

1 **The effects of an 8-week mindful eating intervention on anticipatory reward**  
2 **responses in striatum and midbrain**

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## 26 **Abstract**

27 Obesity is a highly prevalent disease, usually resulting from chronic overeating. Accumulating  
28 evidence suggests that increased neural responses during the anticipation of high-calorie food  
29 play an important role in overeating. A promising method for counteracting enhanced food  
30 anticipation in overeating might be mindfulness-based interventions (MBIs). However, the  
31 neural mechanisms by which MBIs can affect food reward anticipation are unclear. In this  
32 randomized, actively controlled study, the primary objective was to investigate the effect of an  
33 8-week mindful eating intervention on reward anticipation. On the neural level, we  
34 hypothesized that mindful eating would decrease striatal reward anticipation responses.  
35 Additionally, responses in the midbrain – from which the reward pathways originate – were  
36 explored. Using functional magnetic resonance imaging (fMRI), we tested 58 healthy  
37 participants with a wide body mass index range (BMI: 19-35 kg/m<sup>2</sup>), motivated to change their  
38 eating behavior. During scanning they performed an incentive delay task, measuring neural  
39 reward anticipation responses to caloric and monetary cues before and after 8 weeks of  
40 mindful eating or educational cooking (active control). Compared with the educational cooking  
41 intervention, mindful eating affected neural reward anticipation responses, with relatively  
42 reduced caloric versus monetary reward responses. This effect was, however, not seen in the  
43 striatum, but only in the midbrain. The secondary objective was to assess temporary and long-  
44 lasting (one year follow-up) intervention effects on self-reported eating behavior and  
45 anthropometric measures (BMI, waist circumference, waist-to-hip-ratio (WHR)). We did not  
46 observe effects of the mindful eating intervention on eating behavior. Instead, the control  
47 intervention showed temporary beneficial effects on BMI, waist circumference, and diet

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48 quality, but not on WHR or self-reported eating behavior, as well as long-lasting increases in  
49 knowledge about healthy eating. These results suggest that an 8-week mindful eating  
50 intervention may have decreased the relative salience of food cues by affecting midbrain but  
51 not striatal reward responses. However, these exploratory results should be verified in  
52 confirmatory research.

53 The primary and secondary objectives of the study were registered in the Dutch Trial Register  
54 (NTR): NL4923 (NTR5025).

## 55 **Introduction**

56 Reward-related disorders such as addiction, binge-eating disorder and obesity, are  
57 characterized by altered responses to reward cues related to the target of abuse <sup>1-3</sup>.  
58 Mesolimbic regions in the brain, including the striatum and the midbrain – with its  
59 dopaminergic projections to the striatum<sup>4,5</sup> – respond to increases in appetitive motivation  
60 induced by reward cues <sup>6</sup>. Responses of these subcortical reward regions have been related to  
61 eating behavior. For example, greater ventral striatal responses to reward cues have been  
62 associated with subsequent food intake <sup>7</sup> and future weight gain <sup>7-9</sup> (for a review, see <sup>3</sup>).  
63 Reductions in striatal food-cue responses after a weight loss intervention were even predictive  
64 of the later outcome of the weight loss intervention<sup>10</sup>. Moreover, increases in BMI were  
65 associated with increased midbrain responses to high-calorie food cues in adults <sup>11</sup> and to  
66 anticipating rewards during risky choices in adolescents <sup>12</sup>. Interventions targeted at  
67 diminishing subcortical responses to food reward cues may therefore be promising for treating  
68 and preventing obesity.

69  
70 Mindfulness-based interventions are aimed at cultivating attention to present-moment  
71 experience, without judgment <sup>13</sup>. Protocolized mindfulness interventions, such as mindfulness-  
72 based stress reduction (MBSR) have shown to be effective in reducing subcortical responses to  
73 emotional stimuli in anxiety <sup>14</sup> as well as in healthy individuals <sup>15</sup>. Furthermore, mindfulness  
74 meditation training can improve executive control processes such as conflict monitoring and  
75 response inhibition <sup>16</sup>, as well as alter functional connectivity of brain networks involved in  
76 attention, cognitive processing, awareness, sensory integration, and reward processing <sup>17</sup>.

77 Importantly, mindfulness-based interventions aimed at changing eating behavior were able to  
78 reduce obesity-related eating behavior in clinical populations<sup>18,19</sup>, as well as abdominal fat<sup>20,21</sup>,  
79 and to increase self-reported mindful eating<sup>22</sup> and reduce reward-driven eating in obese  
80 individuals<sup>23</sup>. However, only two of these trials were actively controlled<sup>18,22,23</sup>. It is therefore  
81 unclear whether these beneficial effects can be attributed to mindfulness per se. In fact,  
82 Kristeller and colleagues<sup>18</sup> found that both mindfulness-based eating awareness training (MB-  
83 EAT) and a psycho-educational/cognitive-behavioral (i.e., active control) intervention decreased  
84 binge-eating symptoms relative to a waitlist control group to a similar degree. Given the  
85 different nature of these interventions, it is possible that reduced symptomatology was  
86 mediated by distinct brain mechanisms, as was suggested by an actively controlled clinical trial  
87 on social anxiety<sup>14</sup>. In this fMRI study, reduced social anxiety symptoms were observed for  
88 both the mindfulness and the active control intervention, but the interventions had differential  
89 effects on neural responses during self-referential processing. Studies investigating the  
90 neurocognitive mechanism underlying mindful eating are required to assess whether a mindful  
91 eating intervention can diminish neural responses to food reward cues.

92

93 Kirk and colleagues performed three studies on neurocognitive reward mechanisms underlying  
94 mindfulness. They found that meditators, relative to controls, showed lower neural responses  
95 in striatum during reward anticipation<sup>24</sup>, as well as diminished BOLD responses in putamen  
96 during positive and negative prediction errors<sup>25</sup>. In addition, they found that mindfulness  
97 training modulated value signals in vmPFC to primary reward (juice) delivery<sup>26</sup>. However, these  
98 studies do not yet address the question how mindfulness training affects neural responses for

99 food reward anticipation. Specifically, the first two studies were performed in experienced  
100 meditators versus controls instead of in a randomized controlled design, and the third study  
101 investigated reward responses at the moment of reward delivery, instead of anticipation.  
102 Reward anticipation is particularly interesting to investigate in light of overweight and obesity,  
103 as increases in reward anticipation have predictive value for weight gain or overeating-related  
104 behavior in these disorders<sup>1-3,7-9,12</sup>.

105  
106 Here, we present an actively controlled randomized study investigating the effects of  
107 mindfulness on reward anticipation in the brain. We studied the effects of an 8-week mindful  
108 eating intervention aimed at changing undesired eating habits versus a carefully matched  
109 educational cooking intervention (active control). To assess reward anticipation, we used an  
110 incentive delay task<sup>27</sup> during fMRI, which has been shown to produce reliable mesolimbic  
111 responses to reward cues<sup>5</sup>. We hypothesized that the mindful eating intervention would  
112 reduce reward cue responses in the striatum (primary objective), and also explored these  
113 effects in the dopaminergic midbrain as part of the mesolimbic reward circuit. We included  
114 both monetary and caloric rewards in the task, which enabled us to assess whether the effect  
115 on anticipatory reward responses is specific to the caloric domain, or generalizes to the  
116 monetary domain. As a secondary objective, we assessed the effects of mindful eating on  
117 anthropometric measures (BMI, waist-to-hip ratio (WHR), and waist circumference) and on self-  
118 reported questionnaires related to eating behavior and knowledge of healthy eating.

119

## 120 **Materials and methods**

121 **Participants**

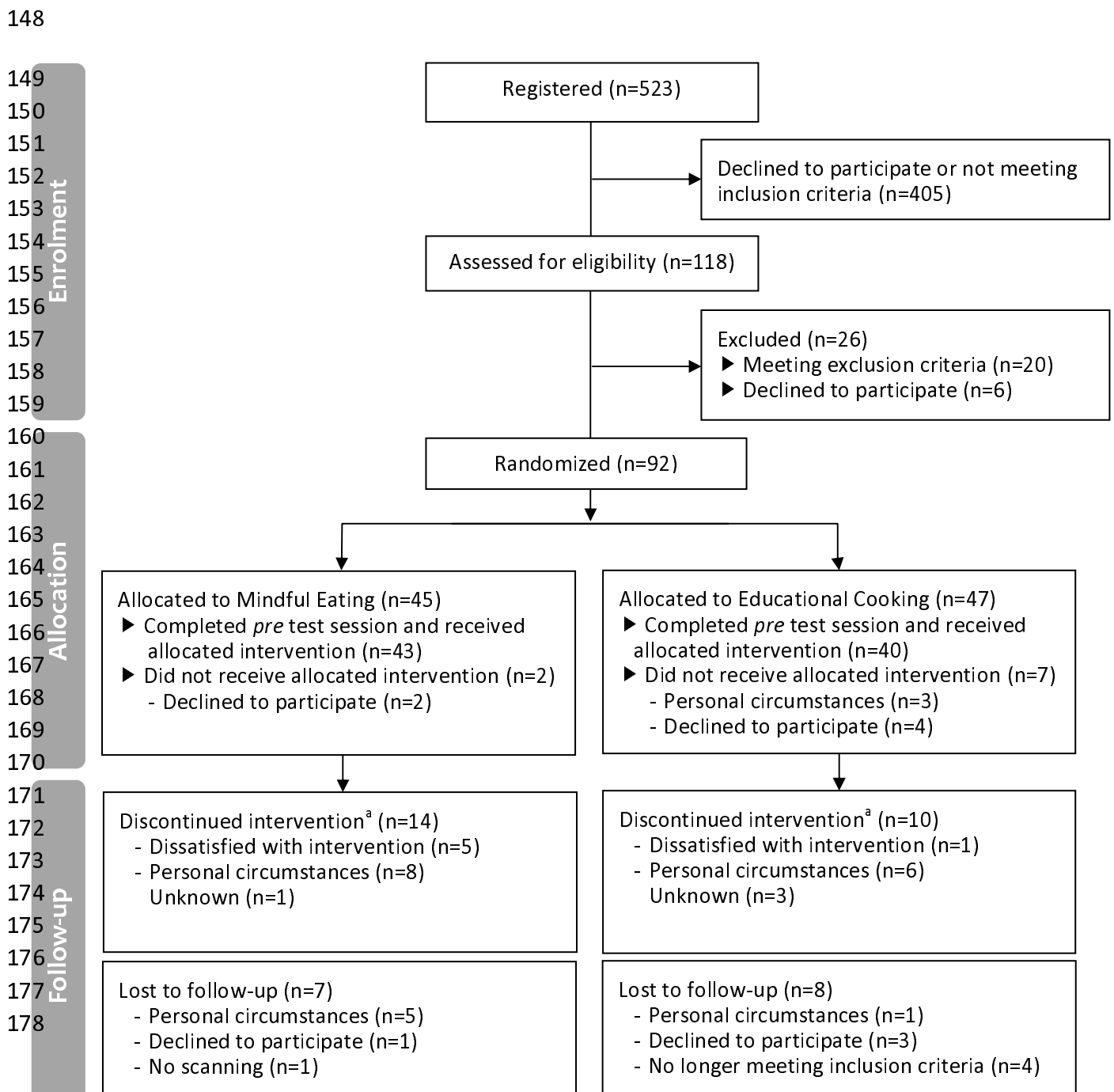
122 The results reported in this study are based on data from 58 healthy, right-handed participants  
123 (48 women; mean age: 31.6, SD: 11.0, range: 19 – 52 years; mean body mass index (BMI): 26.0,  
124 SD: 3.68, range: 19.7 – 34.7 kg/m<sup>2</sup>). Note that this sample is largely overlapping with the  
125 sample reported previously for another task<sup>28</sup>. Participants were recruited from Nijmegen and  
126 surroundings through advertisement. Only participants (aged: 18 – 55 years old; BMI: 19 – 35  
127 kg/m<sup>2</sup>) with no (history of) eating disorders or current dieting and who were highly motivated  
128 to change their eating behavior (not to lose weight per se) were included in the study.

129  
130 Exclusion criteria included MRI-incompatibility; hepatic, cardiac, respiratory, renal, cerebro-  
131 vascular, endocrine, metabolic, pulmonary, or cardiovascular diseases; eating, neurological, or  
132 psychiatric disorders; use of neuroleptica or other psychotropic medication; sensori-motor  
133 handicaps; drug or alcohol addiction; current strict dieting and a change in body weight of more  
134 than 5 kg in the past two months. Crucially, subjects with previous MBSR (Mindfulness-Based  
135 Stress Reduction) or MBCT (Mindfulness-Based Cognitive Therapy) experience were excluded  
136 from the study. Exclusion criteria are further detailed in Janssen et al.<sup>28</sup>.

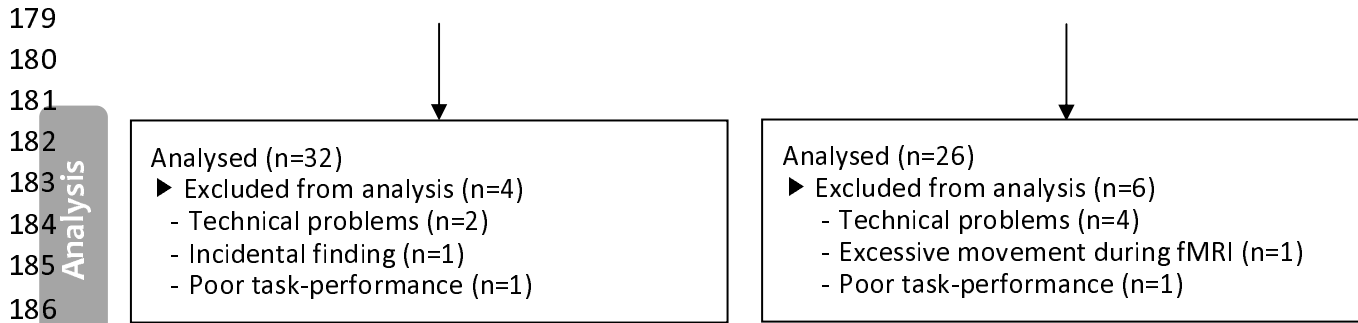
137  
138 Ten participants were excluded from the analyses following testing because of technical  
139 problems (n=6), excessive movement during fMRI scanning (n=1), an incidental finding after the  
140 post-test session (n=1), or because of poor task performance (n=2) (for details see **Methods,**  
141 **Behavioral analyses**). For a flow diagram of all excluded participants, see **Figure 1**.

142

143 All participants gave written informed consent and were reimbursed for participation according  
 144 to the local institutional guidelines (i.e., 8 Euros per hour for behavioral testing, 10 Euros per  
 145 hour for scanning). The study protocol was approved by the local ethics committee (CMO  
 146 region Arnhem-Nijmegen, the Netherlands, 2013-188) and was in accordance with the  
 147 Declaration of Helsinki. The trial was registered at the Dutch trial register (NL4923 (NTR5025)).







187 **Figure 1. CONSORT flow diagram.** <sup>a</sup> **Attended <4 sessions of the intervention program. Note**  
188 **that these participants were invited back to the laboratory for the *post*-intervention test**  
189 **session.**

## 190 Protocol

191 In a separate screening interview, all participants were assessed for in- and exclusion criteria,  
192 and matching criteria (age, gender, BMI, experience with meditation and yoga) by taking  
193 anthropometric measures and administering self-report questionnaires.

194  
195 After inclusion, participants came to the MRI laboratory twice – before and after the  
196 intervention – and a third time to the behavioral lab one year later. Participants were instructed  
197 to abstain from eating foods and drinking anything else than water four hours prior to the start  
198 of the test sessions. Participants were also instructed to abstain from drinking alcohol 24 hours  
199 before the test session. As secondary outcome measures, anthropometric measurements were  
200 taken (weight, height, waist and hip circumference) before scanning and participants  
201 completed self-reported measures of diet quality and eating behaviour: the Dutch Healthy Diet  
202 - Food Frequency Questionnaire <sup>29</sup> (DHD-FFQ) on food intake; a shortened version of the Food  
203 Behavior Questionnaire (FBQ) with subscales on “knowledge of healthy eating” and

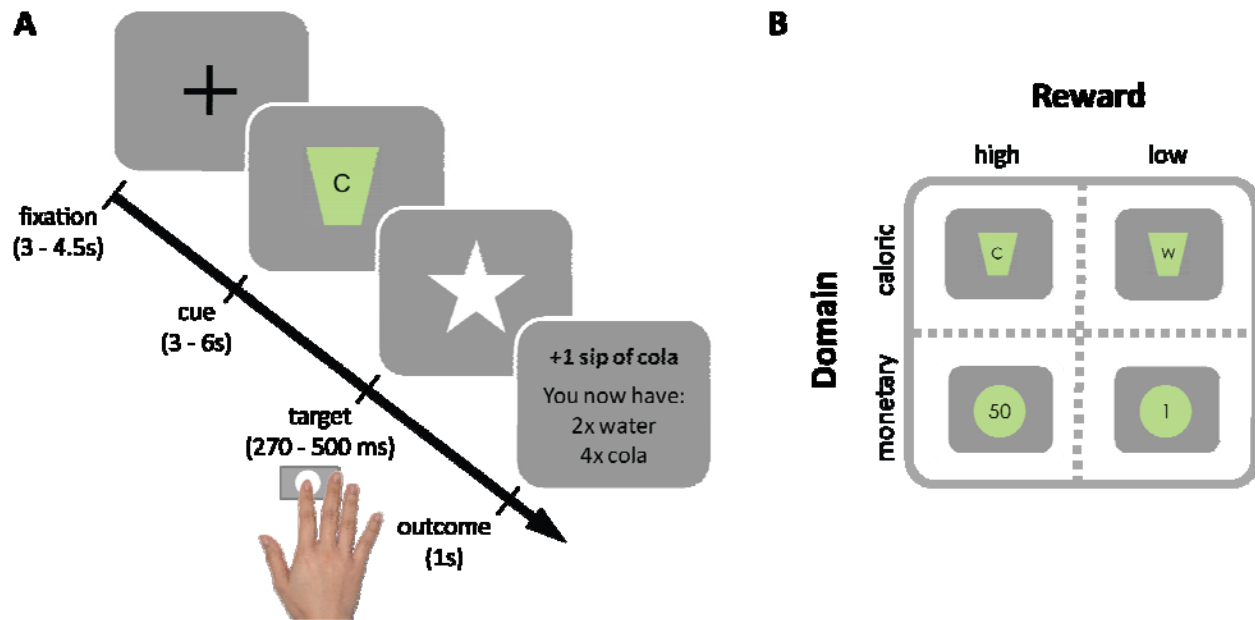
204 “temptation”; and the Dutch Eating Behaviour Questionnaire <sup>30</sup> (DEBQ) with subscales on  
205 restraint, emotional, and external eating behaviors. To further characterize the sample, to  
206 account for between-group differences at baseline that could occur by chance, and to further  
207 explore the effectiveness of the intervention programs, the following self-report questionnaires  
208 and scales were administered: the Five Facet Mindfulness Questionnaire – Short Form <sup>31</sup>  
209 (FFMQ-SF); a Treatment Credibility Questionnaire (TCQ); the Positive And Negative Affect Scale  
210 <sup>32</sup> (PANAS); the Behavioral Inhibition System / Behavioral Approach System questionnaire <sup>33</sup>  
211 (BIS-BAS); the Hospital Anxiety and Depression Scale <sup>34</sup> (HADS); the Fagerstrom Test for  
212 Nicotine Dependence <sup>35</sup> (FTND); the Barratt Impulsiveness Scale-11 <sup>36</sup> (BIS-11); the Kirby  
213 monetary choice, delay discounting questionnaire <sup>37</sup>; and the neuropsychological digit span test  
214 <sup>38</sup>. Note that the pre-training TCQ was filled out at the first training session, not on the pre-  
215 training test session, as participants were unaware of the contents of their training at that time.  
216  
217 After completing the questionnaires, participants underwent a one-hour MR scanning session  
218 in which they performed an incentive delay task. Participants also performed a food Stroop task  
219 inside the scanner, followed by a reversal learning and outcome devaluation task outside the  
220 scanner. These data are reported elsewhere <sup>28,39,40</sup>. One year after the intervention,  
221 participants were re-invited to the laboratory to reassess anthropometric measurements of  
222 obesity (weight, waist and hip circumference) and the self-report questionnaires as  
223 administered on pre- and post-test sessions. Reward anticipation was not re-assessed at one-  
224 year follow-up. The procedure is further detailed in <sup>28</sup>.

225

226 **Paradigm: Incentive Delay task**

227 We adapted the original incentive delay task <sup>27</sup> to assess reward anticipation following  
228 monetary as well as caloric cues. For task details, see **Figure 2**. In short, on each trial  
229 participants were cued as to which of four rewards they could win (monetary: 1 or 50 cents;  
230 caloric: a sip of water or of a high-calorie drink of their choice (orange juice, whole chocolate  
231 milk or regular cola)). As soon as a white star (target) appeared on the screen, participants were  
232 to press a button with their right index finger as fast as possible. If participants responded  
233 within an individually determined time-window, they won and the reward was added to their  
234 cumulative gain. On average, 59.6% (SD: 10.0) of the trials were hit trials. After scanning,  
235 participants received and drank their total caloric gain. Their total monetary gain was added to  
236 their financial reimbursement. Participants received instructions for the incentive delay task  
237 before going into the scanner, and were aware they would receive their gain following  
238 scanning. Before scanning, participants rated how much they *wanted* and *liked* each reward on  
239 a Visual Analogue Scale (VAS, 100mm). To expose participants to the reward outcomes, they  
240 were provided with the actual coins, and one sip (5 mL) of water and one of the chosen drink  
241 while rating the VAS.

242



243

244 **Figure 2. Incentive delay task. A) Each trial started with a fixation cross, followed by a cue**

245 **signaling which reward could be earned on that trial. Subsequently, a white star (i.e. target)**

246 **appeared for a brief period and participants were instructed to press a button as fast as**

247 **possible upon detection using their right index finger. If participants pressed before the**

248 **response deadline (hit trial), the target remained on the screen, informing participants of the**

249 **successful registration of their key press. Subsequently, a brief feedback image informing the**

250 **participants about the total gain was presented. If participants pressed too late or failed to**

251 **press at all (too late or miss trial, respectively), they were presented with the text message**

252 **“you win nothing” plus the total gain so far. To ensure participants won similar amounts of**

253 **each reward (in  $\pm 2/3$  of the trials), target presentation times were determined individually**

254 **and adaptively: following hit trials the response deadline for that reward cue was decreased**

255 **with 10 ms, following too late or miss trials it increased with 10 ms. B) Reward cues for high-**

256 **and low-calorie cues (C: participant’s choice from cola, orange juice or chocolate milk vs. W:**

257 **water) and high and low monetary cues (50 cents vs. 1 cent). The task took between 20 – 25**

258 **minutes to complete. Participants performed 4 blocks of 25 trials (a total of a 100 trials). A**  
259 **block contained either high/low monetary or high/low-calorie trials. Each trial type was**  
260 **repeated approximately 25 times (M: 24.4, SD: 2.78). Block-presentation was pseudo-**  
261 **randomly distributed and counterbalanced across participants (randomization scheme: ABBA**  
262 **or BAAB).**

263

#### 264 **Interventions**

265 Participants were randomly assigned to one of two intervention programs: mindful eating (ME)  
266 or educational cooking (EC; active control). Participants were assigned by a computer through  
267 minimization <sup>41</sup>, which guarantees that groups are balanced in terms of certain *a priori*  
268 determined minimization factors: age (categories: 18-25y, 26-35y, 36-45y, 46-55y), gender  
269 (categories: male, female), BMI (categories: 19 – 24.9 kg/m<sup>2</sup> normal weight, 25 – 29.9 kg/m<sup>2</sup>  
270 overweight, 30 – 35 kg/m<sup>2</sup> moderately obese) and experience with meditation and yoga  
271 (categories: never, 0 – 2 years, 2 – 5 years, 5 – 10 years, > 10 years).

272

273 The intervention programs were matched in terms of time, effort, and group contact, but  
274 differed significantly in terms of content. Both programs consisted of 8 weekly, 2.5 hour group  
275 sessions plus one day (6 hours) dedicated to the intervention goals. Participants were asked to  
276 spend 45 minutes per day on homework assignments and to record the amount of time spent  
277 on homework forms. In the information letters, the intervention programs were described as  
278 “eating with attention” (ME) and “eating with knowledge” (EC) to prevent a selection-bias of  
279 participants interested in mindfulness. Only after the first test session, participants were

280 informed about the intervention to which they were randomized, to ensure that baseline  
281 measurements were not influenced by intervention expectations. Because group size was set to  
282 10 to 15 participants per round, included participants were divided across three rounds for  
283 each intervention (3xME, 3xEC). The final sample for statistical analyses consisted of 32 (from  
284 45 included) participants in the ME intervention and 26 (from 47 included) participants in the  
285 EC intervention (for a flow diagram see **Figure 1**). Despite the numerical difference in dropouts  
286 between groups, the number of people excluded from analysis was not significantly different  
287 (ME: 28.8%, EC: 44.7%,  $\chi^2(1, N = 92) = 2.461, p = .117$ ). We get back to the relatively high  
288 dropout rate in the **Discussion**.

289

#### 290 *Mindful eating (ME)*

291 The aim of the ME intervention was to increase experiential awareness of food and eating. The  
292 ME program was based on the original MBSR program developed by Kabat-Zinn et al.<sup>42</sup>.  
293 Participants performed formal mindfulness practices (i.e. body scan, sitting meditation, walking  
294 meditation and mindful movement), aimed at increasing general mindfulness skills, which were  
295 similar to the original program. In addition, participants performed informal mindfulness  
296 practices based on the Mindful Eating, Conscious Living program (MECL)<sup>43</sup>, which were mainly  
297 directed to mindful eating and not part of the original MBSR program. Sessions focused on  
298 themes, such as: the automatic pilot, perception of hunger and satiation, creating awareness of  
299 boundaries in eating behavior, stress-related eating, coping with stress, coping with (negative)  
300 thoughts, self-compassion, and how to incorporate mindfulness in daily life. Towards the end of  
301 the program, participants had a 'silent day'. During this day, the whole group performed formal

302 mindfulness exercises and ate a meal together in complete silence. Homework consisted of a  
303 formal mindfulness practice and an informal mindfulness practice directed at one moment (e.g.  
304 a meal) a day. The ME intervention was developed and delivered by qualified mindfulness  
305 teachers from the Radboud University Medical Centre for Mindfulness.

306

307 *Educational Cooking (EC)*

308 The aim of the EC intervention was to increase informational awareness of healthy food and  
309 eating. The EC program was based on the Dutch healthy food-based dietary guidelines  
310 ([www.voedingscentrum.nl](http://www.voedingscentrum.nl)). To establish similar (active) group activities as in the ME,  
311 participants were enrolled in cooking workshops during the group meetings of the EC. Sessions  
312 focused on healthy eating, healthy cooking of vegetables and fruit, use of different types of fat  
313 and salt for cooking, reading of nutrition labels on food products, healthy snacking, guidelines  
314 for making healthy choices when eating in restaurants, and how to incorporate healthy eating  
315 and cooking in daily life. Towards the end of the program, participants had a ‘balance day’,  
316 during which the participants adhered to all nutritional health guidelines for every snack and  
317 meal. Homework assignments entailed practicing cooking techniques, or grocery shopping with  
318 informational awareness, and counting the amount of calorie intake for one meal a day. The EC  
319 intervention was developed and delivered by a qualified dietitian from Wageningen University  
320 and a professional chef of the Nutrition and Dietetics faculty of the University of Applied  
321 Sciences of Arnhem-Nijmegen guided the cooking sessions. The interventions are further  
322 detailed in <sup>28</sup>.

323

324 **Behavioral analyses**

325 Between-group comparisons were analyzed using independent-samples t-tests, Fisher's Exact  
326 Tests, or Mann-Whitney U tests. Effects of training on anthropometric, neuropsychological and  
327 self-report measurements were analyzed using repeated-measures ANOVA with Time (pre,  
328 post) as within-participant factor and Intervention (ME, EC) as between-participant factor. To  
329 assess the longevity of measures that exhibited a significant Time x Intervention interaction, we  
330 ran *post hoc* ANOVAs adding the one-year follow-up data as a third level in factor Time for BMI,  
331 waist, DHD-FFQ, and FBQ knowledge. One-year follow-up data was available of 26 participants  
332 in the ME group and 21 participants in the EC group. In case of violation of the assumption of  
333 sphericity as indicated by Mauchly's test, the Huyhn-Feldt correction was used to adjust the  
334 degrees of freedom accordingly (see Results). Planned *post hoc* comparisons were performed  
335 to statistically compare follow-up data to data from both the pre- and post-test sessions  
336 separately. Mean latencies of the manual responses were analyzed using repeated-measures  
337 ANOVA with within-participant factors Reward (high, low), Domain (caloric, monetary), Time,  
338 and the between-participant factor Intervention (ME, EC). Specific effects were tested with  
339 subsequent F-tests. All analyses were performed using two-tailed tests in SPSS (version 23.0,  
340 Chicago, IL). The significance level was set at an alpha of  $p=0.05$ , partial eta squared ( $\eta_p^2$ ) was  
341 reported to indicate effect sizes in the repeated measures ANOVAs.

342

343 **fMRI acquisition**

344 We acquired whole-brain functional images (multi-echo) on a Siemens 3T Skyra MRI scanner  
345 (Siemens Medical system, Erlangen, Germany) using a 32-channel coil to measure blood oxygen



346 level dependent (BOLD) contrast. A multi-echo echo-planar imaging (EPI) sequence was used to  
347 acquire 34 axial slices per functional volume in ascending direction (voxel size 3.5x3.5x3mm;  
348 repetition time (TR) 2070 ms; TE 9ms, 19.25ms, 29.5ms, and 39.75ms; flip angle 90 °; field of  
349 view 224mm). This is a method that uses accelerated parallel imaging to reduce image artifacts  
350 (in plane acceleration 3) and acquire images at multiple TEs following a single excitation<sup>44</sup>.  
351 Before the acquisition of functional images, a high-resolution anatomical scan was acquired  
352 (T1-weighted MPRAGE, voxel size 1x1x1mm, TR 2300ms, TE 3.03ms, 192 sagittal slices, flip  
353 angle 8 °, field of view 256 mm).

354

### 355 **fMRI pre-processing and analysis**

356 Data were pre-processed and analyzed using FSL version 5.0.11,  
357 (<http://www.fmrib.ox.ac.uk/fsl/>) and SPM8 ([www.fil.ion.ucl.ac.uk/spm](http://www.fil.ion.ucl.ac.uk/spm)). Pre-processing and  
358 data analysis were performed using three approaches, which differed in how motion-related  
359 noise was accounted for. The final approach was determined based on the strength of the main  
360 task effect (i.e. the t-value of the high>low reward anticipation contrast) independent of  
361 training, across all participants and sessions. First, we added twelve rigid-body transformation  
362 parameters (three translations and rotations, and their linear derivatives) obtained during  
363 realignment to the first level model. Second, we used non-aggressive ICA-AROMA<sup>45</sup> to reduce  
364 motion-induced signal variations in the fMRI data. Because ICA-AROMA takes out noise  
365 components, the twelve rigid-body transformation parameters obtained during realignment  
366 were not included in the model. For our third approach, we also used ICA-AROMA, however,  
367 rather than reducing motion-related noise in the fMRI data directly, we added the time courses

368 of the independent components accounting for less than 5% of task-related variance to the first  
369 level model. To achieve this, we used the components identified as motion by ICA-AROMA in a  
370 multiple regression analysis with the task regressors as predictors and the motion-related time  
371 courses as dependent variables. From this analysis, the adjusted  $R^2$  was obtained to identify  
372 how much of the total variance in a time course was captured by the task's design. In case the  
373 adjusted  $R^2$  of a component was higher than 5%, they were not included in the first level model  
374 as noise regressors (i.e. regressor of non-interest). The twelve rigid-body transformation  
375 parameters obtained during realignment were also included in the model. The third approach  
376 showed the strongest main task effect (brain responses to high - low reward cues) and was  
377 therefore used as our final approach. Below, we describe this approach in more detail.

378  
379 The volumes for each echo time were realigned to correct for motion artefacts (estimation of  
380 the realignment parameters is done for the first echo and then copied to the other echoes). The  
381 four echo images were combined into a single MR volume based on 31 volumes acquired  
382 before the actual experiment started using an optimized echo weighting method <sup>44</sup>. Combined  
383 functional images were slice-time corrected by realigning the time-series for each voxel  
384 temporally to acquisition of the middle slice. The images were subsequently spatially smoothed  
385 using an isotropic 6 mm full-width at half-maximum Gaussian kernel. Non-aggressive ICA-  
386 AROMA <sup>45</sup> was used to identify motion-induced signal variations in the fMRI data. Participant-  
387 specific structural and functional data were then coregistered to a standard structural or  
388 functional stereotactic space respectively (Montreal Neurological Institute (MNI) template).  
389 After segmentation of the structural images using a unified segmentation approach, structural

390 images were spatially coregistered to the mean of the functional images. The resulting  
391 transformation matrix of the segmentation step was then used to normalize the anatomical and  
392 functional images into Montreal Neurological Institute space. The functional images were  
393 resampled at voxel size 2 x 2 x 2 mm.

394

395 Statistical analyses of fMRI data at the individual participant (first) level were performed using  
396 an event-related approach and included 13 regressors of interest: four regressors for cue  
397 presentation (high- and low-calorie cues, high and low monetary cues), one regressor for target  
398 presentation, four outcome regressors for hits (high- and low-calorie hits, high and low  
399 monetary hits), and four outcome regressors for trials on which participants responded too late  
400 (high- and low- calorie too late, high and low monetary too late). If participants failed to  
401 respond on a trial (i.e. a miss), the trial was excluded from analyses. Onsets of the regressors  
402 were modeled as a stick function (duration=0s) convolved with a canonical hemodynamic  
403 response function<sup>46</sup>. Furthermore, we only added time courses of the independent noise  
404 components that accounted for less than 5% of task-related variance to the first level model as  
405 regressors of non-interest. Note that the number of these regressors varied per subject and  
406 session. In addition, twelve rigid-body parameters, a constant term, and two regressors that  
407 reflected signal variation in white matter and cerebrospinal fluid regions were included as  
408 regressors of non-interest. High pass filtering (128 seconds) was applied to the time series of  
409 the functional images to remove low-frequency drifts and correction for serial correlations was  
410 done using an autoregressive AR(1) model.

411

412 We ran two general linear models (GLMs) at the second level: one for reward anticipation with  
413 high minus low reward cue contrast images, and one for reward receipt with hit minus too late  
414 contrast images. Analysis of variance (ANOVA) was performed in a full-factorial design, with  
415 between-subject factor Intervention and within-subject factors Time and Domain, resulting in 8  
416 cells. Effects were considered statistically significant when reaching a threshold of  $p < 0.05$ ,  
417 family wise error (FWE) corrected for multiple comparisons at the peak level, whole brain or in  
418 the *a priori* defined regions of interest (see below). We report whole-brain and small volume  
419 corrected ( $p_{FWE} < .05$ ) effects in **Table 3 and 4**, and show the statistical maps at  $p < .001$  and  
420  $p < .005$  uncorrected thresholds in **Figure 3** for exploratory purposes.

421

422 To further investigate the effects of intervention on reward anticipation and receipt, region-of-  
423 interest (ROI) analyses were performed using *a priori* defined ROIs for midbrain and striatum.  
424 ROIs were anatomically defined based on a high-resolution probabilistic *in vivo* atlas that  
425 included midbrain and striatal nuclei<sup>47</sup>: bilateral substantia nigra (atlas: region 7), and ventral  
426 tegmental area (region 11) for *midbrain*, and bilateral caudate nucleus (region 2), nucleus  
427 accumbens (region 3) and putamen (region 1) for *striatum* at 100% overlap. Probabilistically  
428 weighted mean beta weights were extracted from all voxels in both ROIs separately using  
429 MarsBar<sup>48</sup>. The probabilistically weighted averaged beta-weights were analyzed per region  
430 using ANOVA with the same factors as in the whole-brain analyses. As two ROIs were tested  
431 (striatum and midbrain), effects for each total region were considered significant when  
432 reaching a threshold of  $p < .025$  (Bonferroni corrected for multiple comparisons). *Post hoc*, the  
433 same effects were tested in the striatal sub-regions (bilateral caudate nucleus, nucleus

434 accumbens, and putamen) because striatal sub-regions have been associated with distinct  
 435 neurocognitive mechanisms.

436

## 437 Results

### 438 Characterization of intervention groups

439 The mindful eating (ME) and educational cooking (EC) groups were well matched in terms of  
 440 the minimization factors age, gender, body mass index (BMI) and experience with meditation  
 441 and yoga (**Table 1**). Note that the groups tended to differ in terms of educational level.  
 442 However, *post hoc* correlation analyses revealed no correlations between educational level and  
 443 the neural effects described below and is therefore unlikely to drive these effects. Furthermore,  
 444 the total time participants spent on the intervention, and the number of sessions participants  
 445 attended did not differ significantly between the two groups (**Table 1**).

446

447 **Table 1** Between-group (mindful eating, ME; educational cooking, EC) comparisons.

	mindful eating (ME) (n=32)			educational cooking (EC) (n=26)			p-value	test- statistic	effect size <sup>d</sup>
<b>Minimization factors</b>									
Gender (Male : Female)	5 : 27			5 : 21			.740	na <sup>a</sup>	na
Age (yrs)	32.3	±10.8	20-52	30.6	±11.3	19-51	.546	.607 <sup>b</sup>	0.154
Body mass index (kg/m <sup>2</sup> )	26.6	±4.1	19-35	25.5	±3.4	20-33	.296	1.054 <sup>b</sup>	0.292
Yoga/meditation experience (yrs)	1.0	±2.6	0-14	1.9	±4.3	0-19	.334	-.974 <sup>b</sup>	0.253
<b>Sample characterization</b>									
Education	6.5	±0.6	5-7	6.2	±0.7	5-7	.053	304.0 <sup>c</sup>	-0.033 <sup>e</sup>
Digit span (total score)	15.6	±3.5	9-23	14.1	±3.5	9-22	.120	1.577 <sup>b</sup>	0.429
Smoking (FTND score)	0.19	±1.1	0-6	0.04	±0.2	0-1	.902	413.5 <sup>c</sup>	-0.002 <sup>e</sup>
<b>Intervention</b>									
Time on training (hrs)	31.0	±14.4	2.5-47.8	23.9	±21.2	0-77.7	.135	1.518 <sup>b</sup>	0.392
Attendance < 4 sessions (n)	5			5			.740	na <sup>a</sup>	na
Attendance (number of sessions)	6.5	±2.5	1-9	6.3	±2.8	1-9	.738	0.336 <sup>b</sup>	0.075

448 If not otherwise stated, values denote mean±SD, and min-max.

449 *FTND*: Fagerstrom Test for Nicotine Dependence.

450 <sup>a</sup>Based on Fisher's Exact Test, <sup>b</sup>Independent samples t-test (degrees of freedom: 56), <sup>c</sup>Mann-Whitney test, <sup>d</sup>If not otherwise  
451 stated, effect sizes indicate Cohen's *d*, <sup>e</sup>*r*, effect size for Mann Whitney U-test (z-value divided by the total sample size (58))

452

### 453 **Behavioral outcomes**

454 As a primary objective, we assessed the effects of the intervention on reward anticipation  
455 during the incentive delay task. We start with the behavioral responses during the task (**Table**  
456 **2**). Across sessions and intervention groups, participants responded faster on high than on low  
457 reward trials (main Reward:  $F(1,56)=25.0$ ,  $p < .001$ ,  $\eta_p^2 = 0.309$ ), thus revealing a reward benefit  
458 (**Table 2**). In addition, participants across sessions and intervention groups responded faster to  
459 monetary relative to caloric reward cues (main Domain:  $F(1,56)=17.4$ ,  $p<.001$ ,  $\eta_p^2 = 0.237$ ). We  
460 observed a reward benefit for both caloric ( $F(1,56)=4.5$ ,  $p=.038$ ,  $\eta_p^2 = 0.074$ ) and monetary  
461 trials ( $F(1,56)=25.6$ ,  $p<.001$ ,  $\eta_p^2 = 0.314$ ), which was, however, larger in the monetary trials  
462 (Reward x Domain interaction:  $F(1,56)=9.0$ ,  $p=.004$ ,  $\eta_p^2 = 0.139$ ). Participants responded faster  
463 on post- relative to pre-intervention test sessions (pre: 310.66 (SD: 21.3), post: 304.60 ms. (SD:  
464 20.8); main Time:  $F(1,56)=4.4$ ,  $p<.041$ ,  $\eta_p^2 = 0.072$ ). However, there was no evidence for effects  
465 of intervention type (4-way interaction between Intervention x Time x Reward x Domain  
466 ( $F(1,56)<1$ ), indicating that the speeding of responding on the second versus the first session  
467 was not qualified by reward magnitude, reward type or intervention type.

468 There were also no effects of Intervention on any other behavioral task-related  
469 measures that we included to control for potentially unexpected group-differences in wanting  
470 and liking of the included rewards, or hunger, thirst, and satiety VAS ratings during the task (no  
471 Time x Intervention interactions (**Table 2**)).

472

473 **Table 2. Task-related outcomes pre- and post-training, for each group (mindful eating, ME;**

	mindful eating (ME)		educational cooking (EC)		<i>p</i>	<i>test-</i> <i>statistic<sup>a</sup></i>	<i>effect</i> <i>size<sup>b</sup></i>
	pre	post	pre	post			
<b>Primary outcome measure: Response times on the incentive delay task</b>							
Response Times per reward type							
Low caloric	313.7 ±41.0	312.4 ±33.8	322.5 ±51.6	312.6 ±43.8	.319	1.0	0.018
High caloric	303.4 ±33.8	299.1 ±31.5	322.2 ±50.0	311.8 ±48.4	.471	< 1	0.009
Low monetary	313.0 ±47.0	311.2 ±44.2	317.4 ±44.8	313.3 ±49.6	.834	< 1	0.001
High monetary	294.7 ±26.2	285.1 ±32.5	302.3 ±41.5	293.9 ±43.0	.874	< 1	<0.001
<b>Exploratory outcome measures (manipulation check): Visual analogue scales</b>							
Wanting per reward type							
Low caloric	4.5 ±2.8	4.6 ±2.8	4.5 ±3.1	4.6 ±2.8	.987	< 1	<0.001
High caloric	6.3 ±2.0	5.8 ±2.4	5.4 ±3.0	5.6 ±2.4	.330	< 1	0.017
Low monetary	1.9 ±2.4	1.5 ±2.0	2.2 ±2.5	2.4 ±2.6	.318	1.0	0.018
High monetary	5.2 ±2.8	5.4 ±2.7	5.0 ±3.2	5.4 ±2.4	.840	< 1	0.001
Liking per reward type							
Low caloric	6.4 ±2.3	6.1 ±2.2	6.2 ±2.7	6.6 ±2.2	.187	1.8	0.031
High caloric	7.2 ±1.6	6.7 ±2.1	6.8 ±2.9	6.4 ±2.7	.783	< 1	0.001
Low monetary	2.2 ±2.4	2.2 ±2.2	2.8 ±2.4	2.8 ±2.3	.967	< 1	<0.001
High monetary	5.1 ±2.5	5.2 ±2.4	4.4 ±2.7	5.3 ±2.2	.143	2.2	0.038
Hunger <sup>c</sup>	5.9 ±2.6	5.9 ±2.7	5.9 ±3.0	5.6 ±2.9	.835	< 1	0.001
Thirst <sup>c</sup>	5.7 ±2.6	5.9 ±2.8	6.0 ±2.4	5.5 ±2.4	.273	1.2	0.023
Satiety <sup>c</sup>	2.3 ±2.1	2.1 ±0.9	1.9 ±1.1	2.1 ±1.2	.345	< 1	0.017

474 **educational cooking, EC) separately, and Time (pre, post) x Intervention (ME, EC) statistics.**

475 If not otherwise stated, values denote mean±SD.

476 <sup>a</sup>The reported test-statistic is the F-value (degrees of freedom: 1,56)

477 <sup>b</sup>The reported effect size is the partial eta squared ( $\eta_p^2$ )

478 <sup>c</sup>Hunger, Thirst, Satiety: N = 55 (N<sub>ME</sub> = 29, N<sub>EC</sub> = 26; degrees of freedom: 1,53)

479

## 480 **Neuroimaging outcomes**

### 481 *Reward Anticipation*

482 Before assessing the intervention effects on the neural responses during reward anticipation

483 (primary outcome), we identified brain regions that responded to reward anticipation across

484 sessions and intervention groups (main effect of Reward condition: high>low). At our whole-

485 brain corrected threshold (FWE<.05, peak-level), this contrast yielded significant responses in

486 striatum (right caudate nucleus, right nucleus accumbens, right putamen, and left pallidum) and  
487 two right midbrain regions, as well as in occipital, motor and frontal regions (**Figure 3a**). Note  
488 that the optimal preprocessing pipeline was selected based on maximal main effects of reward  
489 anticipation (see **Materials and Methods**), so no inference can be made on the magnitude of  
490 these main effects. Reward anticipation differed in mostly posterior regions for monetary  
491 versus caloric reward cues (i.e., interaction of Domain x Reward), independent of sessions and  
492 intervention groups. For all contrasts, see **Table 3**.

493  
494 We were primarily interested in the effects of ME on reward anticipation in our *a priori* defined,  
495 anatomical region-of-interest (ROI): the striatum. We explored the same effects in an  
496 anatomical midbrain ROI. First, we explored these effects using our probabilistic ROIs as small  
497 search volumes. We found five peaks for the Reward x Domain x Time x Intervention interaction  
498 in the striatum (three regions in caudate nucleus, one in putamen, and one in pallidum), as well  
499 as one peak in the midbrain. However, these peaks were not significant when correcting for  
500 multiple comparisons across the two search volumes (i.e., midbrain and striatum), i.e., all pFWE  
501 > 0.025 (**Figure 3b**).

502  
503 Based on our hypotheses, we also performed ROI analyses (**Figure 3c**) using a bilateral  
504 probabilistic structural ROI for the striatum (primary) and the midbrain (see **Materials and**  
505 **methods**). No four-way interaction effect (Intervention x Time x Domain x Reward) was found  
506 for the striatum. *Post hoc* analyses of the separate striatal regions also showed no effect of  
507 intervention (Intervention x Time x Domain x Reward: putamen:  $F(1,56) < 1$ ,  $p = .385$ ,  $\eta_p^2 = 0.014$ ,



508 caudate nucleus:  $F(1, 56)=1.3$ ,  $p = .255$ ,  $\eta_p^2 = 0.023$ , nucleus accumbens:  $F(1, 56)=2.2$ ,  $p = .142$ ,  
509  $\eta_p^2 = 0.038$ ). Interestingly, for the midbrain ROI, we did observe a significant four-way  
510 interaction in the ROI betas, and - in contrast to the observed midbrain effect in the small  
511 volume analysis mentioned above - this effect did survive correction for multiple comparisons  
512 (Intervention x Time x Domain x Reward:  $F(1,56)=7.9$ ,  $p=.007$ ,  $\eta_p^2 = 0.123$ ,  $\alpha=.025$ ). *Post hoc*  
513 analyses showed a significant relative reduction in caloric versus monetary reward anticipation  
514 in midbrain after the mindful eating training (Time x Domain x Reward for ME:  $F(1,31)=4.4$ ,  
515  $p=.043$ ,  $\eta_p^2 = 0.125$ ). This effect was not significant in the EC group (Time x Domain x Reward for  
516 EC:  $F(1,25)=3.7$ ,  $p = .065$ ,  $\eta_p^2 = 0.130$ ) and, if anything, showed the opposite effect. When  
517 further breaking down the interaction in the mindfulness group, we found no significant  
518 training effect in the caloric domain (Time x Reward:  $F(1,31)=2.1$ ,  $p = .156$ ,  $\eta_p^2 = 0.064$ ), or in the  
519 monetary domain (Time x Reward:  $F(1,31)=2.8$ ,  $p = .104$ ,  $\eta_p^2 = 0.083$ ) separately. This means  
520 that we can only interpret the ME effect on midbrain reward anticipation responses as a  
521 *relative* decrease for caloric versus monetary reward (see above-mentioned significant Time x  
522 Domain x Reward effect for ME). Pre-intervention Reward differences could not explain the  
523 observed interaction in the midbrain (caloric:  $t(56)=1.4$ ,  $p = .169$ , *cohen's d* = 0.370, monetary:  
524  $t(56)=1.1$ ,  $p = .272$ , *Cohen's d* = 0.292).

525

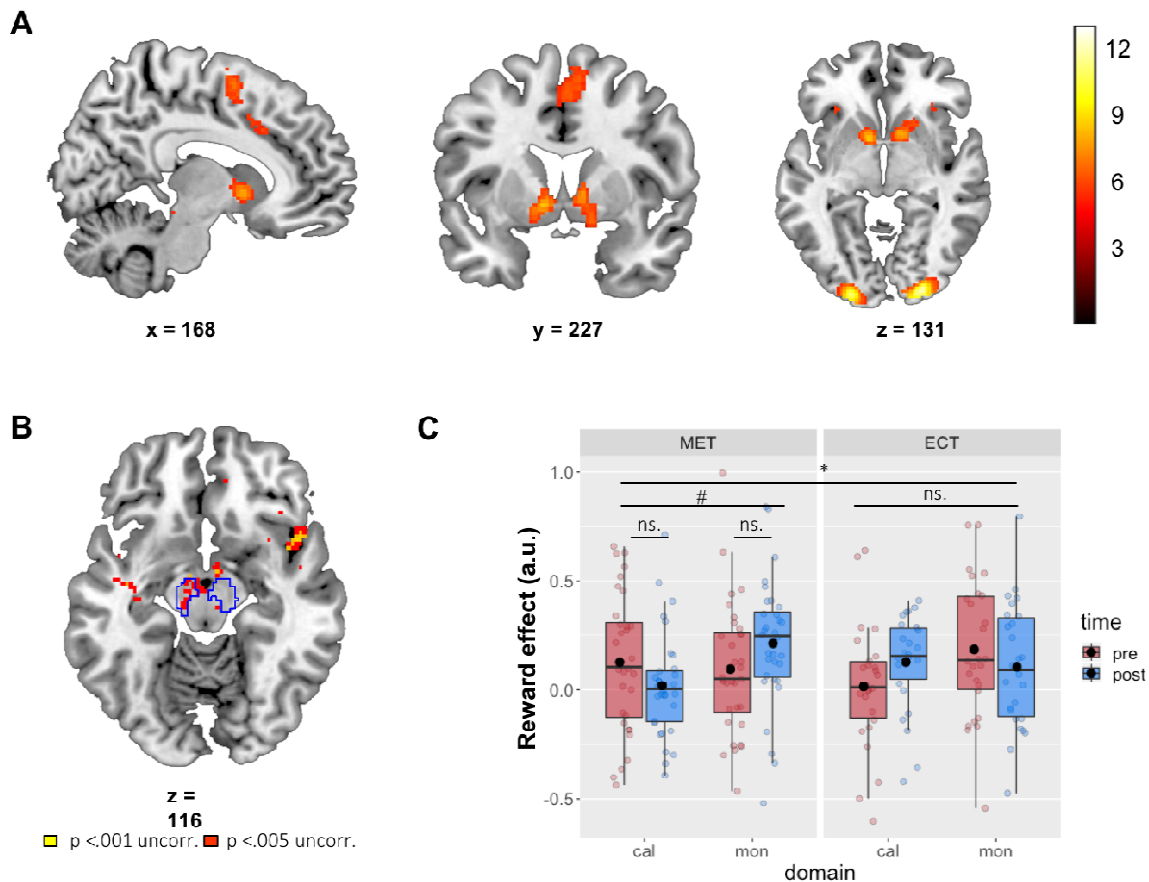
526 To explore whether the time spent on training affected anticipatory reward processing in the  
527 midbrain, we ran a *post hoc* analysis with total time spent on training for each participant as a  
528 covariate. Adding this covariate (and interaction terms) did not change the results (Reward x  
529 Domain x Time x Intervention:  $F(1,55)=7.4$ ,  $p = .009$ ,  $\eta_p^2 = 0.118$ ). Because BMI and waist

530 showed effects of the intervention (see secondary Results: Anthropometric measures), we  
531 added BMI and waist as covariates to the analysis. This also did not change the results  
532 qualitatively (Reward x Domain x Time x Intervention interaction with BMI covariate:  
533  $F(1,55)=5.93$ ,  $p=.018$ ,  $\eta_p^2 = 0.097$ ; with waist circumference covariate:  $F(1,55)=5.94$ ,  $p=.018$ ,  $\eta_p^2$   
534  $= 0.097$ ).

535

### 536 *Reward Receipt*

537 The intervention did not affect neural responses during the receipt of reward. Specifically, no  
538 significant main effects of Intervention or interactions with Intervention were found for BOLD  
539 responses to reward receipt in whole-brain analyses, nor in ROI analyses using *a priori* defined  
540 ROIs for striatum and midbrain. For main effects and other interaction effects of reward receipt  
541 see **Table 4**.



542

543 **Figure 3. Summary of neuroimaging results. A) Main effect of reward. Contrast of high vs. low**

544 **reward cue trials (high > low). Full brain statistical parametric maps were thresholded at  $p <$**

545 **.05 (FWE-corrected, peak-level). B) Axial slice of whole brain interaction effect of Domain x**

546 **Time x Intervention for the Reward contrast (high > low). Statistical parametric maps were**

547 **thresholded at  $p < .001$  (yellow) and  $p < .005$  (red) uncorrected for visualization purposes.**

548 **Outlined regions are corrected for multiple comparisons within our small search volume, at**

549 **peak  $p_{FWE} < .05$ . C) Betas from the bilateral probabilistic midbrain ROI (outlined in blue in**

550 **panel B). Post- minus pre-intervention mean betas based on the high minus low reward**

551 **contrast are presented for each domain (caloric, monetary) and for each intervention group**

552 **(ME, EC) in arbitrary units (a.u.). Box plots show the median and interquartile range, with the**

553 **black dot denoting the mean. All statistical parametric maps are overlaid onto a T1-weighted**  
 554 **canonical image. Slice coordinates are defined in MNI152 space and images are shown in**  
 555 **neurological convention (left=left). \* =  $p < .025$  (Bonferroni corrected for two ROIs) and # =  $p$**   
 556 **< .05.**

557

558 **Table 3. Reward anticipation. Summary of brain regions exhibiting main effects of reward,**  
 559 **domain and/or interactions with domain, intervention, and time. N.B., the preprocessing**  
 560 **pipeline was selected based on maximal main effects of reward anticipation.**

Label	Side (Left/Right)	MNI-coordinates x, y, z (mm)	Size (number of voxels)	$pFWE$ (peak-level)	$t$ -value <sup>a</sup> (peak)
<b>Main effect of Reward: high &gt; low<sup>b</sup></b>					
Inferior occipital lobe	R	24 -94 -4	591	< .001	11.37
		40 -82 -14		< .001	8.82
		34 -86 -8		< .001	7.64
Inferior occipital lobe	L	-22 -96 -4	591	< .001	10.43
Lingual gyrus	L	-34 -88 -14		< .001	7.83
Pallidum	L	-10 6 -4	145	< .001	7.99
Caudate nucleus	R	12 12 -2	267	< .001	7.88
Nucleus accumbens	R	14 6 -12		< .001	6.32
Putamen	R	20 18 -4	2134	< .001	6.05
		0 2 54	323	< .001	6.87
		8 4 60		< .001	6.60
Supplementary motor area	R	10 -2 66		< .001	5.93
		-32 26 -2	18	< .001	6.11
		-6 14 36	9	.001	5.86
Cingulate gyrus, mid part	R	8 20 34	28	.002	5.82
		8 12 42		.012	5.42
Midbrain	R	10 -26 -12	3	.006	5.58
Superior frontal gyrus	R	18 0 58	1	.011	5.45
Inferior frontal gyrus, orbital	R	32 30 -4	7	.027	5.26
		8 -30 -12	1	.048	5.12
<b>Main effect of Reward: low &gt; high reward<sup>b</sup></b>					
Superior temporal gyrus	R	62 -26 8	71	< .001	6.87
Middle occipital lobe	L	-40 -78 4	45	< .001	6.32
Angular gyrus	R	52 -58 28	52	.001	6.02
		54 -62 36		.012	5.44

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Superior frontal gyrus	R	26	18	44	9	.001	5.87
Precuneus	R	10	-50	42	19	.002	5.81
Superior frontal gyrus	R	22	28	56	58	.002	5.79
Inferior frontal gyrus, triangular	L	-46	38	14	3	.003	5.69
Precuneus	R	8	-60	46	4	.004	5.64
Inferior parietal gyrus	L	-44	-40	42	2	.006	5.56
Insula	R	38	-14	18	2	.031	5.22
Inferior parietal gyrus	L	-46	-42	46	1	.033	5.21
Lingual gyrus	L	-28	-58	-4	1	.046	5.13
<b>Interaction effect of Reward x Domain: caloric (high &gt; low reward) &gt; monetary (high &gt; low reward)<sup>b</sup></b>							
Inferior occipital lobe	L	-48	-70	-4	595	< .001	10.47
Fusiform gyrus	L	-38	-54	-12		< .001	6.17
Inferior temporal gyrus	R	50	-68	-6	251	< .001	8.41
Middle temporal gyrus	R	44	-62	-2		< .001	7.06
Inferior temporal gyrus	R	58	-60	-10		.005	5.60
Middle occipital lobe	L	-26	-76	28	92	< .001	6.69
Inferior temporal gyrus	R	50	-54	-18	27	.001	5.97
Inferior frontal gyrus, opercular	L	-46	6	28	24	.001	5.91
Inferior parietal gyrus	L	-42	-40	42	24	.002	5.79
Fusiform gyrus	L	-28	-58	-12	14	.008	5.51
Middle occipital lobe	R	34	-64	36	20	.010	5.47
Inferior parietal gyrus	L	-36	-40	36	2	.018	5.35
Precentral gyrus	L	-38	2	30	1	.018	5.35
Fusiform gyrus	L	-46	-60	-18	5	.018	5.34
Inferior frontal gyrus, triangular	L	-42	34	12	2	.020	5.33
Lingual gyrus	L	-24	-54	-10	1	.023	5.29
Precentral gyrus	L	-42	2	30	1	.039	5.17
Middle occipital lobe	R	32	-76	30	1	.049	5.11
<b>Interaction effect of Reward x Domain: monetary (high &gt; low reward) &gt; caloric (high &gt; low reward)<sup>b</sup></b>							
Inferior occipital lobe	L	-22	-96	-4	1104	< .001	20.14
Lingual gyrus	R	24	-92	-8	995	< .001	18.47
<b>Interaction effect: Reward x Domain x Time x Intervention<sup>c</sup> (Primary objective)</b>							
Midbrain	L	-10	-18	-10	1	.131	3.19
Putamen	R	20	22	-2	12	.250	3.83
Caudate nucleus	R	12	12	2	23	.369	3.69
Caudate nucleus	R	12	8	-6		.369	3.68
Pallidum	R	10	8	0		.619	3.42
Caudate nucleus	R	16	14	4		.769	3.27

561 <sup>a</sup> Degrees of freedom: 1, 224; <sup>b</sup>  $p < .05$ , whole-brain family wise error (FWE) corrected; <sup>c</sup> pFWE value for the smaller midbrain and  
 562 striatum search volumes.

563

564 **Table 4. Reward Receipt. Summary of brain regions exhibiting main effects of reward, domain**  
 565 **and/or interactions with domain, training, and time.**

Label	Side (Left/Right)	MNI-coordinates x, y, z (mm)	Size (number of voxels)	<i>p</i> FWE (peak- level)	<i>t</i> -value <sup>a</sup> (peak)
<b>Main effect of receipt: hits (high &gt; low) &gt; too lates (high &gt; low)<sup>b</sup></b>					
Nucleus accumbens	L	-14 6 -12	880	< .001	13.61
Putamen	L	-18 10 -6		< .001	12.41
Hippocampus	L	-16 -6 -16		< .001	6.89
Putamen	R	18 8 -8	1019	< .001	12.50
		22 14 -4		< .001	12.42
		30 -10 2		< .001	8.63
Middle temporal gyrus	R	48 -72 0	1371	< .001	9.85
Inferior temporal gyrus	R	52 -54 -16		< .001	8.91
Middle occipital lobe	R	32 -80 10		< .001	7.40
Superior frontal gyrus, medial orbital	L	-4 50 -6	1197	< .001	9.63
		-6 42 -8		< .001	8.35
		-6 60 2		< .001	7.87
Superior frontal gyrus	L	-20 30 52	794	< .001	9.38
Middle frontal gyrus	L	-22 18 46		< .001	6.82
Superior frontal gyrus	L	-14 46 38		< .001	6.07
Inferior temporal gyrus	L	-52 -48 -14	499	< .001	9.26
Inferior parietal gyrus	L	-48 -40 48	1530	< .001	8.86
Superior parietal gyrus	L	-30 -66 48		< .001	8.28
Inferior parietal gyrus	L	-42 -40 40		< .001	8.14
Inferior parietal gyrus	R	34 -48 50	1074	< .001	8.72
Supramarginal gyrus	R	46 -36 46		< .001	8.69
Inferior parietal gyrus	R	40 -42 50		< .001	7.22
Inferior frontal gyrus, triangular	L	-40 36 14	324	< .001	8.60
Putamen	L	-30 -12 4	104	< .001	8.19
Inferior frontal gyrus, triangular	L	-36 36 12	142	< .001	7.12
Inferior frontal gyrus, orbital	L	-26 30 -18		< .001	6.70
Caudate nucleus	L	-20 -8 26	92	< .001	7.01
		-20 -16 30		< .001	6.10
Inferior frontal gyrus, opercular	L	-44 6 26	51	< .001	6.41
Superior frontal gyrus	R	22 30 48	28	< .001	6.26
Caudate nucleus	R	18 -8 26	43	.001	6.03
		20 6 20		.005	5.62
		28 36 -14		.001	5.97

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Cingulate gyrus, mid part	R	4	-38	34	27	.001	5.85
Middle occipital lobe	L	-24	-92	8	48	.002	5.77
		-32	-88	10		.007	5.53
Precentral gyrus	R	48	4	28	31	.002	5.76
Inferior occipital lobe	L	-48	-74	-2	12	.002	5.74
Middle occipital lobe	L	-26	-84	20	14	.002	5.67
Precuneus	R	2	-62	24	23	.004	5.66
Paracentral lobule	L	-2	-26	60	28	.004	5.63
	R	8	-24	62		.004	5.45
Hippocampus	L	-32	-34	-6	1	.007	5.55
Inferior parietal gyrus	L	-26	-50	44	1	.035	5.19
Middle temporal gyrus	L	-62	-10	-22	1	.045	5.14
Main effect of receipt: too late (high > low reward) > hits (high > low reward) <sup>b</sup>							
Middle temporal gyrus	R	48	-26	-6	1877	< .001	13.37
		48	-36	0		< .001	10.35
Supramarginal gyrus	R	60	-42	36		< .001	9.06
Inferior frontal gyrus, orbital	R	48	22	-4	956	< .001	9.42
Inferior frontal gyrus, triangular	R	54	22	4		< .001	8.04
		44	22	8		< .001	7.15
Supramarginal gyrus	L	-62	-44	26	342	< .001	8.91
Supplementary motor area	R	6	24	62	1584	< .001	8.58
		8	14	66		< .001	8.45
Superior frontal gyrus, medial	R	4	34	54		< .001	7.70
Middle temporal gyrus	L	-50	-28	-4	437	< .001	8.33
		-50	-48	8		< .001	6.95
Thalamus	L	-8	-16	8	355	< .001	7.51
Thalamus	R	10	-16	10		< .001	7.35
		8	-8	6		< .001	7.02
Middle frontal gyrus	R	30	50	24	274	< .001	7.50
Middle temporal gyrus	L	-56	2	-14	626	< .001	7.29
Insula	L	-34	22	-8		< .001	7.14
		-36	20	8		< .001	6.80
Postcentral gyrus	L	-40	-22	50	320	< .001	7.04
		-48	-20	46		< .001	6.30
		-42	-24	38		.033	5.21
Middle frontal gyrus	L	-26	48	24	90	< .001	6.89
		-24	38	20		.013	5.41
Caudate nucleus	R	12	2	14	20	< .001	6.24
Cingulate gyrus, mid part	R	6	-18	36	15	< .001	6.05
Middle temporal pole	R	52	8	-22	32	.001	5.92
Insula	R	40	0	-14	13	.002	5.80
Caudate nucleus	L	-8	8	6	4	.003	5.71
Cerebellum	R	22	-50	-22	7	.004	5.66
Rolandic operculum	L	-40	-20	18	9	.009	5.48
Superior temporal gyrus	L	-40	-4	-14	2	.016	5.37

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Middle temporal gyrus	R	50	2	-22	1	.038	5.17
Temporal pole: superior temporal gyrus	R	50	16	-18	1	.044	5.14
Midbrain	R	6	-24	-6	1	.046	5.13
Calcarine fissure	R	8	-80	12	1	.047	5.13
Interaction effect of domain x reward: caloric (hits (high > low reward) > toolates (high > low reward)) > monetary (hits (high > low reward) > toolates (high > low reward)) <sup>b</sup>							
Lingual gyrus	R	18	-86	-4	195	< .001	8.96
Calcarine fissure	L	-10	-90	-4	63	.001	6.04
Cerebellum	R	16	-80	-16	5	.005	5.59
Interaction effect of Intervention x Domain x Reward <sup>b</sup>							
Putamen	R	30	-14	8	1	.015	5.38
Interaction effect of domain x receipt x reward: monetary (hits (high > low reward) > toolates (high > low reward)) > caloric (hits (high > low reward) > toolates (high > low reward)) <sup>b</sup>							
Lingual	R	18	-84	-4	116	< .001	7.02
Lingual	L	-14	-88	-4	1	.023	5.01

566 <sup>a</sup> Degrees of freedom: 1,224; <sup>b</sup>  $p < .05$ , whole-brain FWE corrected.

567

568 **Anthropometric outcomes**

569 As a secondary outcome, we analyzed the effects of the two interventions on the  
 570 anthropometric measures. Although we initially intended to assess only BMI and waist-to-hip  
 571 ratio (WHR), we have added the analysis of waist circumference as an additional exploratory  
 572 measure to assess abdominal obesity<sup>49</sup>. Changes in abdominal obesity as measured with WHR  
 573 may be masked because of the relative nature of the measure (i.e., if the interventions affect  
 574 waist and hip circumference similarly, especially in women<sup>50</sup>). The interventions had differential  
 575 effects on the anthropometric measures as indicated by a significant Time x Intervention  
 576 interaction. Specifically, the active control, EC, intervention resulted in both decreased BMI and  
 577 waist circumference (main Time: BMI:  $F(1,25)=6.2$ ,  $p=.020$ ,  $\eta_p^2 = 0.198$ ; waist circumference:  
 578  $F(1,25)=17.9$ ,  $p<.001$ ,  $\eta_p^2 = 0.418$ ), whereas the ME intervention did not affect either of them  
 579 (main Time: BMI:  $F(1,31)<1$ ,  $p=.648$ ,  $\eta_p^2 = 0.007$ ; waist circumference:  $F(1,31)<1$ ,  $p=.504$ ,  $\eta_p^2 =$



580 0.015). Waist-to-hip ratio was not affected by either of the interventions (Time x Intervention:  
581  $F(1,56) < 1$ ,  $p = .379$ ,  $\eta_p^2 = 0.014$ ). For all comparisons see **Table 5**.

582

### 583 **Self-reported and neuropsychological outcomes**

584 As another secondary outcome, we assessed intervention effects on eating-related self-  
585 reported measures. We found that EC participants reported closer compliance to the Dutch  
586 food-based guidelines for healthy eating (main Time:  $F(1,25)=12.8$ ,  $p=.001$ ,  $\eta_p^2 = 0.339$ ) than ME  
587 participants following their intervention (main Time:  $F(1,31)=1.4$ ,  $p=.244$ ,  $\eta_p^2 = 0.044$ ), as  
588 substantiated by a significant Time x Intervention interaction for DHD-FFQ scores. EC  
589 participants also showed a significant increase in knowledge on healthy eating following the  
590 intervention (main Time:  $F(1,25)=48.8$ ,  $p<.001$ ,  $\eta_p^2 = 0.661$ ), whereas ME participants did not  
591 (main Time:  $F(1,31)<1$ ,  $p=.394$ ,  $\eta_p^2 = 0.024$ ), as evidenced by a significant Time x Intervention  
592 interaction for FBQ scores. The other sub-scale of the FBQ (temptation) did not show any  
593 differential intervention effects; neither did any of the sub-scales of the DEBQ (restraint,  
594 emotional, and external eating). For all comparisons see **Table 5**.

595 Analysis of the other self-reported and neuropsychological measurements – including  
596 those related to the intervention (FFMQ-SF, TCQ), affect (PANAS, BIS-BAS, HADS), impulsivity  
597 (FTND, BIS-11, Kirby), and working memory (digit span) revealed no significant interactions  
598 between Time and Intervention (**Table 5**).

599

600 **Table 5 Secondary anthropometric, self-reported eating behaviour, and neuropsychological**  
601 **outcomes. Means and standard deviations, pre- and post-training, for each group (mindful**

602 eating, ME; educational cooking, EC) separately, and Time (pre, post) x Intervention (ME, EC)  
 603 statistics.

	mindful eating (ME)		educational cooking (EC)		<i>p</i>	test- statistic <sup>a</sup>	effect size <sup>b</sup>
	pre	post	pre	post			
<b>Anthropometric outcomes</b>							
BMI (kg/m <sup>2</sup> )	26.6 ±4.1	26.6 ±4.2	25.5 ±3.4	25.2 ±3.5	.023	5.5	0.089
WHR	0.85 ±0.06	0.84 ±0.07	0.85 ±0.06	0.84 ±0.07	.379	< 1	0.014
Waist (cm)	89.6 ±12.8	89.3 ±13.2	86.5 ±11.7	84.4 ±11.7	.026	5.2	0.085
<b>Self-report eating behavior outcomes</b>							
DHD-FFQ	52.2 ±10.4	54.2 ±10.0	51.6 ±12.0	59.5 ±10.8	.036	4.6	0.076
FBQ	64.0 ±7.0	62.8 ±5.6	62.1 ±4.8	62.7 ±6.3	.264	1.3	0.022
Knowledge	15.6 ±1.5	15.8 ±1.3	14.9 ±1.5	16.7 ±0.8	<.001	19.6	0.259
Temptation	15.0 ±3.2	14.4 ±3.3	14.8 ±3.3	14.5 ±4.0	.729	< 1	0.002
<b>DEBQ</b>							
Restraint	2.8 ±0.6	2.9 ±0.6	2.9 ±0.7	2.9 ±0.6	.814	< 1	0.001
Emotional	2.8 ±0.8	2.8 ±0.8	2.8 ±0.7	2.7 ±0.9	.728	< 1	0.002
External	3.2 ±0.4	3.2 ±0.5	3.4 ±0.5	3.1 ±0.5	.120	2.5	0.043
<b>Other self-report and neuropsychological outcomes</b>							
FFMQ-SF <sup>c</sup>	78.1 ±7.7	76.8 ±7.4	76.5 ±8.6	75.7 ±7.9	.671	< 1	0.003
TCQ <sup>d</sup>	30.0 ±7.4	27.8 ±8.4	32.7 ±4.8	32.8 ±8.1	.215	1.6	0.029
<b>PANAS</b>							
Positive Affect	31.8 ±6.5	30.0 ±6.1	31.4 ±4.8	29.8 ±5.1	.772	< 1	0.002
Negative Affect	12.7 ±2.8	13.9 ±4.3	12.7 ±2.6	13.4 ±3.6	.602	< 1	0.005
<b>BIS-BAS</b>							
BIS	20.8 ±3.3	20.3 ±3.2	19.8 ±3.3	19.6 ±3.3	.671	< 1	0.003
BAS	41.5 ±3.3	42.3 ±4.0	43.2 ±4.1	42.7 ±4.1	.101	2.8	0.047
<b>HADS</b>							
Anxiety	4.4 ±2.4	6.0 ±2.5	4.8 ±2.5	6.2 ±3.9	.902	< 1	<0.001
Depression	2.6 ±2.4	2.8 ±2.4	2.4 ±2.3	2.7 ±2.6	.864	< 1	0.001
FTND (smoking score)	0.19 ±1.1	0.19 ±1.1	0.04 ±0.2	0.04 ±0.2	1.000	416 <sup>e</sup>	<0.001 <sup>f</sup>
BIS-11	62.0 ±9.3	62.1 ±9.0	64.5 ±8.7	63.7 ±8.3	.492	< 1	0.008
Kirby	0.013 ±0.02	0.015 ±0.02	0.020 ±0.04	0.011 ±0.01	.094	2.9	0.049
Digit Span <sup>g</sup>	15.6 ±3.5	15.2 ±3.6	14.1 ±3.5	13.5 ±3.7	.689	< 1	0.003

604 If not otherwise stated, values denote mean±SD.

605 Abbreviations: BMI: Body Mass Index; WHR: waist-to-hip ratio; DHD-FFQ: Dutch Healthy Diet Food Frequency Questionnaire;  
 606 FBQ: Food Behavior Questionnaire, a shortened version; DEBQ: Dutch Eating Behaviour Questionnaire; FFMQ-SF: Five Facet  
 607 Mindfulness Questionnaire – Short Form; TCQ: Treatment Credibility Questionnaire; PANAS: Positive And Negative Affect Scale;  
 608 BIS-BAS: Behavioral Inhibition System - Behavioral Approach System questionnaire; HADS: Hospital Anxiety and Depression  
 609 Scale; FTND: Fagerstrom Test for Nicotine Dependence; BIS-11: Barratt Impulsiveness Scale-11; Kirby: delayed reward  
 610 discounting questionnaire.

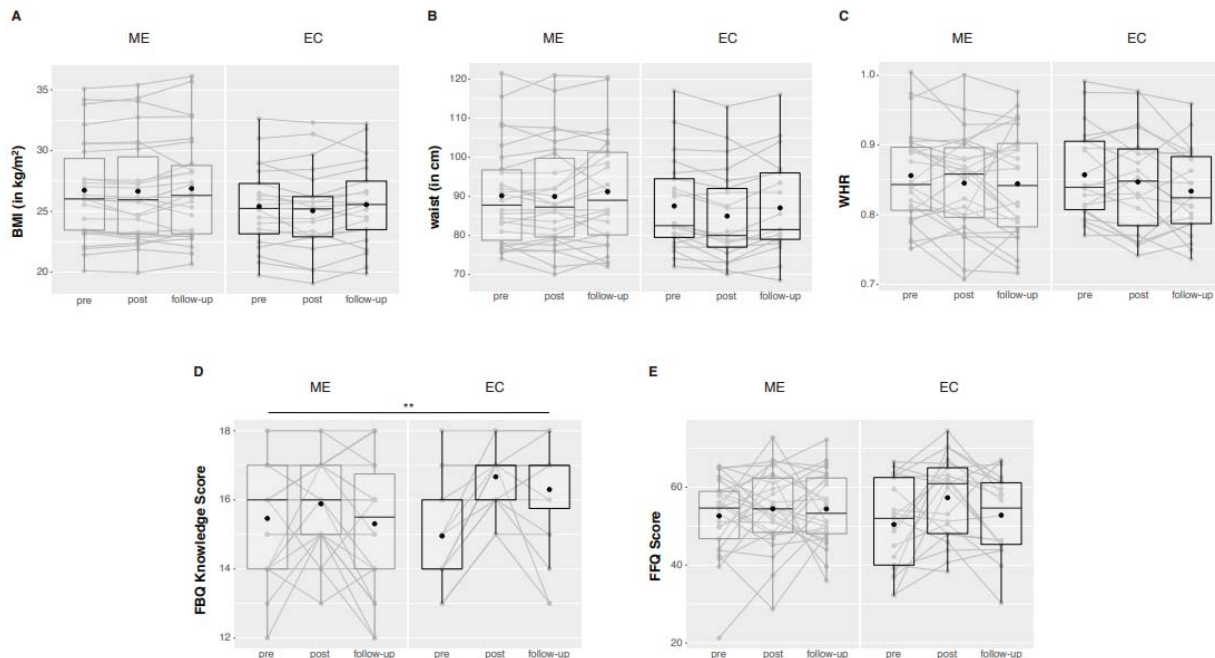
611 <sup>a</sup>If not otherwise stated, the reported test-statistic is the F-value (degrees of freedom: 1,56)

612 <sup>b</sup>If not otherwise stated, the reported effect size is the partial eta squared ( $\eta_p^2$ )

613 <sup>c</sup>FFMQ-SF: N = 48 (N<sub>ME</sub> = 22, N<sub>EC</sub> = 26; degrees of freedom: 1,46)  
614 <sup>d</sup>TCQ, Hunger, Thirst, Satiety: N = 55 (N<sub>ME</sub> = 29, N<sub>EC</sub> = 26; degrees of freedom: 1,53).  
615 <sup>e</sup>Mann-Whitney U  
616 <sup>f</sup>r, effect size for Mann-Whitney U-test (z-value divided by the total sample size (58))  
617 <sup>g</sup>The total score of the digit span is reported  
618

619 To establish whether the observed differential intervention effects (Time x Intervention  
620 interactions) in the anthropometric and eating-related self-report measures were long-lasting,  
621 we ran *post hoc* analyses by adding the one-year follow-up data as an extra level of factor Time  
622 (pre, post, follow-up) in the ANOVAs for all participants from the reported sample that returned  
623 for the follow-up (ME: n=26, EC: n=20)(**Figure 4**). For BMI and waist circumference, degrees of  
624 freedom were corrected using Huynh-Feldt estimates of sphericity due to violation of the  
625 sphericity assumption. BMI, WHR, and waist circumference did not show any long-term  
626 intervention-related changes (Intervention x Time, BMI:  $F(1.550,69.77) < 1$ ,  $p = 0.468$ ,  $\eta_p^2 = 0.015$ ;  
627 WHR:  $F(2,44) < 1$ ,  $p = 0.589$ ,  $\eta_p^2 = 0.024$ ; waist:  $F(1.742,78.384) = 2.213$ ,  $p = 0.123$ ,  $\eta_p^2 = 0.047$ ). BMI,  
628 WHR, and waist circumference changed over time irrespective of the intervention (main Time,  
629 BMI:  $F(1.550,69.77) = 3.730$ ,  $p = 0.039$ ,  $\eta_p^2 = 0.077$ ; WHR:  $F(2,44) = 5.099$ ,  $p = 0.010$ ,  $\eta_p^2 = 0.188$ ;  
630 waist:  $F(1.742,78.384) = 4.837$ ,  $p = 0.014$ ,  $\eta_p^2 = 0.097$ ). Planned *post hoc* comparisons revealed  
631 that the non-significant intervention effects on the anthropometric measures – after including  
632 the follow-up time point – were caused by a lack of significant differences between pre-  
633 intervention measurements and one-year follow-up measurements for either group (all  $p > 0.1$ ).  
634 This means that the BMI- and waist circumference-reducing effects of the active control (EC)  
635 intervention (versus the mindful eating intervention) were no longer visible at one-year follow-  
636 up.

637 The EC-related increase in knowledge on healthy eating remained significant after  
638 including the one-year follow-up time point (Intervention x Time, FBQ knowledge:  $F(2,44)=7.4$ ,  
639  $p=0.002$ ,  $\eta_p^2 = 0.253$ ), caused by a lingering increase in knowledge on healthy eating for EC  
640 participants at one-year follow-up relative to pre-intervention measurements ( $F(1,20)=17.06$ ,  
641  $p=0.001$ ,  $\eta_p^2 = 0.460$ ). In contrast, the effects of the active control (EC) intervention on self-  
642 reported compliance to the Dutch guidelines for healthy diet were not long lasting (Intervention  
643 x Time, DHD-FFQ:  $F(2,43)=2.121$ ,  $p=0.132$ ,  $\eta_p^2 = 0.090$ ). Similar to the anthropometric  
644 measures, planned *post-hoc* comparisons revealed that these DHD-FFQ scores were  
645 comparable between the pre-intervention and one-year follow-up measures for either group  
646 (all  $p>0.1$ ), meaning that the previously observed post-pre effects of the active control (EC)  
647 intervention were only short lasting.  
648



649

650 **Figure 4. Anthropometric (upper panels) and eating-related self-report measures (lower panels) 1 year**  
651 **after the intervention. No long-lasting intervention effects were observed for (A) BMI, (B) waist**  
652 **circumference, (C) waist-to-hip ratio (WHR), and (E) compliance to the Dutch guidelines for healthy**  
653 **diet (DHD-FFQ). Only knowledge on healthy eating (D) remained high following the educational**  
654 **cooking (EC) intervention. No intervention effects were observed for the mindful eating (ME) group.**  
655 **Box plots show the median and interquartile range, with the black dot denoting the mean. Note that**  
656 **the medians of the EC group in figure (D) do not fall in the interquartile range. Individual data points**  
657 **at the different test sessions are connected for illustrative purpose. \*\* asterisks denote a significant**  
658 **Time x Intervention interaction with  $p < 0.01$ .**

659

## 660 **Discussion**

661 The primary objective of this study was to investigate the effects of an 8-week mindful eating  
662 intervention on striatal reward anticipation responses as well as response times during an  
663 incentive delay task. In addition to the striatum, we explored these effects in the midbrain – as  
664 part of the mesolimbic reward circuit with its dopaminergic projections to the striatum<sup>4,5</sup> – as  
665 regions of interests (ROIs). We observed that mindful eating training significantly impacted  
666 reward anticipation in the midbrain relative to the active control training, with relatively  
667 reduced caloric versus monetary reward responses in this region after the intervention. We  
668 found no effect of the interventions in the striatum or on response times during the incentive  
669 delay task. Anthropometric measures of obesity (i.e. secondary outcome: BMI) temporarily  
670 decreased and self-reported (knowledge of) healthy food intake (i.e. secondary outcome:  
671 eating behavior questionnaires) increased following the educational cooking intervention, but  
672 not following the mindful eating intervention.

673

674 We did not observe any intervention effect on the response times or on striatal fMRI (BOLD)  
675 responses during the incentive delay task. Previous studies have shown that greater subcortical  
676 reward responses to caloric cues, particularly in striatum, are associated with obesity<sup>51,52</sup>, with  
677 weight gain<sup>9</sup>, and with increased snack food intake in healthy-weight to overweight individuals  
678<sup>7</sup>. Despite this clear involvement of striatum in food reward anticipation and its relationship  
679 with eating behavior, we found no effects of mindful eating training on striatal BOLD responses.  
680 Below, we interpret these null results.

681

682 We did however observe intervention effects on midbrain reward anticipation in the current  
683 study, with relatively reduced responses to the caloric (i.e. high-calorie drink versus water)  
684 compared with the monetary (50 ct. versus 1 ct.) cues – in an, on average, overweight sample  
685 of participants motivated to improve their dietary habits. Dopaminergic midbrain neurons are  
686 crucial for processing predicted reward value<sup>5,53</sup> and, in concert with striatum, modulate  
687 motivated behavior such as eating<sup>54</sup>. In line with this, Small et al.<sup>55</sup> showed that midbrain  
688 activity, as measured with positron emission tomography ( $H_2^{15}O$ ), decreased with reduced self-  
689 reported reward value of chocolate in a sample of healthy individuals consuming chocolate  
690 beyond satiety. In another study, midbrain BOLD responses to sips of palatable milkshake were  
691 found to positively correlate with subsequent *ad libitum* milkshake intake in a group of healthy-  
692 weight to moderately obese individuals<sup>56</sup>. Moreover, overweight and obese compared with  
693 normal weight adolescents showed increased activations in midbrain during anticipation of  
694 decisions involving risk and reward<sup>12</sup>. Furthermore, both midbrain and striatal BOLD responses

695 to palatable food pictures were found to correlate positively with self-reported reward drive in  
696 healthy individuals<sup>57</sup>. These (indirect) measures of motivated eating behavior are thus  
697 associated with greater mesolimbic responses when processing food reward value.

698

699 Our finding that anticipatory midbrain responses were relatively reduced in the caloric versus  
700 monetary domain is in line with a previous study showing that only a brief 50-min mindful  
701 eating workshop (versus an educational video) reduced subsequent impulsive choice patterns  
702 for food-, but not money-related outcomes<sup>58</sup>. However, in studies comparing meditators with  
703 non-meditating controls, meditators exhibited reduced striatal BOLD responses to primary  
704 reward prediction errors<sup>25</sup> as well as monetary reward anticipation<sup>24</sup>. In the latter study, Kirk  
705 and colleagues<sup>24</sup> compared meditators to non-meditators without a baseline measurement.  
706 The observed decrease in striatal reward processing could thus be due to pre-existing between-  
707 group differences<sup>59</sup>. Since the present study was actively controlled including pre and post  
708 measurements, the current effects can be more reliably ascribed to the mindfulness  
709 intervention. Kirk and colleagues<sup>26</sup> also performed a similar randomized actively controlled  
710 study including pre and post measurements and found that vmPFC value signals were  
711 modulated by the mindfulness intervention for both primary (juice) and secondary (monetary)  
712 rewards. These general reward effects versus our relative caloric versus monetary effects might  
713 be due to both the type of intervention (general MBSR in Kirk et al.<sup>26</sup> versus mindful eating  
714 presently) as well as the study sample. Specifically, in our study, participants were highly  
715 motivated to change undesired eating habits and their mindfulness practice was targeted at  
716 overcoming those – including homework practices such as resisting impulsive eating behaviors.

717 Moreover, note that we did not observe any effects of either the ME or the EC intervention on  
718 neural responses at the time of caloric or monetary reward receipt. One might have expected  
719 reductions in vmPFC BOLD responses following the mindfulness-based intervention as was  
720 reported by Kirk et al.<sup>26</sup> for juice delivery. However, another important difference with the  
721 current study is that we used promised (i.e. delivered after scanning) instead of actual rewards  
722 (delivered during scanning). Moreover, our design was optimized for reward anticipation, with  
723 perhaps not enough successful reward receipt trials (i.e. approximately 33% of all anticipated  
724 rewards were missed). Together, our results suggest that a targeted mindful eating – instead of  
725 general mindfulness – intervention may have more specific effects on caloric versus monetary  
726 reward anticipation.

727

728 The specificity of our results for midbrain, not striatum, finds resonance in a study in healthy  
729 individuals by O’Doherty and colleagues<sup>60</sup>, who found significant responses to cues predicting  
730 the receipt of a glucose solution versus a neutral taste in midbrain only, whereas both midbrain  
731 and striatum were responsive to cues predicting the receipt of a sweet versus an aversive salty  
732 taste. The latter contrast may be a larger one in terms of valence, which might implicate that  
733 our caloric versus water contrast was not sensitive enough to show intervention effects in the  
734 striatum – despite showing main task effects of reward anticipation. Given the coding of  
735 predicted reward in the midbrain, we speculate that the currently observed relative effect of  
736 the mindful eating intervention on anticipatory midbrain responses to caloric versus monetary  
737 cues suggests that mindful eating practice may be able to reduce the impact of food cues on  
738 reward processing.



739

740 The question then arises whether mindfulness affects midbrain responses through top-down or  
741 bottom-up processes. Current theories on mindfulness-based interventions emphasize that  
742 improvements in emotion regulation occur through increased prefrontal cortex-mediated top-  
743 down control of regions processing affect, such as the amygdala<sup>61,62</sup>. An alternative way to  
744 reducing incentive motivation is through extinction during mindfulness practice, akin to  
745 exposure therapy<sup>61,62</sup>, which would rather be a bottom-up process. Practicing mindful eating  
746 requires one to actively withhold or interrupt cue-triggered eating, a process that may lead to  
747 extinction of conditioned responses to highly caloric stimuli<sup>61,63,64</sup> as well as the formation of  
748 new memories related to those stimuli (i.e., not reacting to them). As a result, choices for high  
749 caloric foods may be further reduced<sup>65,66</sup>. However, incentive motivation could also be reduced  
750 through other bottom-up effects on, for example, physiological state rather than through  
751 extinction. Increased awareness of states like hunger or satiety<sup>67</sup> are known to modulate  
752 conditioned responses to reward-related cues<sup>68</sup>. Future confirmatory studies are needed to  
753 verify the exploratory midbrain findings and investigate the underlying bottom-up versus top-  
754 down mechanisms, for instance by employing tasks manipulating top-down control on food  
755 reward processes, addressing the effects of physiological state and interoception, and by  
756 employing connectivity analyses between cortical and mesolimbic regions.

757

758 The present mindful eating effects on caloric versus monetary reward anticipation in the  
759 midbrain were not accompanied by changes in our secondary outcome measures related to  
760 real-life eating behavior, i.e., reductions in weight, waist-hip ratio or waist circumference, or

761 changes in self-reported eating behavior. Several other studies have found that an intensive  
762 mindful eating intervention did lead to reduced measures associated with overeating such as  
763 consumption of sweets<sup>22</sup>, binges, externally and emotionally driven eating<sup>69</sup> and reductions in  
764 BMI<sup>20</sup> in non-clinical populations, as well as number of binges in binge-eating disorder<sup>18</sup>. On  
765 the other hand, a more recent review by Warren and colleagues concludes that there is a lack  
766 of compelling evidence of mindfulness and mindful eating interventions leading to a reduction  
767 in weight<sup>70</sup>. The current lack of mindful eating intervention-related reductions in our secondary  
768 measures of (abdominal) obesity might reflect the heterogeneity of our sample, including  
769 normal-weight, overweight and obese individuals; with larger mindfulness-related reductions in  
770 food intake seen in overweight and obese populations in previous studies<sup>70</sup>. Moreover, the  
771 study design – including sample size – was optimized for the primary outcome measure (i.e.,  
772 neural effects) and plausibly less optimal for showing these behavioral effects after the mindful  
773 eating intervention. We were also not able to show increased self-reported mindfulness after  
774 the intervention on the established short version of the Five Facet Mindfulness Questionnaire<sup>31</sup>,  
775 but this questionnaire was only employed in a sub group (in n=22 of the total n=32 ME vs n=26  
776 EC). In fact, ineffectiveness of our mindful eating intervention is highly unlikely given the  
777 observed midbrain findings in the hypothesized direction here (although exploratory) and our  
778 previously published effects on behavioral flexibility<sup>71</sup>. Sampling a greater and more  
779 homogeneous population in terms of BMI is advised for future studies to be able to  
780 demonstrate a link between reduced mesolimbic reward responses and altered eating behavior  
781 following a mindful eating intervention. For now, it is unclear how mindfulness-induced  
782 reductions in midbrain responses to caloric versus monetary reward anticipation contribute to

783 changes in real-life eating behavior.

784

785 In contrast, we did observe beneficial effects of the educational cooking intervention on  
786 anthropometric measures of obesity and self-reported eating behavior, whereas this group did  
787 not demonstrate any intervention effects on mesolimbic reward anticipatory responses. The  
788 beneficial effects might not be surprising for this group, since the educational cooking  
789 intervention was explicitly aimed at promoting healthy food intake, with reduced intake of  
790 sugar, fats and salt as part of the homework assignments. This led to short-term reductions in  
791 weight and waist circumference, as well as increased self-reported adherence to the Dutch  
792 healthy diet (DHD-FFQ). Given those health benefits of the educational cooking intervention  
793 and the relatively reduced food reward anticipation responses of the mindful eating  
794 intervention, it might be fruitful to develop a combined program for therapeutic practice or for  
795 preventive strategies. Although weight control and diet interventions are often successful in  
796 producing significant weight loss on the short term, they often fail to produce long-term weight  
797 maintenance<sup>72</sup>. This is supported by our analyses of BMI, waist circumference, and self-  
798 reported compliance to the Dutch healthy diet guidelines (DHD-FFQ) at one-year follow-up in  
799 the present study. These secondary measures returned to baseline one year after the  
800 educational cooking intervention, despite the fact that knowledge of healthy eating remained  
801 significantly higher compared with baseline in the educational cooking group. Previous studies  
802 investigating factors contributing to successful weight maintenance have shown that reductions  
803 in subcortical responses to food reward cues may be beneficial for prevention or treatment of  
804 obesity<sup>7-9</sup>. Therefore, we speculate that a combination of the two interventions with a focus on

805 both information and behavior might lead to longer-lasting health benefits than either  
806 intervention on its own.

807

808 We note that the lack of a – likely, very subtle - effect of mindful eating, e.g. on striatal reward  
809 anticipation, might well reflect the inclusion of a well-matched active control intervention;  
810 enabling the observed effects to be actually attributed to mindfulness practice <sup>62</sup>. The  
811 randomized, active-controlled nature of the study was probably also the reason for a high  
812 dropout rate. This may reflect a lack of motivation to take part in the interventions, although  
813 the dropout rate in the mindful eating group was more than 15% lower (non-significantly) than  
814 in the active control condition (that showed clear effects on secondary outcome measures). We  
815 speculate that dropout rates could have been lower and motivation higher in the current study  
816 had we been able to offer participants to take part in the other intervention program after  
817 completion of the study, which is commonly done for mindfulness studies that include a waitlist  
818 control group. To address differences in results of previous mindfulness or meditation studies  
819 without active control condition, future mindfulness intervention studies, especially those  
820 aimed at unraveling subtle mechanistic effects, are recommended to not only include a well-  
821 matched active control intervention but also a waitlist control group.

822

823 In conclusion, we found that an intensive mindful eating intervention reduced midbrain food,  
824 relative to monetary, reward anticipation. These results have to be confirmed in future studies,  
825 as we primarily hypothesized striatal effects, and the midbrain findings are the result of  
826 exploratory analyses. Future studies are also required to demonstrate the clinical relevance of

827 mindfulness-mediated reductions in food anticipation for counteracting reward cue-driven  
828 overeating, particularly given that we did not observe mindfulness-related changes in  
829 anthropometric or eating behavior measures. Given the success of mindfulness-based programs  
830 in reducing symptoms of other reward-related disorders such as substance use<sup>73,74</sup> and  
831 problem gambling<sup>75</sup>, our findings of relatively specific reduced anticipatory reward responses  
832 may also be relevant for these other targets of abuse.

833

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851

### 852 **Author contributions**

853 EA acquired funding for the study. EA, LKJ, RC, AEMS, and JHMdV designed the study. LKJ, ID,  
854 lvL, and JW acquired and analyzed the data, supervised by EA and RC. AEMS and JHMdV  
855 supervised the execution of the interventions. LKJ, ID, and EA wrote the first version of the  
856 manuscript. All authors corrected the manuscript and approved it for final submission.

857

### 858 **Competing interests**

859 The author(s) declare no competing interests.

860

### 861 **Data availability**

862 The datasets analysed during the current study are available on

863 <http://dx.doi.org/10.17632/fthcv3kns9.1>.

864

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