

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/m<sup>2</sup>), 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/m<sup>2</sup>) 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](http://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](http://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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## 542 **References**

- 543 Alberts HJEM, Thewissen R, Raes L (2012) Dealing with problematic eating behaviour. The  
544 effects of a mindfulness-based intervention on eating behaviour, food cravings,  
545 dichotomous thinking and body image concern. *Appetite* 58:847–851 Available at:  
546 <http://www.sciencedirect.com/science/article/pii/S0195666312000104>.
- 547 Bays JC (2009) *Mindful eating: A guide to rediscovering a healthy and joyful relationship with*  
548 *food*. Shambhala Publications.
- 549 Beaver JD, Lawrence AD, van Ditzhuijzen J, Davis MH, Woods A, Calder AJ (2006) Individual  
550 Differences in Reward Drive Predict Neural Responses to Images of Food. *J Neurosci*  
551 26:5160–5166 Available at: <http://www.jneurosci.org/content/26/19/5160.abstract>.
- 552 Berridge KC (2009) “Liking” and “wanting” food rewards: Brain substrates and roles in eating  
553 disorders. *Physiol Behav* 97:537–550 Available at:  
554 <http://www.sciencedirect.com/science/article/pii/S0031938409001206>.
- 555 Bishop SR, Lau M, Shapiro S, Carlson L, Anderson ND, Carmody J, Segal Z V, Abbey S, Speca M,  
556 Velting D, Devins G (2004) Mindfulness: A Proposed Operational Definition. *Clin Psychol Sci*  
557 *Pract* 11:230–241 Available at: <http://dx.doi.org/10.1093/clipsy.bph077>.
- 558 Brett M, Anton JL, Valabregue R, Poline JB (2002) Region of interest analysis using an SPM  
559 toolbox. *Neuroimage* 16:497.
- 560 Brewer JA, Mallik S, Babuscio TA, Nich C, Johnson HE, Deleone CM, Minnix-Cotton CA, Byrne SA,  
561 Kober H, Weinstein AJ, Carroll KM, Rounsaville BJ (2011) Mindfulness training for smoking  
562 cessation: Results from a randomized controlled trial. *Drug Alcohol Depend* 119:72–80  
563 Available at: <http://www.sciencedirect.com/science/article/pii/S0376871611002535>.

- 564 Daubenmier J, Kristeller J, Hecht FM, Maninger N, Kuwata M, Jhaveri K, Lustig RH, Kemeny M,  
565 Karan L, Epel E (2011) Mindfulness intervention for stress eating to reduce cortisol and  
566 abdominal fat among overweight and obese women: an exploratory randomized  
567 controlled study. *J Obes* 2011.
- 568 Delgado-Rico E, Soriano-Mas C, Verdejo-Román J, S. Río-Valle J, Verdejo-García A (2013)  
569 Decreased insular and increased midbrain activations during decision-making under risk in  
570 adolescents with excess weight. *Obesity* 21:1662–1668 Available at:  
571 <http://dx.doi.org/10.1002/oby.20375>.
- 572 Demos KE, Heatherton TF, Kelley WM (2012) Individual Differences in Nucleus Accumbens  
573 Activity to Food and Sexual Images Predict Weight Gain and Sexual Behavior. *J Neurosci*  
574 32:5549–5552 Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3377379/>.
- 575 Friston KJ, Fletcher P, Josephs O, Holmes a, Rugg MD, Turner R (1998) Event-related fMRI:  
576 characterizing differential responses. *Neuroimage* 7:30–40.
- 577 García-García I, Horstmann A, Jurado MA, Garolera M, Chaudhry SJ, Margulies DS, Villringer A,  
578 Neumann J (2014) Reward processing in obesity, substance addiction and non-substance  
579 addiction. *Obes Rev* 15:853–869 Available at: <http://dx.doi.org/10.1111/obr.12221>.
- 580 Goldin P, Ziv M, Jazaieri H, Gross JJ (2012) Randomized controlled trial of mindfulness-based  
581 stress reduction versus aerobic exercise: effects on the self-referential brain network in  
582 social anxiety disorder. *Front Hum Neurosci* 6.
- 583 Gousias IS, Rueckert D, Heckemann RA, Dyet LE, Boardman JP, Edwards AD, Hammers A (2008)  
584 Automatic segmentation of brain MRIs of 2-year-olds into 83 regions of interest.  
585 *Neuroimage* 40:672–684.
- 586 Groth-Marnat G (2009) *Handbook of psychological assessment*. John Wiley & Sons.
- 587 Haber SN, Knutson B (2010) The Reward Circuit: Linking Primate Anatomy and Human Imaging.  
588 *Neuropsychopharmacology* 35:4–26 Available at: <http://dx.doi.org/10.1038/npp.2009.129>.
- 589 Hammers A, Allom R, Koepp MJ, Free SL, Myers R, Lemieux L, Mitchell TN, Brooks DJ, Duncan JS  
590 (2003) Three-dimensional maximum probability atlas of the human brain, with particular  
591 reference to the temporal lobe. *Hum Brain Mapp* 19:224–247.
- 592 Hendrickson KL, Rasmussen EB (2013) Effects of mindful eating training on delay and probability  
593 discounting for food and money in obese and healthy-weight individuals. *Behav Res Ther*  
594 51:399–409 Available at:  
595 <http://www.sciencedirect.com/science/article/pii/S0005796713000697>.
- 596 Kabat-Zinn J (1984) An outpatient program in behavioral medicine for chronic pain patients  
597 based on the practice of mindfulness meditation: theoretical considerations and  
598 preliminary results. *Revision* 7:71–72.
- 599 Kabat-Zinn J (1990) *Full catastrophe living: Using the wisdom of your body and mind to face*  
600 *stress, pain and illness*. New York: Delacorte.
- 601 Kirk U, Brown KW, Downar J (2014a) Adaptive neural reward processing during anticipation and

- 602 receipt of monetary rewards in mindfulness meditators. *Soc Cogn Affect Neurosci*  
603 Available at:  
604 <http://scan.oxfordjournals.org/content/early/2014/10/02/scan.nsu112.abstract>.
- 605 Kirk U, Gu X, Harvey AH, Fonagy P, Montague PR (2014b) Mindfulness training modulates value  
606 signals in ventromedial prefrontal cortex through input from insular cortex. *Neuroimage*  
607 100:254–262 Available at:  
608 <http://www.sciencedirect.com/science/article/pii/S1053811914005126>.
- 609 Kirk U, Montague PR (2015) Mindfulness meditation modulates reward prediction errors in a  
610 passive conditioning task. *Front Psychol* 6:90 Available at:  
611 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4325661/>.
- 612 Knutson B, Fong GW, Adams CM, Varner JL, Hommer D (2001) Dissociation of reward  
613 anticipation and outcome with event-related fMRI. *Neuroreport* 12 Available at:  
614 [http://journals.lww.com/neuroreport/Fulltext/2001/12040/Dissociation\\_of\\_reward\\_anticipation\\_and\\_outcome.16.aspx](http://journals.lww.com/neuroreport/Fulltext/2001/12040/Dissociation_of_reward_anticipation_and_outcome.16.aspx).
- 615  
616 Knutson B, Taylor J, Kaufman M, Peterson R, Glover G (2005) Distributed neural representation  
617 of expected value. *J Neurosci* 25:4806–4812.
- 618 Kristeller J, Wolever R, Sheets V (2013) Mindfulness-Based Eating Awareness Training (MB-EAT)  
619 for Binge Eating: A Randomized Clinical Trial. *Mindfulness (N Y)*:1–16 Available at:  
620 <http://dx.doi.org/10.1007/s12671-012-0179-1>.
- 621 Lawrence NS, Hinton EC, Parkinson JA, Lawrence AD (2012) Nucleus accumbens response to  
622 food cues predicts subsequent snack consumption in women and increased body mass  
623 index in those with reduced self-control. *Neuroimage* 63:415–422 Available at:  
624 <http://www.sciencedirect.com/science/article/pii/S1053811912006866>.
- 625 Leahey TM, Crowther JH, Irwin SR (2008) A cognitive-behavioral mindfulness group therapy  
626 intervention for the treatment of binge eating in bariatric surgery patients. *Cogn Behav*  
627 *Pract* 15:364–375.
- 628 Lutz J, Herwig U, Opialla S, Hittmeyer A, Jäncke L, Rufer M, Grosse Holtforth M, Brühl AB (2013)  
629 Mindfulness and emotion regulation—an fMRI study. *Soc Cogn Affect Neurosci* Available  
630 at: <http://scan.oxfordjournals.org/content/early/2013/05/29/scan.nst043.abstract>.
- 631 Mascaro JS, Rilling JK, Negi LT, Raison CL (2013) Pre-existing brain function predicts subsequent  
632 practice of mindfulness and compassion meditation. *Neuroimage* 69:35–42 Available at:  
633 <http://www.sciencedirect.com/science/article/pii/S1053811912012062>.
- 634 Mason AE, Epel ES, Kristeller J, Moran PJ, Dallman M, Lustig RH, Acree M, Bacchetti P, Laraia BA,  
635 Hecht FM, Daubenmier J (2015) Effects of a mindfulness-based intervention on mindful  
636 eating, sweets consumption, and fasting glucose levels in obese adults: data from the  
637 SHINE randomized controlled trial. *J Behav Med*:1–13 Available at:  
638 <http://dx.doi.org/10.1007/s10865-015-9692-8>.
- 639 Muller-Oehring EM, Jung Y-C, Sullivan E V, Hawkes WC, Pfefferbaum A, Schulte T (2013)

- 640 Midbrain-Driven Emotion and Reward Processing in Alcoholism.  
641 Neuropsychopharmacology 38:1844–1853 Available at:  
642 <http://dx.doi.org/10.1038/npp.2013.102>.
- 643 Nolan-Poupart S, Veldhuizen MG, Geha P, Small DM (2013) Midbrain response to milkshake  
644 correlates with ad libitum milkshake intake in the absence of hunger. *Appetite* 60:168–174  
645 Available at: <http://www.sciencedirect.com/science/article/pii/S0195666312004035>.
- 646 O’Doherty JP, Deichmann R, Critchley HD, Dolan RJ (2002) Neural Responses during Anticipation  
647 of a Primary Taste Reward. *Neuron* 33:815–826 Available at:  
648 <http://www.sciencedirect.com/science/article/pii/S0896627302006037>.
- 649 Poser BA, Versluis MJ, Hoogduin JM, Norris DG (2006) BOLD contrast sensitivity enhancement  
650 and artifact reduction with multiecho EPI: Parallel-acquired inhomogeneity-desensitized  
651 fMRI. *Magn Reson Med* 55:1227–1235 Available at:  
652 <http://dx.doi.org/10.1002/mrm.20900>.
- 653 Rothmund Y, Preuschhof C, Bohner G, Bauknecht H-C, Klingebiel R, Flor H, Klapp BF (2007)  
654 Differential activation of the dorsal striatum by high-calorie visual food stimuli in obese  
655 individuals. *Neuroimage* 37:410–421 Available at:  
656 <http://www.sciencedirect.com/science/article/pii/S1053811907004302>.
- 657 Schmand B, Bakker D, Saan R, Louman J (1991) De Nederlandse Leestest voor Volwassenen:  
658 een maat voor het premorbide intelligentieniveau. *Tijdschr Gerontol Geriatr* 22:15–19.
- 659 Schultz W (2006) Behavioral theories and the neurophysiology of reward. *Annu Rev Psychol*  
660 57:87–115 Available at:  
661 [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=16318590](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16318590).
- 662
- 663 Scott NW, McPherson GC, Ramsay CR, Campbell MK (2002) The method of minimization for  
664 allocation to clinical trials: A review. *Control Clin Trials* 23:662–674.
- 665 Small DM, Zatorre RJ, Dagher A, Evans AC, Jones-Gotman M (2001) Changes in brain activity  
666 related to eating chocolate. *Brain* 124:1720–1733 Available at:  
667 <http://brain.oxfordjournals.org/content/124/9/1720.abstract>.
- 668 Stice E, Yokum S, Burger KS, Epstein LH, Small DM (2011) Youth at Risk for Obesity Show  
669 Greater Activation of Striatal and Somatosensory Regions to Food. *J Neurosci* 31:4360–  
670 4366 Available at: <http://www.jneurosci.org/content/31/12/4360.abstract>.
- 671 Stoeckel LE, Weller RE, Cook 3rd EW, Twieg DB, Knowlton RC, Cox JE (2008) Widespread  
672 reward-system activation in obese women in response to pictures of high-calorie foods.  
673 *Neuroimage* 41:636–647 Available at:  
674 [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=18413289](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18413289).
- 675
- 676 Tang Y-Y, Holzel BK, Posner MI (2015) The neuroscience of mindfulness meditation. *Nat Rev*  
677 *Neurosci* 16:213–225 Available at: <http://dx.doi.org/10.1038/nrn3916>.

- 678 Tapper K, Shaw C, Ilesley J, Hill AJ, Bond FW, Moore L (2009) Exploratory randomised controlled  
679 trial of a mindfulness-based weight loss intervention for women. *Appetite* 52:396–404.
- 680 Toneatto T, Pillai S, Courtice EL (2014) Mindfulness-Enhanced Cognitive Behavior Therapy for  
681 Problem Gambling: A Controlled Pilot Study. *Int J Ment Health Addict* 12:197–205  
682 Available at: <http://dx.doi.org/10.1007/s11469-014-9481-6>.
- 683 Val-Laillet D, Aarts E, Weber B, Ferrari M, Quaresima V, Stoeckel LE, Alonso-Alonso M, Audette  
684 M, Malbert CH, Stice E (2015) Neuroimaging and neuromodulation approaches to study  
685 eating behavior and prevent and treat eating disorders and obesity. *Neuroimage (Amst)*  
686 8:1–31 Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4473270/>.
- 687 van Strien T, Frijters JER, Bergers GPA, Defares PB (1986) The Dutch Eating Behavior  
688 Questionnaire (DEBQ) for assessment of restrained, emotional, and external eating  
689 behavior. *International J Eat Disord* 5:295–315.
- 690 Volkow ND, Wang G-J, Fowler JS, Telang F (2008) Overlapping neuronal circuits in addiction and  
691 obesity: evidence of systems pathology. *Philos Trans R Soc London B Biol Sci* 363:3191–  
692 3200 Available at: <http://rstb.royalsocietypublishing.org/content/363/1507/3191.abstract>.
- 693 Wing RR, Phelan S (2005) Long-term weight loss maintenance. *Am J Clin Nutr* 82:222S–225S.
- 694 Witkiewitz K, Warner K, Sully B, Barricks A, Stauffer C, Thompson BL, Luoma JB (2014)  
695 Randomized Trial Comparing Mindfulness-Based Relapse Prevention with Relapse  
696 Prevention for Women Offenders at a Residential Addiction Treatment Center. *Subst Use*  
697 *Misuse* 49:536–546 Available at:  
698 <http://www.tandfonline.com/doi/abs/10.3109/10826084.2013.856922>.
- 699 Zigmond AS, Snaith RP (1983) The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand*  
700 67:361–370 Available at: <http://dx.doi.org/10.1111/j.1600-0447.1983.tb09716.x>.
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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 <sup>a</sup>
Age (yrs)	32.3	±10.8	20-52	30.6	±11.3	19-51	.546	.607 <sup>b</sup>
Education (NLV)	6.5	±0.6	5-7	6.2	±0.7	5-7	.053	304.0 <sup>c</sup>
Digit span (total score)	15.6	±3.5	9-23	14.1	±3.5	9-22	.120	1.577 <sup>b</sup>
Smoking (FTND score)	0.19	±1.1	0-6	0.04	±0.2	0-1	.902	413.5 <sup>c</sup>
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>
Waist circumference (cm)	89.6	±12.8	72-122	86.5	±11.7	70-117	.338	.967 <sup>b</sup>
Yoga/meditation experience (yrs)	1.0	±2.6	0-14	1.9	±4.3	0-19	.334	-.974 <sup>b</sup>
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>
Attendance < 4 sessions (n)	5			5			.740	na <sup>a</sup>
Attendance (number of sessions)	6.5	±2.5	1-9	6.3	±2.8	1-9	.738	0.336 <sup>b</sup>

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 <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

709

710

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<sup>a</sup></i>
	pre	post	pre	post		
Physical measurements						
BMI (kg/height(m) <sup>2</sup> )	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 <sup>b</sup>
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 <sup>c</sup>	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 <sup>d</sup>	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 <sup>b</sup>	5.9	±2.6	5.9	±2.7	5.9	±3.0	5.6	±2.9	.835	< 1
Thirst <sup>b</sup>	5.7	±2.6	5.9	±2.8	6.0	±2.4	5.5	±2.4	.273	1.2
Satiety <sup>b</sup>	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 <sup>a</sup>If not otherwise stated, the reported test-statistic is the F-value (degrees of freedom: 1,56)

722 <sup>b</sup>Mann-Whitney U

723 <sup>c</sup>FFMQ-SF: N = 48 (N<sub>ME</sub> = 22, N<sub>EC</sub> = 26; degrees of freedom: 1,46)

724 <sup>d</sup>TCQ, Hunger, Thirst, Satiety: N = 55 (N<sub>ME</sub> = 29, N<sub>EC</sub> = 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 <sup>a</sup> (peak)
<b>Main effect of Reward: high &gt; low<sup>b</sup></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	
<b>Main effect of Reward: low &gt; high reward<sup>b</sup></b>								
Frontal superior lobe	R	18	26	50	7	.023	4.97	
<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	-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

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Interaction effect: Reward x Domain x Time x Intervention<sup>c</sup>

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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

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729 <sup>a</sup>Degrees of freedom: 1, 224; <sup>b</sup> $p < .05$ , whole brain family wise error (FWE) corrected; <sup>c</sup> $p < .05$ , small volume, FWE corrected.

730

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 <sup>a</sup> (peak)
<b>Main effect of receipt: hits (high &gt; low) &gt; too lates (high &gt; low)<sup>b</sup></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
<b>Main effect of receipt: too lates (high &gt; low reward) &gt; hits (high &gt; low reward)<sup>b</sup></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)) <sup>b</sup>							
Lingual	R	18	-84	-4	116	< .001	7.02
Lingual	L	-14	-88	-4	1	.023	5.01

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

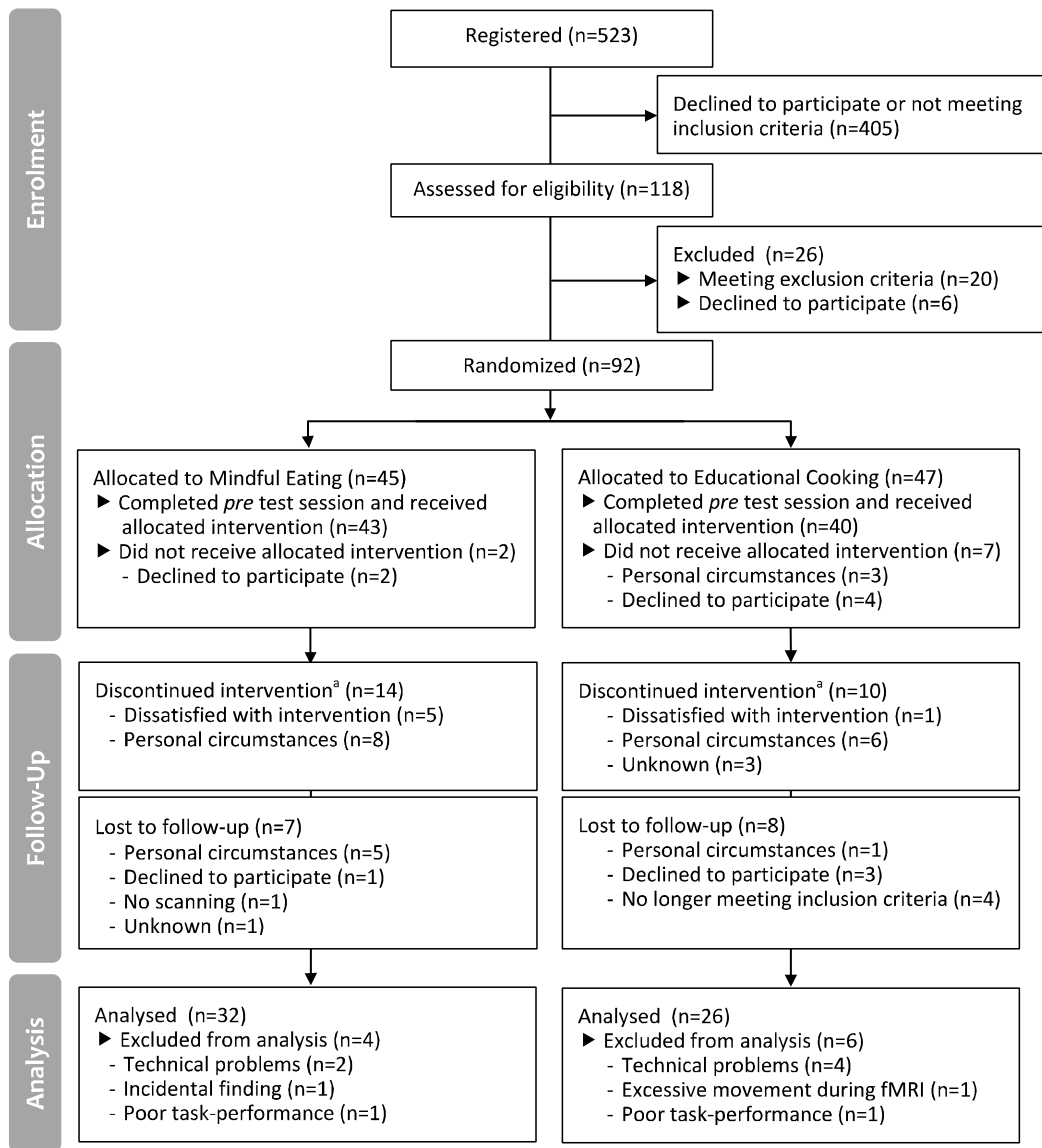
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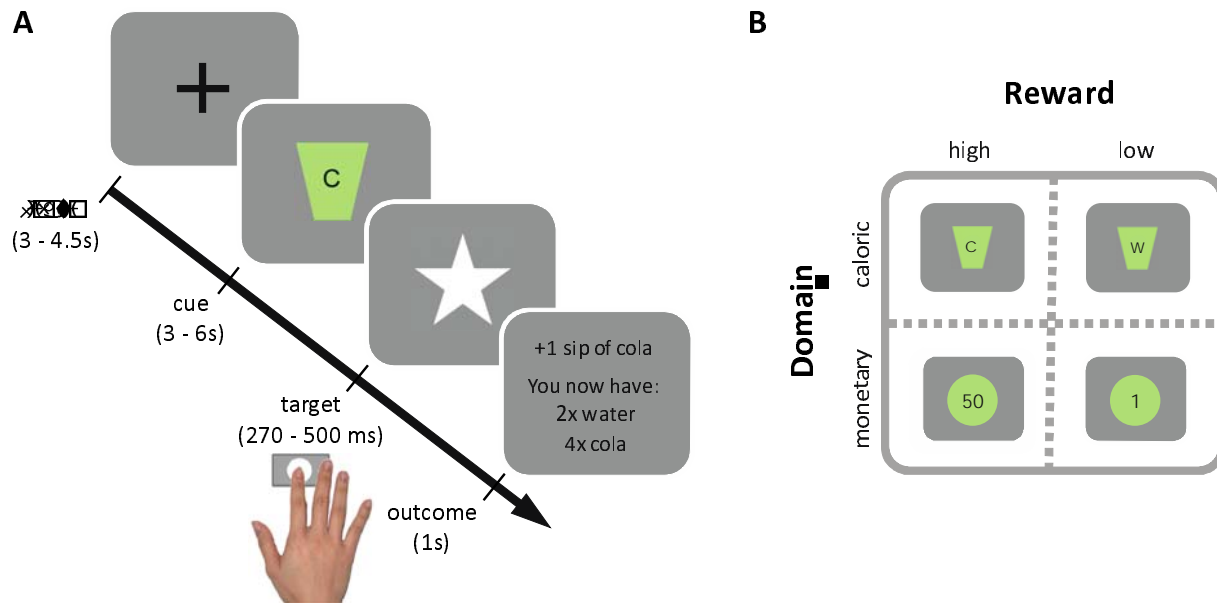
739 **Figures**



740

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

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



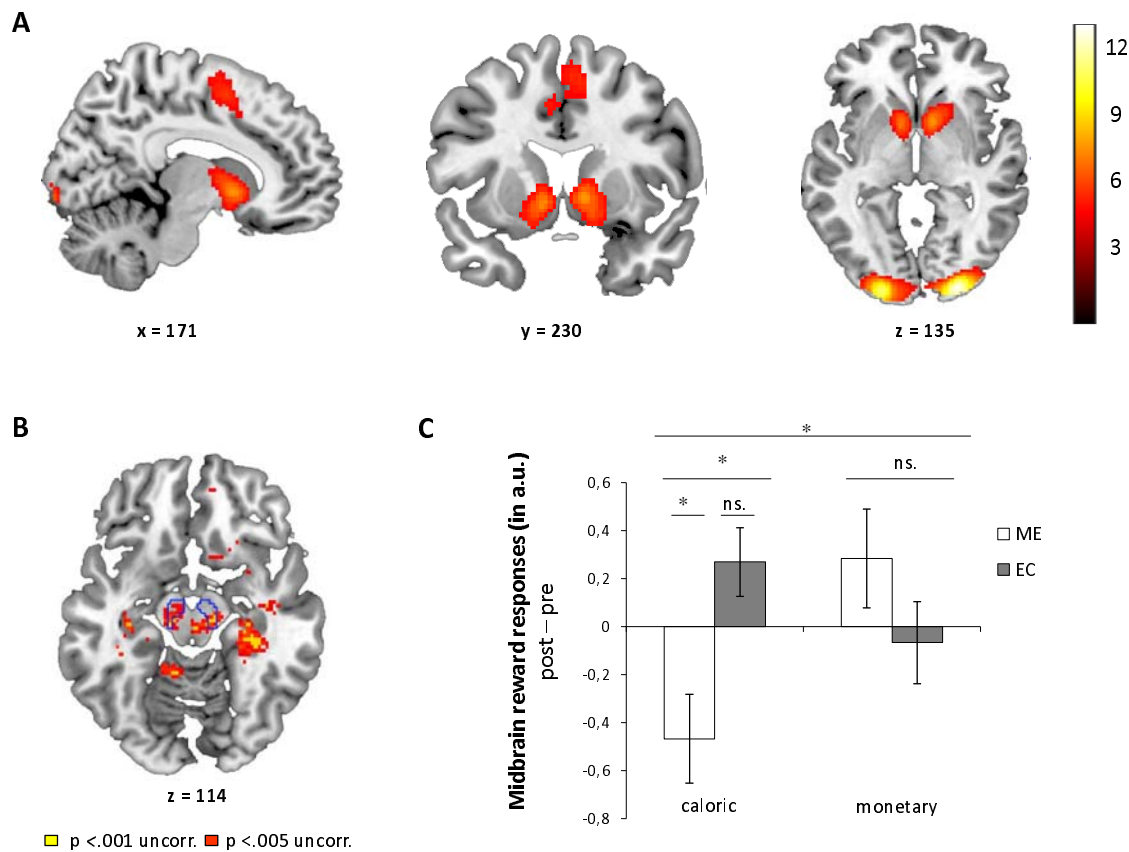
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745 **Figure 2.** Incentive delay task. **A)** Each trial started with a fixation cross, followed by a cue  
746 signaling which reward could be earned on that trial. Subsequently, a white star (i.e. target)  
747 appeared for a brief period and subjects 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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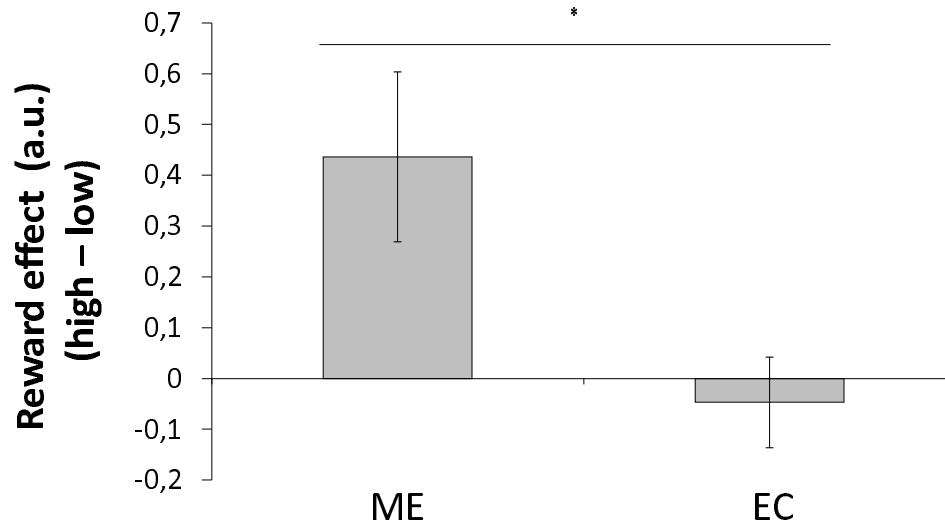
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765  
766 **Figure 3.** Summary of neuroimaging results. **A)** Main effect of reward. Contrast of high vs. low  
767 reward cue trials (high > low). Full brain statistical parametric maps were thresholded at  $p < .05$   
768 (FWE-corrected, peak-level). **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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779  
780  
781



782  
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  $p = .021$ .