

1 Running title: Mindful eating and reward anticipation

2 The effect of an 8-week mindful eating intervention on
3 anticipatory reward responses in the midbrain

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43

44 **Abstract**

45 Obesity is a highly prevalent disease, usually resulting from chronic overeating. Accumulating
46 evidence suggests that increased neural responses during the anticipation of high caloric food
47 play an important role in overeating. A promising method to counteract enhanced food
48 anticipation in overeating might be mindfulness-based interventions (MBIs). However, how
49 MBIs can affect food reward anticipation neurally has never been studied. In this randomized,
50 actively controlled study we aimed to investigate whether an 8-week mindful eating
51 intervention decreases reward anticipation in striatal and midbrain reward regions. Using
52 functional Magnetic Resonance Imaging, we tested 58 healthy subjects with a wide body mass
53 index range (BMI: 19-35 kg/m²), who were motivated to change their eating behavior. During
54 scanning they performed an incentive delay task, measuring neural reward anticipation
55 responses to caloric and monetary cues before and after 8 weeks of mindful eating or
56 educational cooking (active control). Relative to educational cooking (active control), mindful
57 eating decreased reward anticipation responses to food, but not to monetary reward cues, in
58 the midbrain, but not the striatum. The effects were specific to reward anticipation and did not
59 extend to reward receipt. These results show that an 8-week mindful eating intervention may
60 decrease the salience of food cues specifically, which could result in decreased food-cue
61 triggered overeating on the long term.

62

63 **Significance statement**

64 Mindfulness-based interventions have been shown effective in reducing disordered eating
65 behavior in clinical as well as non-clinical populations. Here, we present the first randomized
66 actively controlled study investigating the effects of mindfulness on reward anticipation in the
67 brain. Using fMRI we show that midbrain responses to caloric, but not monetary, reward cues
68 are reduced following an 8-week intervention of mindful eating relative to educational cooking
69 (active control). Mindful eating interventions may thus be promising in counteracting reward
70 cue-driven overeating, particularly in our obesogenic environment with food cues everywhere.
71 Moreover, our data show that specific mindfulness-based interventions can target specific
72 reward-cue responses in the brain, which might be relevant in other compulsive behaviors such
73 as addiction.

74

75 **Introduction**

76 Reward-related disorders such as addiction, binge-eating disorder and obesity, are
77 characterized by altered responses to reward cues related to the target of abuse (Volkow et al.,
78 2008; García-García et al., 2014; Val-Laillet et al., 2015). Regions in the striatum and midbrain
79 respond to increases in appetitive motivation induced by reward cues (Knutson et al., 2005).
80 Altered responses of these subcortical reward regions have been related to reward-related
81 disorders. For example, greater BMI was associated with increased midbrain responses to risky
82 rewards in adolescents (Delgado-Rico et al., 2013). Furthermore, greater midbrain responses to
83 alcohol-related stimuli have been suggested to contribute to an attentional bias towards those
84 stimuli in alcoholics (Muller-Oehring et al., 2013). In addition, greater responses of ventral
85 striatum to reward cues have been associated with subsequent food intake (Lawrence et al.,
86 2012) and future weight gain (Stice et al., 2011; Demos et al., 2012; Lawrence et al., 2012).
87 Interventions that diminish subcortical responses to food reward cues may therefore be
88 promising for treating and preventing obesity.

89
90 Mindfulness-based interventions are aimed at cultivating attention to present-moment
91 experience, without judgment (Kabat-Zinn, 1984). Protocolized mindfulness interventions, such
92 as mindfulness-based stress reduction (MBSR) have shown to be effective in reducing
93 subcortical responses to emotional stimuli in anxiety (Goldin et al., 2012) as well as in healthy
94 individuals (Lutz et al., 2013). Importantly, mindfulness-based interventions aimed at changing
95 eating behavior reduced obesity-related eating behavior in clinical populations (Leahey et al.,
96 2008; Kristeller et al., 2013) as well as abdominal fat (Tapper et al., 2009; Daubenmier et al.,

97 2011), and increased self-reported mindful eating in obese individuals (Mason et al., 2015).
98 However, only two of these studies were actively controlled (Kristeller et al., 2013; Mason et
99 al., 2015). It is therefore unclear whether these beneficial effects can be attributed to
100 mindfulness per se. In fact, Kristeller and colleagues (2013) found that mindfulness-based
101 eating awareness training (MB-EAT) and a psycho-educational/cognitive-behavioral (i.e., active
102 control) intervention similarly decreased binge-eating symptoms relative to a waitlist control
103 group. Given the different nature of these interventions, it is possible that reduced
104 symptomatology was mediated by distinct brain mechanisms, as was suggested by an actively
105 controlled clinical trial on social anxiety (Goldin et al., 2012). Studies investigating the
106 neurocognitive mechanism underlying mindful eating are required to address this issue.

107
108 Here, we present the first actively controlled randomized study investigating the effects of
109 mindfulness on reward anticipation in the brain to be able to understand its mechanisms of
110 action. Using functional Magnetic Resonance Imaging (fMRI) we investigated the effects of an
111 8-week mindful eating intervention and a carefully matched educational cooking intervention
112 (active control) on subcortical reward region responses when rewards could be earned in an
113 incentive delay task (Knutson et al., 2001) that has been consistently shown to produce reliable
114 subcortical responses to reward cues (Haber and Knutson, 2010). We hypothesized that the
115 mindful eating intervention would reduce reward cue responses of these subcortical reward
116 regions. We included both monetary and caloric rewards in the task, which enabled us to
117 explore whether the effect on anticipatory reward responses is specific to the caloric domain,
118 or generalizes to the monetary domain.

119 **Materials and methods**

120 **Subjects**

121 The results reported in this study are based on data from 58 healthy right-handed subjects (48
122 women; mean age: 31.6, SD: 11.0, range: 19 – 52 years; mean body mass index (BMI): 26.0, SD:
123 3.68, range: 19.7 – 34.7). Subjects were recruited from Nijmegen and surroundings through
124 advertisement. Only subjects (aged: 18 – 55 years old; BMI: 19 – 35 kg/m²) with no (history of)
125 eating disorders or current dieting and who were highly motivated to change their eating
126 behavior were included in the study (not per se to lose weight). All subjects gave written
127 informed consent and were reimbursed for participation according to institutional guidelines of
128 the local ethics committee (CMO region Arnhem-Nijmegen, the Netherlands, 2013-188).

129
130 Crucially, subjects who previously participated in an MBSR (Mindfulness-Based Stress
131 Reduction) or MBCT (Mindfulness-Based Cognitive Therapy) course were not included in the
132 study. Other exclusion criteria were: left-handedness, inadequate demand of Dutch, current
133 pregnancy, MRI-incompatibility, diabetes mellitus, (history of) hepatic, cardiac, respiratory,
134 renal, cerebrovascular, endocrine, metabolic or pulmonary diseases, uncontrolled hypertension
135 (diastolic pressure > 90 mmHg, systolic pressure > 160 mmHg), (history of) eating, neurological,
136 or psychiatric disorders, depression/anxiety state scores > 11 on the Hospital Anxiety and
137 Depression Scale (HADS, Zigmond & Snaith, 1983), current strict dieting, high restrained eating
138 score on the Dutch Eating Behavior Questionnaire (DEBQ \geq 3.60 for females and \geq 4.00 for
139 males; Strien & Frijters, JER, 1986), current psychological or dietary treatment, taste or smell
140 impairments, use of neuroleptica or other psychotropic medication, food allergies relevant to

141 the study, deafness, blindness, and sensori-motor handicaps, drug or alcohol addiction, and a
142 change in body weight of more than 5 kg in the past two months. Crucially, subjects with
143 previous MBSR (Mindfulness-Based Stress Reduction) or MBCT (Mindfulness-Based Cognitive
144 Therapy) experience were excluded from the study. For a flow diagram of all excluded subjects,
145 see **Figure 1**.

146

147 **Protocol**

148 All subjects were screened for inclusion and exclusion criteria, and matching criteria (age,
149 gender, BMI, experience with meditation and yoga) were assessed by taking physical measures
150 and administering self-report questionnaires on a separate intake session. To assess education,
151 the Dutch version of the National Adult Reading Test was administered at the (Schmand et al.,
152 1991).

153

154 After inclusion, subjects came to the laboratory twice, before and after the intervention. Test
155 sessions started at 11:00 AM or 12:30 PM. Pre-measurements were performed in the month
156 prior to the start of the intervention. Post-measurements were performed in the month
157 following the last group session. Subjects were instructed to abstain from eating foods and
158 drinking anything else than water four hours prior to the start of the test sessions. Subjects
159 were encouraged to have a light breakfast before fasting. Furthermore, subjects were
160 instructed to abstain from drinking alcohol 24 hours before the test session. Before scanning,
161 physical measurements were taken (weight, waist and hip circumference), digit span was
162 assessed (Groth-Marnat, 2009), and the following self-report questionnaires were

163 administered: the Fagerstrom Test for Nicotine Dependence (Heatherton et al., 1991) to assess
164 smoking and nicotine dependence; the Positive And Negative Affect Scale (Watson et al., 1988)
165 to assess positive and negative affect before scanning; the Barratt Impulsiveness Scale-11
166 (Barratt and Patton, 1995) to assess impulsivity; the Behavioral Inhibition System / Behavioral
167 Approach System questionnaire (Carver and White, 1994) to assess punishment and reward
168 sensitivity; the Kirby questionnaire (Kirby, 2009) to assess delayed reward discounting; the Food
169 Frequency Questionnaire, Dutch Healthy Diet (van Lee et al., 2013) to assess the degree to
170 which subjects eat according to the national guidelines for a Dutch healthy diet; a shortened
171 version of the Food Behavior Questionnaire to assess behaviour towards food; the Dutch Eating
172 Behaviour Questionnaire (van Strien et al., 1986) to assess emotional, external and restraint
173 eating behavior; the Five Facet Mindfulness Questionnaire – Short Form (Baer et al., 2006) to
174 assess degree of mindfulness; the Hospital Anxiety and Depression Scale (Zigmond and Snaith,
175 1983) to assess levels of anxiety and depression; a Treatment Credibility Questionnaire (TCQ) to
176 assess how much subjects believed the intervention would work for them. Note that the pre-
177 training TCQ was filled out at the first training session, not on the pre-training test session, as
178 subjects were unaware of the contents of their training at that time. Subsequently, subjects
179 underwent a one hour MR scanning session in which they performed an incentive delay task.

180

181 **Paradigm: Incentive Delay task**

182 We adapted the original incentive delay task (Knutson et al., 2001) to assess reward
183 anticipation to monetary as well as caloric cues. For task details see **Figure 2**. In short, on each
184 trial subjects were cued as to which of four rewards they could win (monetary: 1 or 50 cents;

185 caloric: a sip of water or a high-caloric drink of their choice (orange juice, chocolate milk or
186 regular cola)). As soon as a white star (target) appeared on the screen subjects were to press a
187 button with their right index finger as fast as possible. If subjects responded within an
188 individually-determined time-window they won and the reward was added to their cumulative
189 gain. After scanning, subjects received and drank their total caloric gain. Their total monetary
190 gain was added to their financial reimbursement. Subjects received instructions for the
191 incentive delay task before going into the scanner, and were aware they would receive their
192 gain following scanning. Before scanning, subjects rated how much they *wanted* and *liked* each
193 reward on a Visual Analogue Scale (VAS). To expose subjects to the reward outcomes, they
194 were provided with the actual coins, and one sip (5 mL) of water and one of the chosen drink
195 while rating the VAS.

196

197 **Interventions**

198 Subjects were randomly assigned to one of two intervention programs: mindful eating (ME) or
199 educational cooking (EC; active control), using minimization with respect to age, gender, BMI
200 and experience with meditation and yoga. Subjects were assigned through minimization (Scott
201 et al., 2002), which guarantees that groups are balanced in terms of certain *a priori* determined
202 minimization factors. An algorithm randomly assigned subjects to one of the groups by taking
203 into account the minimization factors: age (categories: 18-25, 26-35, 36-45, 46-55), gender
204 (categories: male, female), BMI (categories: 19 – 24.9 normal weight, 25 – 29.9 overweight, 30
205 – 35 moderately obese) and experience with meditation and yoga (categories: never, 0 – 2

206 years, 2 – 5 years, 5 – 10 years, > 10 years). Experience with meditation and yoga was assessed
207 by means of an in-house self-report questionnaire.

208

209 The programs were matched in terms of time, effort, and group contact, but differed
210 significantly in terms of content. Both programs consisted of 8 weekly, 2.5 hour group sessions
211 from 7PM-9:30PM, plus one day dedicated (6 hours) to the intervention goals. Subjects were
212 asked to spend 45 minutes per day on homework assignments and to record the amount of
213 time spent on homework forms. The intervention programs were described as “eating with
214 attention” (ME) and “eating with knowledge” (EC) to prevent a selection-bias of subjects
215 interested in mindfulness. Only after the first test session, subjects were informed about the
216 intervention to which they were randomized, to ensure that baseline measurements were not
217 influenced by intervention expectations. Because group size was set to 10 to 15 subjects per
218 round, included subjects were divided across three rounds for each intervention (3xME, 3xEC).
219 The final sample for analyses consisted of 32 subjects in the ME intervention and 26 subjects in
220 the EC intervention (for a flow diagram see **Figure 1**). Between groups, the number of people
221 excluded from analysis was not significantly different (ME: 28.8%, EC: 44.7%, $\chi^2(1, N = 92) =$
222 2.461, $p = .117$).

223

224 *Mindful eating (ME)*

225 The aim of the ME intervention was to increase experiential awareness of food and eating (e.g.
226 being more aware of food taste and smell, thoughts and feelings during eating or cravings, and
227 internal signals like satiety). The ME program was based on the original MBSR program

228 developed by Kabat-Zinn et al. (1990) at the Stress Reduction and Relaxation Clinic,
229 Massachusetts Medical Center. Subjects performed formal mindfulness practices (i.e. body
230 scan, sitting meditation, walking meditation and mindful movement), aimed at increasing
231 general mindfulness skills, which were similar to the original program. In addition, subjects
232 performed informal mindfulness practices based on the Mindful Eating, Conscious Living
233 program (MECL; Bays, 2009), which were mainly directed to mindful eating and not part of the
234 original MBSR program. Sessions focused on themes, such as: the automatic pilot, perception of
235 hunger and other internal states, creating awareness for boundaries in eating behavior, stress-
236 related eating, coping with stress, coping with (negative) thoughts, self-compassion, and how to
237 incorporate mindfulness in daily life. Towards the end of the program, subjects had a silent day.
238 During this day, the whole group performed formal mindfulness exercises and ate a meal
239 together in complete silence. Homework consisted of a formal mindfulness practice, using CDs
240 with guided mindfulness exercises, and an informal mindfulness practice directed at one
241 moment (e.g. a meal) a day. Time spent on homework was noted on homework forms every
242 day. The ME intervention was developed and delivered by qualified psychologists/psychiatrists,
243 who graduated from the post-graduate mindfulness teacher training at the Radboud University
244 Medical Centre for Mindfulness.

245

246 *Educational Cooking (EC)*

247 The aim of the EC intervention was to increase informational awareness of food and eating. The
248 program was based on the Dutch healthy diet guidelines (www.voedingscentrum.nl). The EC
249 program was based on the Dutch healthy diet guidelines (voedingscentrum.nl). To establish

250 similar group contact and activities (vs. passive listening) as in the ME, subjects were actively
251 enrolled in cooking workshops during the group meetings of the EC. Sessions focused on
252 healthy eating, healthy cooking of vegetables and fruit, use of different types of fat and salt for
253 cooking, reading of nutrition labels on food products, healthy snacking, guidelines for making
254 healthy choices when eating in restaurants, and how to incorporate healthy eating and cooking
255 in daily life. Towards the end of the program, subjects had a balance day, during which the
256 subjects adhered to all nutritional health guidelines for every snack and meal. Homework
257 assignments entailed practicing cooking techniques, or grocery shopping with informational
258 awareness (i.e. reading food labels for nutritional content), and counting the amount of calorie
259 intake for one meal a day (to be noted in a homework diary). The EC intervention was
260 developed and delivered by a qualified dietitian from Wageningen University and the cooking
261 sessions were guided by a professional chef. Sessions took place at a large kitchen facility of the
262 Nutrition and Dietetics faculty of the Hogeschool of Arnhem-Nijmegen.

263

264 **Behavioral analyses**

265 Between-group comparisons were analyzed using independent-samples t-tests, Fisher's Exact
266 Tests, or Mann-Whitney U tests. Effects of training on physical and neuropsychological
267 measurements were analyzed using repeated-measures ANOVA with Time (pre, post) as within-
268 subject factor and Intervention (ME, EC) as between-subject factor. Mean latencies of the
269 correct manual responses (i.e. when subjects pressed in time) were analyzed using repeated-
270 measures ANOVA with within-subject factors Reward (high, low), Domain (caloric, monetary),
271 Time, and the between-subject factor Intervention (ME, EC). Specific effects were tested with

272 subsequent F-tests. All analyses were performed using two-tailed tests in SPSS (version 23.0,
273 Chicago, IL). The significance level was set at an alpha of $p=0.05$.

274

275

276

277 **fMRI acquisition and analyses**

278 We acquired whole-brain functional images (multi-echo) on a Siemens 3T Skyra MRI scanner
279 (Siemens Medical system, Erlangen, Germany) using a 32-channel coil to measure blood oxygen
280 level dependent (BOLD) contrast. A multi-echo echo-planar imaging (EPI) sequence was used to
281 acquire 34 axial slices per functional volume in ascending direction (voxel size 3.5x3.5x3mm;
282 repetition time (TR) 2070 ms; TE 9ms, 19.25ms, 29.5ms, and 39.75ms; flip angle 90 °; field of
283 view 224mm). This is a method that uses accelerated parallel imaging to reduce image artifacts
284 (in plane acceleration 3) and acquire images at multiple TEs following a single excitation (Poser
285 et al., 2006). Before the acquisition of functional images, a high-resolution anatomical scan was
286 acquired (T1-weighted MPRAGE, voxel size 1x1x1mm, TR 2300ms, TE 3.03ms, 192 sagittal slices,
287 flip angle 8 °, field of view 256 mm).

288

289 Data were pre-processed and analyzed using SPM8 (www.fil.ion.ucl.ac.uk/spm). The volumes
290 for each echo time were realigned to correct for motion artefacts (estimation of the
291 realignment parameters is done for the first echo and then copied to the other echoes). The
292 four echo images were combined into a single MR volume based on 31 volumes acquired
293 before the actual experiment started using an optimised echo weighting method (Poser et al.,

294 2006). Combined functional images were slice-time corrected by realigning the time-series for
295 each voxel temporally to acquisition of the middle slice. Subject-specific structural and
296 functional data were then coregistered to a standard structural or functional stereotactic space
297 (Montreal Neurological Institute (MNI) template). After segmentation of the structural images
298 using a unified segmentation approach, structural images were spatially coregistered to the
299 mean of the functional images. The resulting transformation matrix of the segmentation step
300 was then used to normalize the anatomical and functional images into Montreal Neurological
301 Institute space (resampled at voxel size 2 x 2 x 2). Finally, the normalized functional images
302 were spatially smoothed using an isotropic 8 mm full-width at half-maximum Gaussian kernel.

303
304 Statistical analyses of fMRI data at the individual subject (first) level were performed using an
305 event-related approach and included 13 regressors-of-interest: four regressors for cue
306 presentation (high and low caloric cues, high and low monetary cues), one regressor for target
307 presentation, four outcome regressors for hits (high and low caloric hits, high and low
308 monetary hits), and four outcome regressors for trials on which subjects responded too late
309 (high and low caloric too late, high and low monetary too late). If subjects failed to respond on
310 a trial (i.e. a miss), the trial was excluded from analyses. Onsets of the regressors were modeled
311 as a stick function (duration=0) convolved with a canonical hemodynamic response function
312 (Friston et al., 1998). Twelve rigid-body transformation parameters (three translations and
313 rotations, and their linear derivatives) obtained during realignment and a constant term were
314 included as regressors of no-interest. High pass filtering (128 seconds) was applied to the time

315 series of the functional images to remove low-frequency drifts and correction for serial
316 correlations was done using an autoregressive AR(1) model.

317

318 We ran two general linear models (GLMs) at the second level: one for reward anticipation with
319 high minus low reward cue contrast images, and one for reward receipt with hit minus too late
320 contrast images. Analysis of variance (ANOVA) was performed in a full-factorial design, with
321 between-subject factor Intervention and within-subject factors Time and Domain, resulting in 8
322 cells. Effects were considered statistically significant when reaching a threshold of $p < 0.05$,
323 family wise error (FWE) corrected for multiple comparisons at the peak level, whole brain or in
324 the *a priori* defined regions of interest (see below). Interaction effects of interest are also
325 reported at $p < .001$ (uncorrected for multiple comparisons at the peak level).

326

327 To further investigate the effects of intervention on reward anticipation and receipt, region-of-
328 interest (ROI) analyses were performed for midbrain and striatum using *a priori* defined ROIs for
329 midbrain and striatum. ROIs were anatomically defined based on the Hammersmith atlas (Hammers et
330 al., 2003): bilateral substantia nigra for *midbrain* (74;75; Gousias et al., 2008), and bilateral caudate
331 nucleus (34;35), nucleus accumbens (36;37) and putamen (38;39) for *striatum* (Hammers et al., 2003).
332 Mean beta weights were extracted from all voxels in both ROIs separately using MarsBar (Brett
333 et al., 2002). The regionally averaged beta-weights were analyzed using ANOVA with the same
334 factors as in the whole-brain analyses. As two ROIs were tested, effects were considered
335 significant when reaching a threshold of $p < .025$ (Bonferroni corrected for multiple
336 comparisons).

337

338 **Results**

339 **Behavioral results**

340 *Characterization of intervention groups*

341 The mindful eating (ME) and educational cooking (EC) groups were well matched in terms of
342 the minimization factors age, gender, body mass index (BMI) and experience with meditation
343 and yoga (**Table 1**). Note that the groups differed marginally significantly in terms of
344 educational level. However, *post hoc* correlation analyses revealed no correlations between
345 educational level and the neural effects described below and is therefore unlikely to drive these
346 effects. Furthermore, the total time subjects spent on the intervention, and the number of
347 sessions subjects attended did not differ significantly between the two groups (**Table 1**).

348

349 *Anthropometric and neuropsychological measures*

350 The interventions had differential effects on the anthropometric measures as indicated by a
351 significant Time x Intervention interaction (**Table 2**), i.e. BMI and waist were decreased
352 following EC (main Time: BMI: $F(1,25)=6.2$, $p=.020$; waist circumference: $F(1,25)=17.9$, $p<.001$),
353 but not following ME (main Time: BMI: $F(1,31)<1$, $p=.647$; waist circumference: $F(1,31)<1$,
354 $p=.504$). Furthermore, we found that EC subjects reported closer compliance to the Dutch
355 guidelines for healthy eating (main Time: $F(1,25)=12.8$, $p=.001$) than ME subjects (main Time:
356 $F(1,31)=1.4$, $p=.244$) as substantiated by a significant Time x Intervention interaction for FFQ-
357 DHD scores (**Table 2**). EC subjects also showed a significant increase in knowledge on healthy
358 eating following the intervention (main Time; $F(1,25)=48.8$, $p<.001$), whereas ME subjects did

359 not (main Time: $F(1,31)<1$, $p=.394$) as evidenced by a significant Time x Intervention interaction
360 for FBQ scores (**Table 2**). Analysis of the other neuropsychological measurements revealed no
361 significant interactions between Time and Intervention (**Table 2**).

362

363 *Response times*

364 On average, 59.6% (SD: 10.0) of the trials were hit trials. Subjects responded faster on high
365 rather than low reward hit trials (main Reward: $F(1,56)=25.0$, $p < .001$), thus revealing a reward
366 benefit. In addition, subjects responded faster to monetary relative to caloric reward cues
367 (main Domain: $F(1,56)=17.4$, $p<.001$). We observed a reward benefit for both caloric
368 ($F(1,115)=5.8$, $p=.018$) and monetary trials ($F(1,115)=37.3$, $p<.001$), which was, however, larger
369 in the latter trials (Reward x Domain interaction: $F(1,56)=9.0$, $p=.004$). Finally, subjects' mean
370 response times were lower on post relative to pre test sessions (pre: 310.66 (SD: 21.3), post:
371 304.60 (SD: 20.8) ms; main Time: $F(1,56)=17.4$, $p<.001$). We found no significant 4-way
372 interaction with Intervention ($F(1,56)<1$).

373

374 **Neuroimaging results**

375 *Reward Anticipation*

376 First, brain regions were identified that responded to reward anticipation (main effect of
377 Reward condition: high>low). At our whole-brain corrected threshold ($FWE<.05$, peak-level),
378 this contrast yielded significant responses in striatum (bilateral caudate nucleus) and bilateral
379 midbrain regions, as well as in occipital, motor and frontal regions (**Figure 3a; Table 3**). In
380 addition, striatal (left putamen and right caudate nucleus) and bilateral inferior occipital regions

381 demonstrated greater responses for anticipation to monetary than caloric reward cues (i.e.
382 interaction of Domain x Reward)(Table 3).

383

384 Second, we were interested in the effects of ME on reward anticipation in *a priori* defined
385 regions-of-interest (ROIs: striatum and midbrain). When using our ROIs as small search
386 volumes, we found a significant Reward x Domain x Time x Intervention interaction in bilateral
387 midbrain (FWE<.05, SVC, peak-level; Figure 3b; Table 3), but not in the striatum. To disentangle
388 the observed four-way interaction in the midbrain, we performed ROI analyses (Figure 3c) using
389 a bilateral structural ROI (see Materials and methods). As expected, we found the same four-
390 way interaction in the ROI betas ($F(1,56)=6.0$, $p=.018$, $\alpha=.025$). *Post hoc* analyses revealed that
391 this effect was driven by a significant reduction in midbrain responses on post relative to pre
392 measurement in anticipation of specifically caloric cues following the ME (Time x Reward:
393 $F(1,31)=6.4$, $p=.016$, $\alpha=.025$), but not the EC intervention (Time x Reward: $F(1,25)=3.6$, $p=.070$).
394 There was no significant difference for the monetary domain following either the ME (Time x
395 Reward: $F(1,31)=1.9$, $p=.181$) or the EC intervention (Time x Reward: $F(1,25)<1$).

396

397 Because we observed significant pre-intervention differences in midbrain caloric reward
398 anticipatory activity between the two groups ($t(56)=2.4$, $p=.021$)(Figure 4), we performed *post*
399 *hoc* sub-group analyses to test whether the observed four-way interaction was the result of a
400 potential floor effect in the EC group. For this analysis, we only included subjects with midbrain
401 ROI betas for caloric reward anticipation larger than zero. This resulted in a sample of 20 ME,
402 and 10 EC subjects. The same analyses as described previously were performed on this sample.

403 There were no between-group pre-differences on the midbrain caloric betas ($t(56)=1.3$, $p=.213$)
404 in this sample. Importantly, the four-way interaction remained marginally significant
405 ($F(1,28)=3.5$, $p=.072$), again driven by a significant post versus pre reduction in caloric reward
406 anticipation in ME (Time x Reward: $F(1,19)=10.5$, $p=.004$, $\alpha=.025$), but not in EC (Time x Reward:
407 $F(1,9)<1$).

408
409 To rule out that the observed interaction effect in midbrain can be explained by the group
410 difference in BMI and waist circumference, we added difference scores for BMI and waist
411 circumference (post-pre) as covariates to the analyses of the midbrain ROI betas. The Reward x
412 Domain x Time x Intervention interaction remained significant when correcting for BMI and
413 waist circumference (4-way interaction with BMI covariate: $F(1,55)=5.2$, $p=.026$; with waist
414 circumference covariate: $F(1,55)=7.3$, $p=.009$).

415
416 *Reward Receipt*
417 No significant main effects of Intervention or interactions with Intervention were found for
418 BOLD responses to reward receipt in whole-brain analyses, nor in ROI analyses using *a priori*
419 defined ROIs for striatum and midbrain. For main effects and other interaction effects of
420 reward receipt see **Table 4**.

421
422 **Discussion**
423 The aim of this study was to investigate the effects of an 8-week mindful eating intervention on
424 subcortical reward anticipation using an incentive delay task. Consistent with our hypothesis,

425 we found that anticipatory midbrain BOLD responses to caloric reward cues were decreased
426 following the mindful eating (ME), but not the educational cooking (EC; active control)
427 intervention. Anticipatory sub-cortical BOLD responses to monetary reward cues were not
428 affected by either intervention. The effects were specific to reward anticipation and did not
429 extend to reward receipt. Physical measures of obesity (i.e. BMI and waist circumference) were
430 decreased following the educational cooking intervention, but not following the mindful eating
431 intervention.

432

433 Dopaminergic midbrain neurons are crucial for processing predicted reward value (Schultz,
434 2006; Haber and Knutson, 2010) and, in concert with striatum, modulate motivated behavior
435 such as eating (Berridge, 2009). In line with this, Small et al. (2001) showed that midbrain
436 activity as measured by positron emission tomography ($H_2^{15}O$) decreased with reduced self-
437 reported reward value of chocolate while a sample of healthy individuals ate chocolate beyond
438 satiety. In another study, midbrain BOLD responses to sips of palatable milkshake were found
439 to positively correlate with subsequent *ad libitum* milkshake intake in a group of healthy-weight
440 to moderately obese individuals (Nolan-Poupart et al., 2013). More specifically, previous
441 studies have shown that reduced subcortical reward responses to caloric cues, particularly in
442 striatum are associated with obesity (Rothmund et al., 2007; Stoeckel et al., 2008), with
443 weight gain (Demos et al., 2012), and with increased snack food intake in healthy-weight to
444 overweight individuals (Lawrence et al., 2012). Furthermore, both midbrain and striatal BOLD
445 responses to palatable food pictures was found to correlate positively with self-reported
446 reward drive in healthy individuals (Beaver et al., 2006). These (indirect) measures of motivated

447 eating behavior are thus associated with greater subcortical responses when processing
448 predicted food reward value. In this study we observed intervention effects on caloric reward
449 anticipation (i.e. high caloric drink versus water) – in an, on average, overweight sample of
450 subjects motivated to change their bad eating habits – only in the midbrain, and not in the
451 striatum. This is in accordance with a study in healthy individuals by O’Doherty and colleagues
452 (2002), who found significant responses to cues predicting the receipt of a glucose solution
453 versus a neutral taste in midbrain only, whereas both midbrain and striatum were responsive to
454 cues predicting the receipt of a sweet versus an aversive salty taste; the latter may be a larger
455 contrast in terms of valence. Given the coding of predicted reward in the midbrain, the
456 currently observed effect of the mindful eating intervention on anticipatory midbrain responses
457 to caloric cues suggests that mindfulness may be able to affect overeating by reducing the
458 impact of food cues on reward processing, as it has been shown to reduce subcortical amygdala
459 responses to emotional stimuli (Tang et al., 2015).

460

461 Indeed, several studies have found that an intensive mindful eating intervention led to reduced
462 measures of overeating such as consumption of sweets (Mason et al., 2015), binges, externally
463 and emotionally driven eating (Alberts et al., 2012) and reductions in BMI (Tapper et al., 2009)
464 in non-clinical populations, as well as number of binges in binge-eating disorder (Kristeller et al.,
465 2013). However, in this study we did not find evidence for decreased overeating, as physical
466 measures of obesity (i.e. BMI and waist circumference) were not affected in the month
467 following the ME intervention. A reason for not finding ME intervention-related reductions in
468 our secondary measures such as BMI or waist circumference is that it may take a few months

469 before mindfulness manifests itself in an individual's behavior following a mindfulness-based
470 intervention (Tapper et al., 2009; Mason et al., 2015). In addition, mindfulness is aimed at
471 stimulating acceptance (Bishop et al., 2004) and has been found to decrease body image
472 concern in healthy women with disordered eating behavior (Alberts et al., 2012). Although we
473 did not measure body image concern, this may have reduced the explicit motivation to lose
474 weight in part of our healthy subject sample. Alternatively, the heterogeneity of our sample in
475 terms of motivation might explain the lack of mindfulness-mediated changes in eating behavior
476 as measured in this study. Although all subjects were motivated to change their bad eating
477 habits, some wanted to lose weight, whereas others aimed for a healthier or more regular
478 eating pattern. Unfortunately, we did not systematically record individuals' motivations.
479 Sampling from a more homogeneous population in terms of motivation or recording these data
480 is advised for future studies.

481

482 In contrast, we did observe beneficial effects of the EC intervention on physical measures of
483 obesity and self-reported eating behavior in the absence of effects on subcortical reward
484 anticipatory responses. The beneficial effects might not be surprising for this group, since the
485 EC intervention was explicitly aimed at more healthy food intake, with reduced intake of sugar,
486 fats and salt as part of the homework assignments and, thus, more likely to result in reduced
487 BMI and waist circumference, independent of subjects' motivation. However, it is unclear how
488 the small reductions in physical measures of obesity that were observed in the current study
489 translate to long-term health benefits, in particular considering the low success rate of weight

490 loss maintenance following standard weight loss programs (Wing and Phelan, 2005), and the
491 absence of changes in neurocognitive measures as measured here.

492

493 Our finding that reduced anticipatory midbrain responses were specific to the caloric domain is
494 in line with a previous study showing that only a brief 50-min mindful eating workshop (versus
495 an educational video) reduced subsequent impulsive choice patterns for food-, but not money-
496 related outcomes (Hendrickson and Rasmussen, 2013). However, meditators have been found
497 to exhibit reduced striatal BOLD responses to primary reward prediction errors (Kirk and
498 Montague, 2015) as well as monetary reward anticipation (Kirk et al., 2014a) relative to non-
499 meditating controls. In the latter study, Kirk and colleagues (2014a; 2015) compared meditators
500 to non-meditators without a baseline measurement. The observed decrease in striatal reward
501 processing could thus be due to pre-existing between-group differences (Mascaro et al., 2013).
502 Since the present study is actively controlled including pre and post measurements, the current
503 effects can be ascribed to the mindfulness intervention. Kirk and colleagues (2014b) recently
504 also performed a randomized actively controlled study including pre and post measurements
505 and found that vmPFC value signals were modulated by the mindfulness intervention for both
506 primary (juice) and secondary (monetary) rewards. These general reward effects versus our
507 specific caloric effects might be due to both the type of intervention (general MBSR in Kirk et al.
508 (2014b) versus mindful eating presently) as well as the study sample. Specifically, in our study,
509 subjects were highly motivated to change undesired eating habits and their mindfulness
510 practice was targeted at overcoming those. Note that we did not observe any effects of either
511 intervention on neural responses at the time of caloric or monetary reward receipt. One might

512 expect reductions in vmPFC BOLD responses following the mindfulness-based intervention as
513 was recently reported by Kirk et al. (2014b) for juice delivery. However, another important
514 difference with the current study is that we used promised (i.e. delivered after scanning)
515 instead of actual rewards (delivered during scanning). Moreover, our design was optimized for
516 reward anticipation, with perhaps not enough successful reward receipt trials (i.e.
517 approximately 33% of all anticipated rewards were missed). Together, our results suggest that a
518 targeted mindfulness-based intervention – including homework practices such as resisting
519 impulsive eating behaviors – may have highly specific effects on (here, food) reward
520 anticipation.

521
522 In conclusion, we found that an intensive mindful eating intervention reduced midbrain food
523 anticipation. Future studies are required to demonstrate the clinical relevance of mindfulness-
524 mediated reductions in food anticipation for counteracting reward cue-driven overeating,
525 particularly in our obesogenic environment with food cues everywhere. Given the success of
526 mindfulness-based programs in reducing symptoms of other reward-related disorders such as
527 substance use (Brewer et al., 2011; Witkiewitz et al., 2014) and problem gambling (Toneatto et
528 al., 2014), these interventions may also act by reducing anticipatory reward responses to the
529 target of abuse and thereby reducing consumption and relapse rate.

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703 **Tables**

704 **Table 1** Between-group (ME, EC) comparisons.

	mindful eating (ME)			educational cooking (EC)			<i>p</i> -value	<i>test-statistic</i>
n	32			26				
Gender (Male:Female)	5 : 27			5 : 21			.740	na ^a
Age (yrs)	32.3	±10.8	20-52	30.6	±11.3	19-51	.546	.607 ^b
Education (NLV)	6.5	±0.6	5-7	6.2	±0.7	5-7	.053	304.0 ^c
Digit span (total score)	15.6	±3.5	9-23	14.1	±3.5	9-22	.120	1.577 ^b
Smoking (FTND score)	0.19	±1.1	0-6	0.04	±0.2	0-1	.902	413.5 ^c
Body mass index (kg/m ²)	26.6	±4.1	19-35	25.5	±3.4	20-33	.296	1.054 ^b
Waist circumference (cm)	89.6	±12.8	72-122	86.5	±11.7	70-117	.338	.967 ^b
Yoga/meditation experience (yrs)	1.0	±2.6	0-14	1.9	±4.3	0-19	.334	-.974 ^b
Time on training (hrs)	31.0	±14.4	2.5-47.8	23.9	±21.2	0-77.7	.135	1.518 ^b
Attendance < 4 sessions (n)	5			5			.740	na ^a
Attendance (number of sessions)	6.5	±2.5	1-9	6.3	±2.8	1-9	.738	0.336 ^b

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

706 *NLV*: the Dutch version of the National Adult Reading Test was administered to assess education ; *FTND*: Fagerstrom Test for

707 Nicotine Dependence .

708 ^a Based on Fisher's Exact Test, ^b Independent samples t-test (degrees of freedom: 56) ^c Mann-Whitney test

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711 **Table 2** Means and standard deviations, pre- and post-training, for each group (ME, EC) separately, and

712 Time (pre, post) x Intervention (ME, EC) statistics.

	mindful eating (ME)		educational cooking (EC)		<i>p</i>	<i>test-statistic^a</i>
	pre	post	pre	post		
Physical measurements						
BMI (kg/height(m) ²)	26.6 ±4.1	26.6 ±4.2	25.5 ±3.4	25.2 ±3.5	.023	5.5
Waist (cm)	89.6 ±12.8	89.3 ±13.2	86.5 ±11.7	84.4 ±11.7	.026	5.2
Neuropsychological measurements / self-report						
Digit Span (total score)	15.6 ±3.5	15.2 ±3.6	14.1 ±3.5	13.5 ±3.7	.689	< 1
PANAS						
<i>Positive Affect</i>	31.8 ±6.5	30.0 ±6.1	31.4 ±4.8	29.8 ±5.1	.772	< 1
<i>Negative Affect</i>	12.7 ±2.8	13.9 ±4.3	12.7 ±2.6	13.4 ±3.6	.602	< 1
FTND (smoking score)	0.19 ±1.1	0.19 ±1.1	0.04 ±0.2	0.04 ±0.2	1.000	416 ^b
BIS-11	62.0 ±9.3	62.1 ±9.0	64.5 ±8.7	63.7 ±8.3	.492	< 1
BIS	20.8 ±3.3	20.3 ±3.2	19.8 ±3.3	19.6 ±3.3	.671	< 1
BAS	41.5 ±3.3	42.3 ±4.0	43.2 ±4.1	42.7 ±4.1	.101	2.8
Kirby	0.01 ±0.023	0.015 ±0.023	0.020 ±0.045	0.011 ±0.017	.094	2.9
3						
FFQ – DHD	52.2 ±10.4	54.2 ±10.0	51.6 ±12.0	59.5 ±10.8	.036	4.6
FBQ – short version	64.0 ±7.0	62.8 ±5.6	62.1 ±4.8	62.7 ±6.3	.264	1.3
<i>Knowledge</i>	15.6 ±1.5	15.8 ±1.3	14.9 ±1.5	16.7 ±0.8	<.001	19.6
<i>Temptation</i>	15.0 ±3.2	14.4 ±3.3	14.8 ±3.3	14.5 ±4.0	.729	< 1
DEBQ						
<i>Restraint</i>	2.8 ±0.6	2.9 ±0.6	2.9 ±0.7	2.9 ±0.6	.814	< 1
<i>Emotional</i>	2.8 ±0.8	2.8 ±0.8	2.8 ±0.7	2.7 ±0.9	.728	< 1

<i>External</i>	3.2 ±0.4	3.2 ±0.5	3.4 ±0.5	3.1 ±0.5	.120	2.5
FFMQ-SF ^c	78.1 ±7.7	76.8 ±7.4	76.5 ±8.6	75.7 ±7.9	.671	< 1
HADS						
<i>Anxiety</i>	4.4 ±2.4	6.0 ±2.5	4.8 ±2.5	6.2 ±3.9	.902	< 1
<i>Depression</i>	2.6 ±2.4	2.8 ±2.4	2.4 ±2.3	2.7 ±2.6	.864	< 1
TCQ ^d	30.0 ±7.4	27.8 ±8.4	32.7 ±4.8	32.8 ±8.1	.215	1.6
Wanting						
<i>Low caloric reward</i>	4.5 ±2.8	4.6 ±2.8	4.5 ±3.1	4.6 ±2.8	.987	< 1
<i>High caloric reward</i>	6.3 ±2.0	5.8 ±2.4	5.4 ±3.0	5.6 ±2.4	.330	< 1
<i>Low monetary reward</i>	1.9 ±2.4	1.5 ±2.0	2.2 ±2.5	2.4 ±2.6	.318	1.0
<i>High monetary reward</i>	5.2 ±2.8	5.4 ±2.7	5.0 ±3.2	5.4 ±2.4	.840	< 1
Liking						
<i>Low caloric reward</i>	6.4 ±2.3	6.1 ±2.2	6.2 ±2.7	6.6 ±2.2	.187	1.8
<i>High caloric reward</i>	7.2 ±1.6	6.7 ±2.1	6.8 ±2.9	6.4 ±2.7	.783	< 1
<i>Low monetary reward</i>	2.2 ±2.4	2.2 ±2.2	2.8 ±2.4	2.8 ±2.3	.967	< 1
<i>High monetary reward</i>	5.1 ±2.5	5.2 ±2.4	4.4 ±2.7	5.3 ±2.2	.143	2.2
Response Times						
<i>Low caloric reward</i>	313.7 ±41.0	312.4 ±33.8	322.5 ±51.6	312.6 ±43.8	.319	1.0
<i>High caloric reward</i>	303.4 ±33.8	299.1 ±31.5	322.2 ±50.0	311.8 ±48.4	.471	< 1
<i>Low monetary reward</i>	313.0 ±47.0	311.2 ±44.2	317.4 ±44.8	313.3 ±49.6	.834	< 1
<i>High monetary reward</i>	294.7 ±26.2	285.1 ±32.5	302.3 ±41.5	293.9 ±43.0	.874	< 1
Hunger ^b	5.9 ±2.6	5.9 ±2.7	5.9 ±3.0	5.6 ±2.9	.835	< 1
Thirst ^b	5.7 ±2.6	5.9 ±2.8	6.0 ±2.4	5.5 ±2.4	.273	1.2
Satiety ^b	2.3 ±2.1	2.1 ±0.9	1.9 ±1.1	2.1 ±1.2	.345	< 1

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

714 PANAS: Positive And Negative Affect Scale; FTND: Fagerstrom Test for Nicotine Dependence ; BIS-11: Barratt Impulsiveness

715 Scale-11; BIS/BAS: Behavioral Inhibition System / Behavioral Approach System questionnaire; Kirby: delayed reward discounting

716 questionnaire; *FFQ-DHD*: Food Frequency Questionnaire, Dutch Healthy Diet; *FBQ*: Food Behavior Questionnaire, a shortened
717 version; *DEBQ*: Dutch Eating Behaviour Questionnaire; *FFMQ-SF*: Five Facet Mindfulness Questionnaire – Short Form; *HADS*:
718 Hospital Anxiety and Depression Scale; *TCQ*: Treatment Credibility Questionnaire. Note that the pre-training TCQ was filled out
719 at the first training session, not on the pre-training test session, as subjects were unaware of the contents of their training at
720 that time.

721 ^aIf not otherwise stated, the reported test-statistic is the F-value (degrees of freedom: 1,56)

722 ^bMann-Whitney U

723 ^cFFMQ-SF: N = 48 (N_{ME} = 22, N_{EC} = 26; degrees of freedom: 1,46)

724 ^dTCQ, Hunger, Thirst, Satiety: N = 55 (N_{ME} = 29, N_{EC} = 26; degrees of freedom: 1,53).

725

726 **Table 3** Summary of brain regions exhibiting main effects of reward, domain and/or interactions with
 727 domain, intervention, and time at the time of reward anticipation.
 728

Label	Side (Left/Right)	MNI-coordinates x, y, z (mm)				Size (number of voxels)	<i>p</i> FWE (peak-level)	<i>t</i> -value ^a (peak)
Main effect of Reward: high > low^b								
Inferior occipital lobe	R	24	-94	-4	1319	< .001	12.99	
Cerebellum	R	36	-58	-20		< .001	5.96	
Inferior occipital lobe	L	-22	-96	-4	1459	< .001	11.47	
Caudate nucleus	R	10	10	-2	1145	< .001	7.70	
Caudate nucleus	L	-8	10	-4		< .001	7.49	
Thalamus	L	-4	-18	8		.003	5.48	
Superior motor area	L	-6	-2	58	2134	< .001	6.32	
Precentral	L	-38	-14	52		< .001	6.23	
Superior motor area	R	6	6	56		< .001	6.23	
Precentral	R	52	0	50	25	.012	5.13	
Premotor cortex	R	42	0	58		.037	4.85	
Insula	L	-32	28	4	2	.026	4.94	
Midbrain	R	8	-28	-8	1	.043	4.81	
Midbrain	L	-6	-28	-8	2	.044	4.80	
Insula	L	-30	28	0	2	.050	4.77	
Main effect of Reward: low > high reward^b								
Frontal superior lobe	R	18	26	50	7	.023	4.97	
Interaction effect of Reward x Domain: monetary (high > low reward) > caloric (high > low reward)^b								
Inferior occipital lobe	L	-20	-96	-4	1511	< .001	19.96	

Inferior occipital lobe	R	24	-92	-6	1349	< .001	18.71
Putamen	L	-20	22	-8	1	.037	4.85
Caudate nucleus	R	12	10	4	1	.047	4.79
<hr/>							
Interaction effect: Reward x Domain x Time x Intervention ^c							
<hr/>							
Midbrain	R	12	-18	-12	8	.005	3.64
Midbrain	L	-10	-22	-12	13	.005	3.64
Midbrain	L	-12	-18	-12		.006	3.54
Midbrain	L	-8	-18	-14		.010	3.40
<hr/>							

729 ^aDegrees of freedom: 1, 224; ^b $p < .05$, whole brain family wise error (FWE) corrected; ^c $p < .05$, small volume, FWE corrected.

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731

732 **Table 4.** Summary of brain regions exhibiting main effects of reward, domain and/or interactions with
 733 domain, training, and time at the time of reward receipt.

Label	Side (Left/Right)	MNI-coordinates x, y, z (mm)			Size (number of voxels)	<i>p</i> FWE (peak- level)	<i>t</i> -value ^a (peak)
Main effect of receipt: hits (high > low) > too lates (high > low) ^b							
Temporal inferior lobe	L	-52	-48	-14	36815	< .001	13.32
Striatum	L	-14	6	-12		< .001	12.08
Caudate	R	12	10	-8		< .001	11.27
Frontal medial lobe	L	-20	24	50	1612	< .001	9.34
Frontal medial lobe	L	-30	18	54		< .001	8.95
Frontal superior lobe	R	22	30	48	318	< .001	6.16
Frontal medial lobe	R	30	12	52		< .001	6.08
Frontal superior lobe	L	22	6	48		.025	4.98
Frontal inferior lobe	R	46	38	16	63	.001	5.70
Thalamus	L	0	-14	18	5	.022	5.01
Temporal medial lobe	L	-62	-12	-22	3	.035	4.89
Main effect of receipt: too lates (high > low reward) > hits (high > low reward) ^b							
Temporal medial lobe	R	48	-28	-6	1183	< .001	11.47
Supramarginal	R	62	-46	32		< .001	9.15
Temporal medial lobe	R	62	-46	12		.004	5.43
Frontal inferior lobe	R	46	22	4	837	< .001	7.83
Frontal inferior lobe	R	56	24	16		.002	5.53
Insula	L	-32	20	-10	339	< .001	6.85
Insula	L	-36	20	8		< .001	6.83
Insula	L	-30	28	0		.001	5.75

Superior motor area	R	8	16	60	235	< .001	6.61
Supramarginal	L	-62	-44	28	144	< .001	6.61
Temporal medial lobe	L	-50	-28	-4	61	< .001	6.16
Frontal medial lobe	R	26	50	24	108	< .001	5.89
Anterior cingulate	R	8	26	32	41	.007	5.30
Anterior cingulate	R	10	16	38		.026	4.97
Midbrain	L	-6	-26	-2	6	.010	5.19
Midbrain	R	6	-26	-2	7	.011	5.18
Temporal medial lobe	L	-54	6	-16	6	.019	5.04

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))^b

Lingual	R	18	-84	-4	116	< .001	7.02
Lingual	L	-14	-88	-4	1	.023	5.01

734 ^a Degrees of freedom: 1,224; ^b $p < .05$, whole brain FWE corrected.

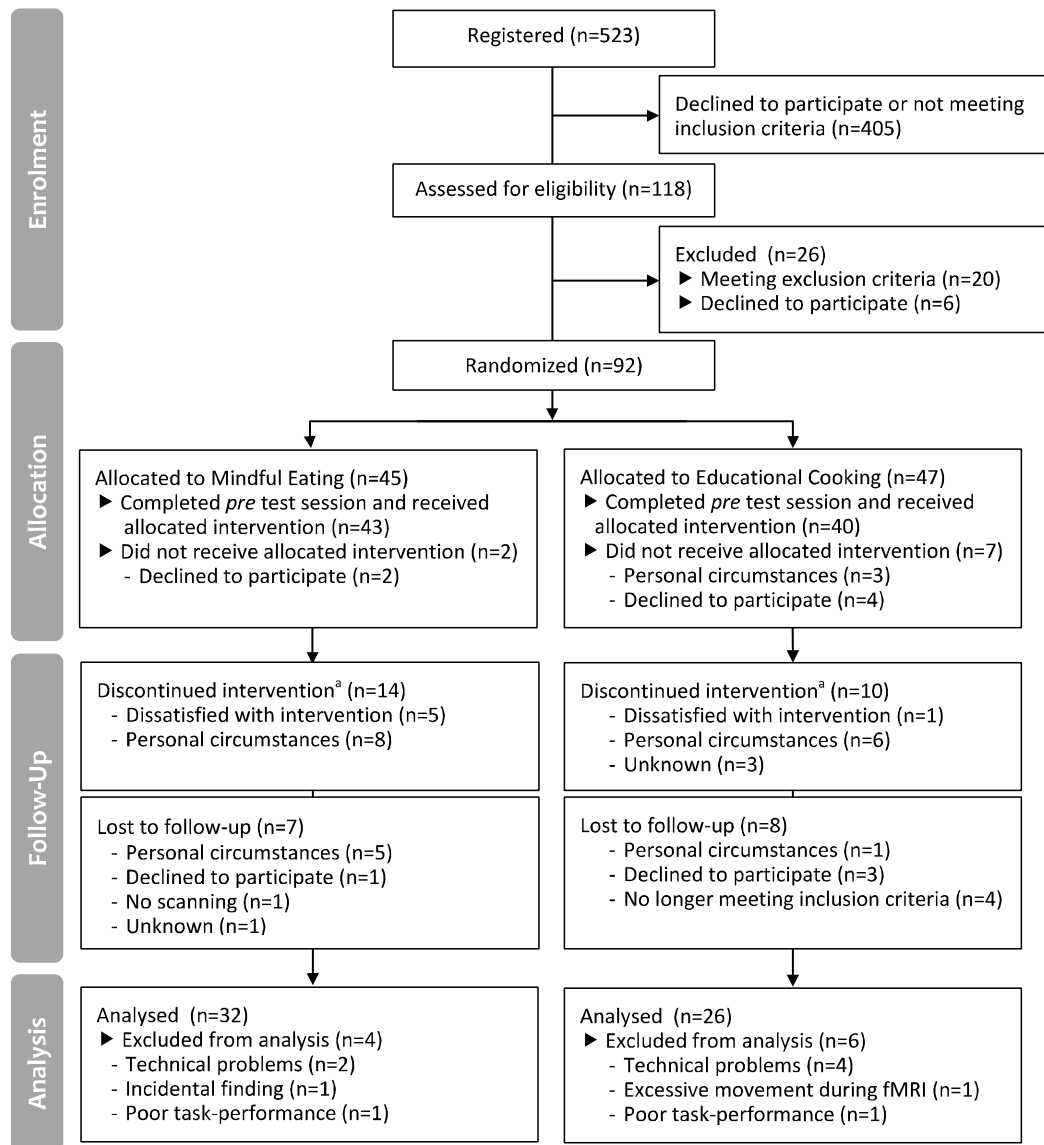
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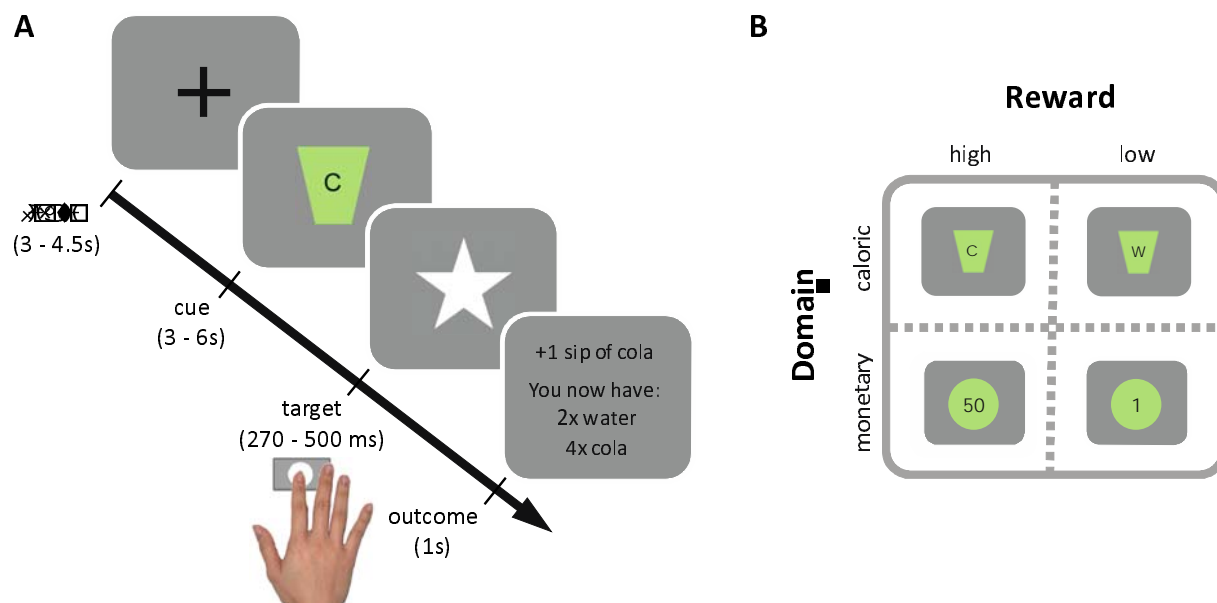
739 **Figures**



740

741 **Figure 1.** CONSORT flow diagram.

742 ^a Attended <4 sessions of the intervention program. Note that these subjects were invited back
743 to the laboratory for the *post* test session

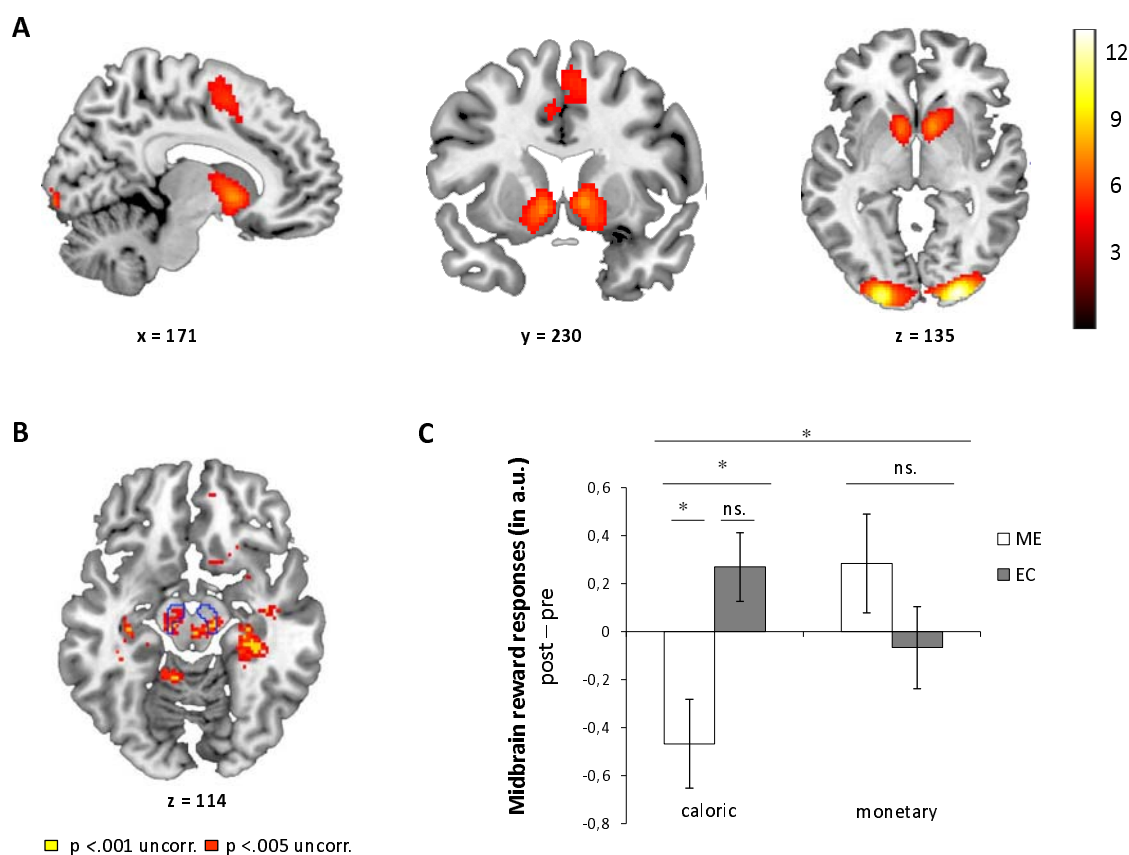


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745 **Figure 2.** Incentive delay task. **A)** Each trial started with a fixation cross, followed by a cue
746 signaling which reward could be earned on that trial. Subsequently, a white star (i.e. target)
747 appeared for a brief period and subjects were instructed to press a button as fast as possible
748 upon detection using their right index finger. If subjects pressed before the response deadline
749 (hit trial), the target remained on the screen, informing subjects of the successful registration of
750 their key press. Subsequently, a brief feedback image informing the subjects about the total
751 gain was presented. If subjects pressed too late or failed to press at all (too late or miss trial,
752 respectively), they were presented with the text message “you win nothing” plus the total gain
753 so far. To ensure subjects won similar amounts of each reward (in $\pm 2/3$ of the trials), target
754 presentation times were determined individually and adaptively: following hit trials the
755 response deadline for that reward cue was decreased with 10 ms, following too late or miss
756 trials it increased with 10 ms. **B)** Reward cues for high and low caloric cues (C: subject’s choice
757 from cola, orange juice or chocolate milk vs. W: water) and high and low monetary cues (50
758 cents vs. 1 cent). The task took between 20 – 25 minutes to complete. Subjects performed 4
759 blocks of 25 trials (a total of a 100 trials). A block contained either high/low monetary or
760 high/low caloric trials. Each trial type was repeated approximately 25 times (M: 24.4, SD: 2.78).
761 Block-presentation was pseudo-randomly distributed and counterbalanced across subjects
762 (randomization scheme: ABBA or BAAB).

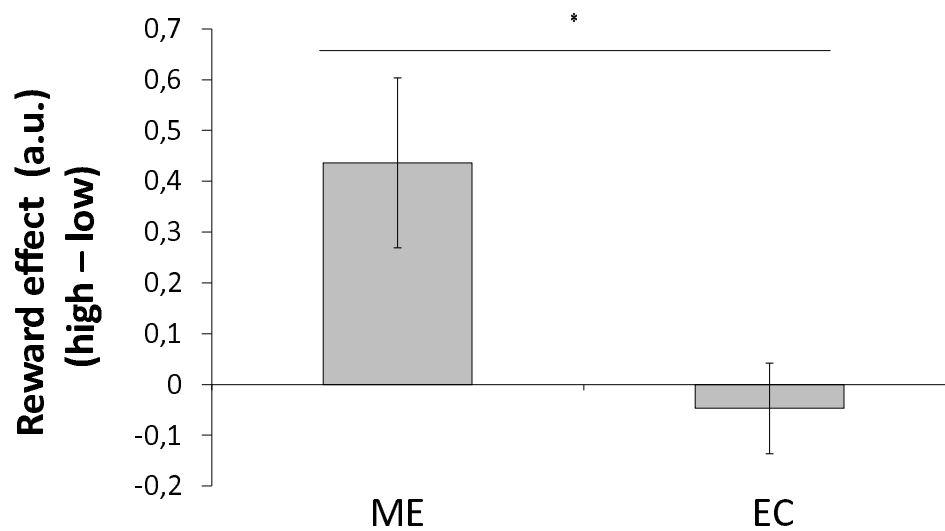
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 766 **Figure 3.** Summary of neuroimaging results. **A)** Main effect of reward. Contrast of high vs. low
 767 reward cue trials (high > low). Full brain statistical parametric maps were thresholded at $p < .05$
 768 (FWE-corrected, peak-level). **B)** Axial slice of whole brain interaction effect of Domain x Time x
 769 Intervention for the Reward contrast (high > low). Statistical parametric maps were thresholded
 770 at $p < .001$ (yellow) and $p < .005$ (red) uncorrected for visualization purposes. Outlined regions
 771 are corrected for multiple comparisons within our small search volume, at peak $p_{FWE} < .05$. **C)**
 772 Betas from the bilateral structural midbrain ROI (outlined in blue in panel B). Post- minus pre-
 773 intervention mean betas based on the high minus low reward contrast are presented for each
 774 domain (caloric, monetary) and for each intervention group (ME, EC) in arbitrary units (a.u.).
 775 Asterisks indicate $p < .025$ (Bonferroni corrected for multiple ROIs). All statistical parametric
 776 maps are overlaid onto a T1-weighted canonical image. Slice coordinates are defined in MNI152
 777 space and images are shown in neurological convention (left=left).

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783 **Figure 4.** Midbrain caloric ROI betas are presented to indicate between-group pre-differences in
784 midbrain reward (high - low) anticipatory activity. Asterisk indicates $p = .021$.