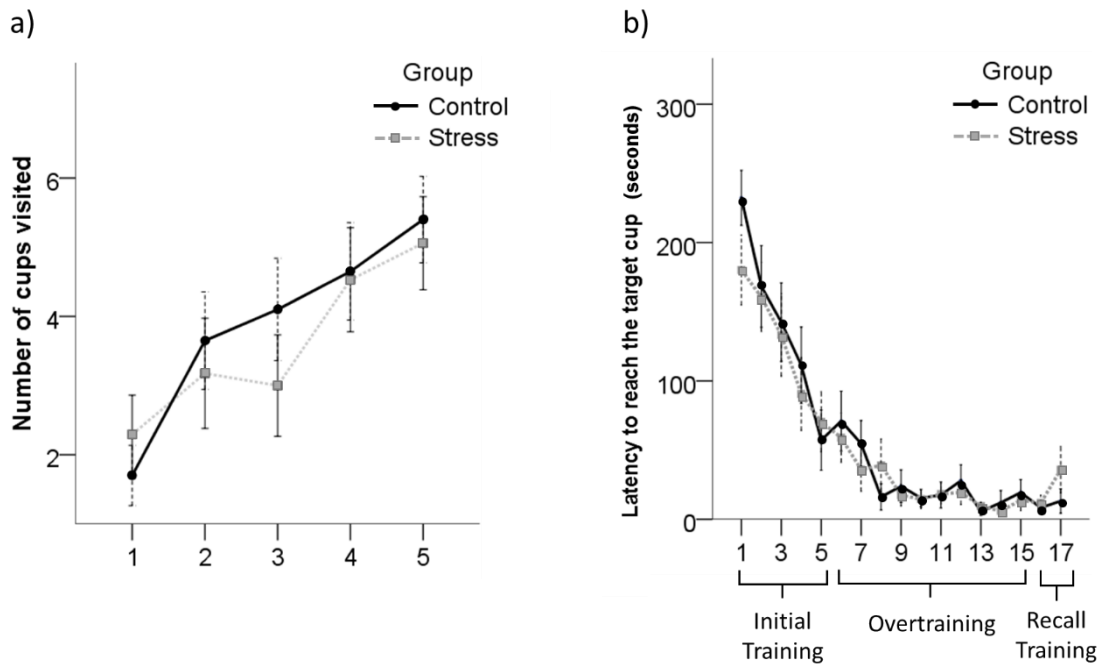
3.1. Effect of chronic stress on habituation and training in the dual spatial/cued task

During habituation, both groups visited more cups and ate significantly more mealworms over days without any differences between control and chronically stress quail (effect of days: $F_{4,140}=18.15$, $p<0.001$; effect of stress: $F_{1,35}=0.13$, $p=0.72$; interaction days x stress: $F_{4,140}=1.11$, $p=0.35$; Figure 2a).

During the initial training period, both groups similarly learned the location of the target cup since the latency to find the target cup significantly decreased over days (effect of days: $F_{4,140}=19.60$, $p<0.001$; effect of stress: $F_{1,35}=0.28$, $p=0.60$; interaction days x stress: $F_{4,140}=0.93$, $p=0.45$; Figure 2). Similarly, during the overtraining period, the latency to reach the target cup significantly decreased without any effect of chronic stress (effect of days: $F_{9,315}=5.89$, $p<0.001$; stress effect: $F_{1,35}=0.13$, $p=0.73$; interaction days x stress: $F_{9,315}=0.58$, $p=0.81$; Figure 2b).

The latency between the last day of overtraining (the fifteenth day of training) and the recall period between tests (last two additional days) was not different between days, nor between control

339 and chronically stressed quail (effect of days: $F_{2,70}=1.12$, $p=0.33$; effect of stress: $F_{1,35}=0.65$, $p=0.42$;
 340 interaction days x stress: $F_{2,70}=1.10$, $p=0.33$), indicating that animals reached a learning plateau.
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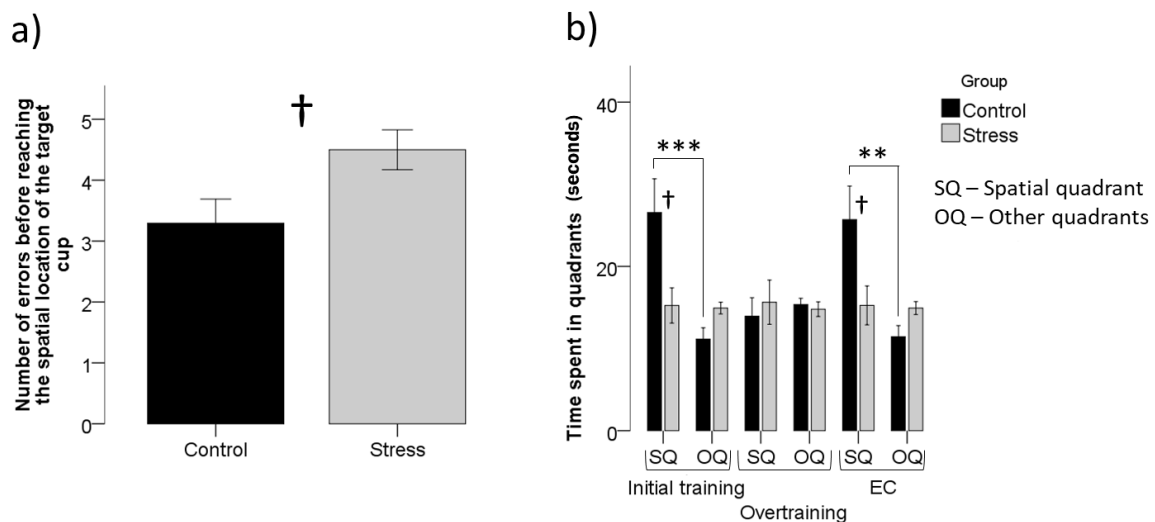
342
 343 **Figure 2: Effects of chronic stress on habituation and training performances in the dual**
 344 **spatial/cued task. a)** Number of visited cups over days of habituation in control and chronically
 345 stressed quail. During habituation, all eight cups were rewarded with mealworms. **b)** Latency to reach
 346 the location of the target cup over days of training in control and chronically stressed quail. Mean \pm
 347 SEM are given. ($n_{\text{control quail}} = 17$, $n_{\text{chronically stressed quail}} = 20$)

3.2. Effect of chronic stress during the spatial test

351 The number of errors made before reaching the spatial cup was significantly increased in
 352 chronically stressed quail (effect of stress: $F_{1,35}=5.62$, $p=0.023$, Figure 3a), independently of the test
 353 occasion and the interaction with stress (effect of test occasion: $F_{2,70}=1.45$, $p=0.24$; interaction test
 354 occasion x stress: $F_{2,70}=2.72$, $p=0.072$).

355 The time spent in the spatial quadrant compared to other quadrants was affected by the
 356 quadrant considered, stress, and the interaction quadrant, test occasion, and stress (effect of quadrant:
 357 $F_{1,35}=7.58$, $p=0.009$; effect of stress: $F_{1,35}=6.13$, $p=0.018$; interaction quadrant x test occasion x stress:
 358 $F_{2,70}=3.36$, $p=0.040$). Post-hoc analyses revealed that, during the tests after the initial training and the
 359 emotional challenge, control birds spent significantly more time in the spatial quadrant compared to
 360 other quadrants ($p<0.001$ and $p=0.001$, for the tests after the initial training and the emotional
 361 challenge, respectively). In contrast, chronically stressed birds spent an equivalent time in the spatial
 362 quadrant compared to other quadrants ($p=1$ and $p=1$ for the tests after the initial training and the

363 emotional challenge, respectively, Figure 3b). No differences were found for the test after
 364 overtraining: both control and chronically stressed quail spent an equivalent time in the spatial
 365 quadrant compared with other quadrants ($p=1$ and $p=1$, for control and chronically stressed quail,
 366 respectively, Figure 3b).
 367



368
 369 **Figure 3. Effects of chronic stress in spatial memory tests performed after initial training (5**
 370 **days), overtraining (15 days), and after an emotional challenge (EC, exposure to an open field).**
 371 **a) Number of errors before reaching the spatial location of the target cup, and b) Time (in seconds)**
 372 **spent in different quadrants of the arena (spatial and other quadrants). † $p \leq 0.05$, significant difference**
 373 **between control and chronically stressed quail. ** $p \leq 0.01$; *** $p \leq 0.001$, significant difference**
 374 **between the spatial quadrant and other quadrants. Mean \pm SEM are given. ($n_{\text{control quail}} = 17$, $n_{\text{chronically$**
 375 **stressed quail} = 20)**

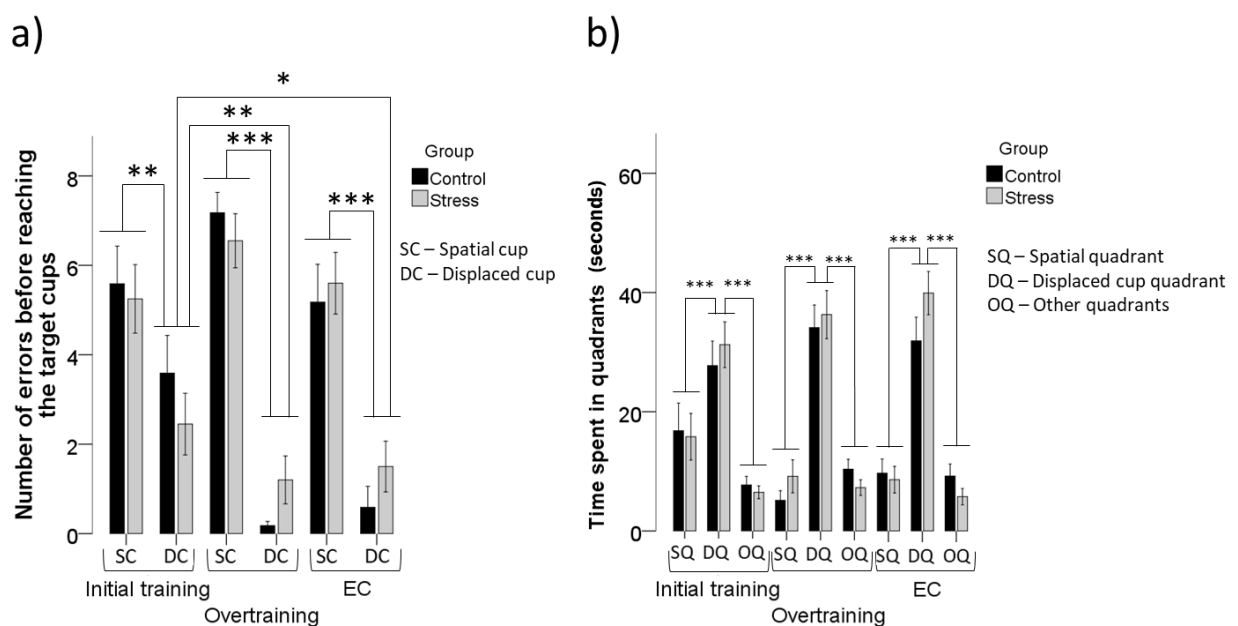
376 3.3. Effect of chronic stress during the displacement test

377
 378 Analyses on the number of errors made before reaching the target cups (either the spatial cup
 379 or the displaced cup) showed that animals were more performant to reach the displaced cup,
 380 independent of their treatment group. There was also a significant interaction between the test
 381 occasion and the target cups (effect of target cup: $F_{1,35}=100.71$, $p<0.001$; effect of test occasion:
 382 $F_{2,70}=3.22$, $p=0.046$; effect of stress: $F_{1,35}=0.010$, $p=0.92$; interaction target cup x stress: $F_{1,35}=0.27$,
 383 $p=0.6$; interaction target cup x test occasion: $F_{2,70}=8.26$, $p=0.001$; interaction target cup x test occasion
 384 x stress: $F_{2,70}=0.87$, $p=0.42$). Post-hoc analyses revealed animals did significantly fewer errors before
 385 reaching the displaced cup on all test occasions, compared to the errors before reaching the spatial cup
 386 ($p=0.001$, $p<0.001$ and $p<0.001$, for the tests performed after initial training, overtraining, and just
 387 after the emotional challenge, respectively, Figure 4a). Between test occasions and within-target cup,

388 post-hoc comparisons revealed that animals made significantly fewer errors before reaching the
 389 displaced cup during the tests after overtraining and after the emotional challenge, compared to the test
 390 after initial training ($p=0.001$ and $p=0.005$, respectively, Figure 4a).

391 Analyses on time spent in different quadrants showed that animals did not spend their time
 392 evenly between quadrants. They spent significantly more time than the chance level in the displaced
 393 cup quadrant independent of their treatment group. There was also a significant interaction between
 394 the test occasion and the time spent in different quadrants (effect of quadrants: $F_{2,70}=67.19$, $p<0.001$;
 395 effect of test occasion: $F_{2,70}=0.82$, $p=0.44$; effect of stress: $F_{1,35}=3.81$, $p=0.059$; interaction quadrants x
 396 stress: $F_{2,70}=1.09$, $p=0.34$; interaction quadrants x test occasion: $F_{4,140}=3.25$, $p=0.014$. interaction
 397 quadrants x test occasion x stress: $F_{4,140}=0.42$, $p=0.78$). Post-hoc analyses revealed that the time spent
 398 in the displaced cup quadrant was higher for all test occasions compared to those spent on the spatial
 399 quadrant and other quadrants ($p<0.05$, for the tests performed after initial training, overtraining, and
 400 just after the emotional challenge, respectively, Figure 4b).

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404 **Figure 4. Effects of chronic stress in the displacement tests performed after initial training (5**
 405 **days), overtraining (15 days), and after an emotional challenge (EC, exposure to an open field).**

406 **a) Number of errors before reaching the target cups (spatial cup or displaced cup), and b) Time (in**
 407 **seconds) spent in different quadrants of the arena (either the spatial quadrant, SQ, the displaced cup**
 408 **quadrant, DQ, or the other quadrants, OQ). * $p\leq 0.05$; ** $p\leq 0.01$; *** $p\leq 0.001$, significant difference**
 409 **between the spatial cup and displaced cup or between spatial quadrant, displaced cup quadrant, and**
 410 **other quadrants. Mean \pm SEM are given. ($n_{\text{control quail}} = 17$, $n_{\text{chronically stressed quail}} = 20$)**

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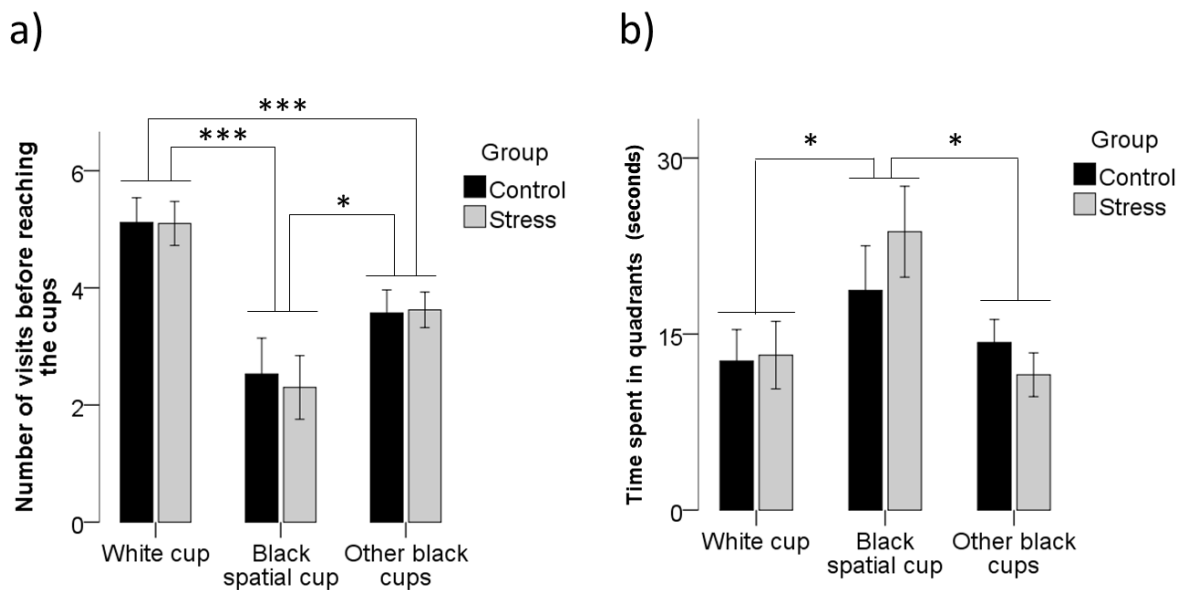
413

3.4. Effect of chronic stress during the color test

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415 During the colour test, independently of chronic stress, the number of visits made before
416 reaching a cup was different depending on the cup considered (effect of cup: $F_{2,70}=18.60$, $p<0.0001$;
417 effect of stress: $F_{1,35}=0.03$, $p=0.87$; interaction cup x stress: $F_{2,70}=0.06$, $p=0.95$; Figure 5). Post-hoc
418 analyses showed that the number of visits before reaching the spatial black cup was significantly lower
419 than those performed before reaching other black cups or the white cup ($p=0.02$ and $p<0.001$,
420 respectively, Figure 5a).

421 Finally, the time spent in the different quadrants was also significantly dependent on the
422 quadrant considered (effect of quadrants: $F_{2,70}=3.62$, $p=0.032$). Post-hoc analyses revealed a
423 significantly larger amount of time spent in the black spatial cup quadrant compared to other black
424 cups and white cup quadrants ($p=0.01$). No differences were found between the treatment groups, nor
425 for the interaction quadrants and treatment groups (effect of stress: $F_{1,35}=1.02$, $p=0.31$; interaction
426 quadrants x stress: $F_{2,70}=0.59$, $p=0.55$, Figure 5b).



427

428 **Figure 5. Effects of chronic stress on the color test. a)** Number of visits before reaching the white
429 cup, the black spatial cup, or other black cups in chronically stressed and control birds and **b)** Time (in
430 seconds) spent in different quadrants of the arena containing the white cup, the spatial black cup, other
431 black cups in chronically stressed and control birds. * $p\leq 0.05$; ** $p\leq 0.01$; *** $p\leq 0.001$, significant
432 difference between the white cup, black spatial cup, and other black cups. Mean \pm SEM are given.

433 ($n_{\text{control quail}} = 17$, $n_{\text{chronically stressed quail}} = 20$)

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4. DISCUSSION

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Since the majority of the studies investigating the relationship between chronic stress and training level comes from studies on rodents, until now, we have had little understanding on how these interactions apply to other taxa, such as birds. To fill this gap, using Japanese quail as the animal model, the main objective of the present study was to address whether chronic stress can differentially impact two forms of long-term memory, the declarative spatial and the non-declarative cue-based memories, according to the level of training. To this end, control and chronically stressed Japanese quail were trained in a task that could be solved using spatial and cue-based memory, the dual spatial/cued task, and tested for their performances on each type of memory after 5 and 15 days of training (initial training and overtraining, respectively). Our results showed that the spatial memory of quail was sensitive to the deleterious effect of chronic stress. Performances of chronically stressed birds during the spatial test after initial training were impaired compared to that of control birds. During the test after overtraining, however, these differences were lowered. Interestingly, during the test after an emotional challenge, when birds were exposed to an open field, the negative impact of chronic stress on spatial memory performance seemed to be fully reinstated. These findings indicate that the relationships between chronic stress, training level, and spatial memory are complex and dynamic. By contrast, cue-based memory was not affected in chronically stressed birds and control birds on any test occasion, which indicates that this form of memory is relatively resistant to the negative effect of chronic stress. Finally, a test conducted to better qualify birds' cue-based memory performance, the color test, provided support that chronically stressed birds were still able to efficiently remember the spatial location of the target cup when this location was signaled by a color similar to that used during training. This suggests that chronically stressed birds cannot efficiently recall stored spatial information in a context different from the one experienced during training, which highlights that chronic stress reduces the ability to use spatial memory flexibly.

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Our results from habituation showed that the number of mealworms eaten increased over days without any significant effect of chronic stress. Moreover, the latency to reach the target cup decreased over days of training in both groups. These findings indicate that both control and chronically stressed birds similarly habituated to the arena and the cups and similarly learned the dual spatial/cued task. They also indicate differences between groups observed during the different tests performed could not be attributed to evident motor or motivational differences and instead reflect stress-related changes in memory performance.

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During the spatial test, the number of errors before reaching the spatial location of the target cup was higher in all test occasions (initial training, overtraining, after an emotional challenge) for chronically stressed birds compared to control birds, evidencing the negative impact of chronic stress

473 on spatial memory performance. Although not significant ($p=0.07$), the interaction between test
474 occasion and stress suggests that the performance of both groups during overtraining tests was similar,
475 compared to initial training and after emotional challenge tests, when their performances differed
476 more. Confirming this tendency, the time spent in different quadrants revealed some specificities of
477 the animals' performance over the different test occasions. During spatial tests performed after initial
478 training, chronically stressed birds spent their time evenly between the quadrants, while control birds
479 spent significantly more time in the spatial quadrant. The same did not occur after overtraining.
480 Indeed, performances of both control and chronically stressed birds were relatively low during the
481 spatial test performed after overtraining. Contrasting the spatial tests, chronic stress did not affect cue-
482 based memory performance in all displacement tests performed. On all test occasions, chronically
483 stressed birds and control had the same performance and followed the displaced black cup
484 preferentially. These findings show that, similar to what is already known in rodents, chronic stress in
485 birds differentially impacts memory depending on the memory system, with the spatial memory being
486 much more sensitive to the adverse effects of chronic stress than cue-based memory [1,6,40]. They
487 also confirm that more complicated tasks are more impacted by chronic stress than simple tasks [3],
488 corroborating our previous work on chickens and quail where we found different level of cognitive
489 performance between animals from different groups (hippocampal lesioned vs non-lesioned, stressed
490 vs non-stressed, fearful vs non-fearful, exploratory vs non-exploratory) only during complex tasks,
491 which are more cognitively demanding, rather than during simple tasks, where animals may use
492 stimulus-response strategies [13,16,17,19,41,42].

493 The low spatial memory performance after overtraining for control individuals may be
494 explained by a progressive acquisition of a predominant cue-based strategy to solve the spatial test
495 over days of training. In mammals, it is well documented that the involvement of memory systems is a
496 dynamic process that can vary over time of training. In particular, overtraining in mammals favours
497 cue-based memory [20,21,23,24]. In line with this, the number of errors to reach the black target cup
498 during the displacement tests decreased with training, evidencing an improvement of this type of
499 memory over time. These results highlight the importance of taking training level into account when
500 testing memory in birds, since, similar to mammals a progressive shift from declarative, spatial
501 memory use to a non-declarative, cue-based memory use may occur.

502 An alternative explanation for these results could be that extensive exposure to the task was
503 perceived, by the control animals, as stressful on its own, in other words, control quail may have
504 become stressed with overtraining which caused a worsening in their performance. In previous work
505 we confirmed that stressed quail have poor spatial memory, but improved cue-based memory [19],
506 which gives support to this alternative hypothesis. If indeed stress from overtraining is behind the
507 worsening in spatial memory for control individuals, it is noteworthy to state that the different
508 stressors (overtraining vs chronic stress) were probably perceived differently by the birds, since the
509 differences between control and chronically stressed quail on spatial memory performance were

510 restored after an emotional challenge. Once more, our results give us further understanding of the
511 relationship between chronic stress and memory in birds and reveal it is not that different from that of
512 mammals: previous studies in rodents highlighted that acute stress or stress hormone injections
513 experienced just before testing can induce the reemergence of an extinguished memory [31,32].
514 Another possibility for the suddenly use of spatial information in control birds is that, exposure to an
515 open field is also an exposure to a novel spatial environment, that induces hippocampus dependent
516 mechanisms. Such process may contribute to reactivate hippocampus dependent spatial memory in
517 control birds. More studies need to be done to disentangle these two hypotheses. In any case, the
518 worsening in performance of control birds after an extending period of training seems to not be due to
519 an elimination of the spatial memory, which can re-emerge depending on the more immediate
520 psychological state of the quail. Moreover, the reappearance, even after overtraining, of chronic stress
521 adverse effects on the spatial memory of stressed quail could indicate a long-lasting sensibility of this
522 memory system.

523 Finally, our study highlighted that chronic stress affected specific characteristics of spatial
524 memory but did not make it impossible for stressed animals to have this form of memory. Indeed, in
525 the last test, the color test, control, and chronically stressed birds made fewer visits before reaching the
526 black cup located in the same spatial location used during training. Chronically stressed birds seemed
527 thus able to remember the location of the target cup when this cup was black, as during training. It
528 suggests that chronic stress specifically impaired the capacity of birds to remember a previously
529 learned location when this location was no more signaled by the cue (black color). This capacity is
530 crucial to perform the spatial test efficiently. Numerous studies conducted in chicks and quail
531 evidenced that spatial memory critically requires the hippocampus [13,19,43]. In mammals, the
532 hippocampus was shown to be critically involved in forming distinct memories from events with a
533 high level of similarities (pattern separation) and to re-establish previously acquired memory by using
534 incomplete information as recall cues (pattern completion) [44,45]. During spatial tests, the spatial
535 location was no more signaled by the cue (all cups were white). Birds should re-establish the complete
536 spatial-cued information learned during training (one rewarded black cup among seven non-rewarded
537 white cups) from this incomplete information. Under this framework, chronic stress, which negatively
538 affects the hippocampus's functioning in quail [19], may impair hippocampus-dependent processing of
539 pattern completion.

540 In conclusion, the present study presents evidence that chronic stress can negatively impact the
541 birds' declarative spatial memory. It highlights that chronic stress specifically alters the ability to use
542 spatial memory flexibly. Also, we show for the first time in birds that an extended period of training
543 can lower the spatial memory differences between control and chronically stressed individuals, either
544 by a progressive shift to cue-based memory or by the fact that overtraining can be in itself perceived as
545 stressful by control animals, hindering their performance. These hypotheses should be tested further.
546 Before testing, an emotional challenge was capable of reinstating the differences in performance

547 between chronically stressed and control quail, showing the spatial memory system's long-lasting
548 sensibility. To our knowledge, this is the first work that highlights the dynamic dialogue between
549 stress, training level, and memory systems in birds, increasing the scientific understanding of these
550 interactions and their applicability to other taxa than mammals.

551

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553

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