

1 **Effects of self-conditioning techniques (self-hypnosis) in promoting weight loss in**
2 **patients with severe obesity: a randomized controlled trial.**

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23 **What is already known about this subject?**

- 24
- Overeating often involves loss of control and compulsive behaviors
 - Hypnosis has been suggested as an effective tool for weight reduction
 - The hypnotic techniques previously employed were long, demanding, and difficult to be performed in
27 clinical practice on a large number of patients
- 28

29 **What does this study add?**

- 30 • Self-hypnosis added to a lifestyle intervention was effective in ameliorated satiety, quality of life, and
31 inflammation
- 32 • Individuals who used more frequently self-hypnosis lost more weight and greatly reduced their caloric
33 intake
- 34 • Self-hypnosis was safe and the obtained results were independent of the susceptibility to hypnosis

35 ***Abstract***

36 *Objectives:* The usefulness of the rapid-induction techniques of hypnosis as adjunctive
37 weight-loss treatments is not defined. This randomized controlled trial evaluated whether self-
38 conditioning techniques (self-hypnosis) added to lifestyle interventions were effective in
39 determining weight-loss, changes in metabolic/inflammatory variables, and quality-of-life
40 (QoL) improvement with respect to traditional lifestyle approaches in severe obesity.

41 *Methods:* Individuals (BMI=35-50kg/m²) without organic/psychiatric comorbidity were
42 randomly assigned to the intervention (n=60) or control arm (n=60). All received
43 exercise/behavioral recommendations and individualized diets. The intervention consisted of 3
44 hypnosis sessions, during which self-hypnosis was taught to increase self-control before
45 eating. Diet, exercise, satiety, QoL, anthropometric measurements, blood variables were
46 collected/measured at enrolment and at 1-year (trial-end). *Results:* Participants reduced their
47 caloric intake and lost weight, without significant between-group difference (-423.8kcal, -
48 6.5kg intervention arm; -379.0kcal, -5.6kg controls). However, habitual self-hypnosis users
49 lost more weight (-9.6kg; β =-10.2; 95%CI -14.2 -6.18; p<0.001) and greatly reduced their
50 caloric intake (-682.5kcal; β =-643.6; -1064.0 -223.2; p=0.005) in linear regression models. At
51 trial-end, intervention group showed lower C-reactive protein values (β =-2.55; -3.80 -1.31;
52 p<0.001), higher satiety (β =19.2; 7.71 30.6; p=0.001) and better QoL (β =0.09; 0.02 0.16;
53 p=0.01). *Conclusions:* In severe obesity, self-hypnosis ameliorated satiety, QoL,
54 inflammation, and determined greater weight loss in more frequent users.

55 ***Introduction***

56 Due to the rising epidemic of obesity, little success and high rates of relapse of its treatment,
57 the finding of new approaches for its care has become increasingly important.

58 In the past, some studies have evaluated the effectiveness of hypnosis as an adjunctive
59 therapy for weight loss (1-3). Clinical hypnosis is a procedure in which changes in sensation,
60 perception, thought and behavior are suggested by a therapist; the hypnotic induction
61 produces either “a distinct state of consciousness” or a normal state with heighten
62 suggestibility according to the different theoretical conceptions of hypnosis (1,4).

63 Overall, hypnosis has been recognized as an effective tool for weight reduction, even if many
64 methodological limitations of the published research (small cohorts, lack of long-term follow-
65 up, variations in procedures, different response measurements) have been identified, making
66 the evaluation of treatment efficacy difficult (5). Usually, traditional hypnotic techniques
67 were combined with social, cognitive and behavioral psychological approaches. The hypnotic
68 procedure used varied greatly among studies, ranging e.g. from a 9-weeks program, with the
69 presentation of eating and dieting rules during the hypnotic sessions (6), a total 24-h hypnotic
70 treatment with a therapist, and the successive utilization of audiotapes (7), to a combination of
71 hypnotic and behavioral therapy for twelve 120-min sessions over a period of 8.5-months (8),
72 a multifaceted program with suggestions for relaxation, self-control, self-esteem,
73 strengthening motivation towards change (9). Most of these treatments are long, demanding,
74 and difficult to be performed in clinical practice on a large number of patients. Moreover,
75 during the hypnotic sessions many researchers gave suggestions targeting aversion to specific
76 high-calorie foods, persuading that overeating is a poison, or employing other techniques of
77 aversion (10-11), rather than purposeful messages or pleasant suggestions for heightening the
78 awareness of self-control and healthy functioning.

79 Recently, techniques with a rapid-induction phase allow the patient to go into hypnosis in a
80 few minutes. Trained individuals can repeat the experience in complete autonomy (self-
81 hypnosis), using little time of the day.

82 Overeating often involves loss of control and compulsive behaviors (12), and frequently
83 people bring with themselves the daily stress and worries during meals, thus eating in less
84 conscious ways and consuming more calories than necessary.

85 We hypothesized that self-hypnosis could be applied before eating occasions or circumstances
86 of irrational food need, as an aid to increase awareness and self-control.

87 Therefore, our aims were evaluating whether in patients with severe obesity self-conditioning
88 techniques (self-hypnosis) added to traditional lifestyle approach (diet, exercise and
89 behavioral recommendations) were effective in determining weight loss, changes in metabolic
90 and inflammatory variables, and improvement in the quality of life, with respect to the
91 traditional lifestyle approach.

92

93 ***Methods***

94 The methods of the present trial have been previously reported (13). The trial was conducted
95 at the Unit of Clinical Nutrition of the “Città della Salute e della Scienza” Hospital of Turin,
96 Italy. Participants were enrolled between January 2015-June 2016.

97 Inclusion criteria were: BMI 35-50 kg/m²; age 20-70 years; being able to give written
98 informed consent and accepting hypnosis. The exclusion criteria were: current/previous
99 mental disorders diagnosed by an expert clinician and/or use of any psychotropic drug; insulin
100 treatment; candidates to bariatric surgery; current (or discontinued for <6-months) treatment
101 with anti-obesity drugs; at risk of heart failure, edema, ascites (known heart diseases, chronic
102 liver diseases, nephrotic syndrome, renal failure; untreated or uncompensated thyroid
103 diseases). Before enrolment, in order to exclude clinically relevant psychiatric symptoms

104 below diagnostic thresholds, patients were submitted to the following questionnaires: the
105 Hamilton rating scale for depression (14), the Hamilton anxiety scale (15), and the Binge
106 Eating Scale (16). Only individuals who satisfied all the three scores (respectively <8, <17
107 and <17) were considered for enrolment.

108 This prospective, randomized controlled, open-label monocentric trial was registered at
109 ClinicalTrials.gov (identifier NCT02978105).

110 *Intervention*

111 Eligible patients were randomized either to the experimental arm (self-conditioning
112 techniques plus standard care) or the control arm (standard care, i.e. diet plus exercise plus
113 behavioral recommendations) (**Figure 1**).

114 All the participants received a personalized diet by a trained dietician (energy
115 ~1500±100kcal/day, 15-20% protein, 55-60% carbohydrates, 25-30% lipids), and the
116 recommendation of performing at least 20-minutes/day of brisk walking, according to the
117 Borg scale criteria (17). Verbal and written behavioral recommendations were given to all
118 patients, i.e. recommendations about exercise inclusion in daily activities and simple tips to
119 favor diet adherence (i.e. don't buy foods on an empty stomach, do not do anything else when
120 eating, etc).

121 The participants were followed-up every 3-months (at 3,6,9, and 12-months after enrolment)
122 by a dietician and a medical doctor, and a physical assessment, the recording of adverse
123 events or effects, and a check of compliance to the protocol were performed. During visit
124 intervals (at 1.5, 4.5, 10.5-months after enrollment), participants were called by phone and
125 asked about adverse events and compliance to the intervention.

126 Subjects who withdrew from the study before 12-months for any reasons or those who during
127 the trial took slimming products/drugs or employed techniques to lose weight other than those

128 recommended (e.g. very-low-calorie diets, or highly unbalanced diets) were considered as
129 drop-outs.

130 *Self-hypnosis*

131 The experimental group received three individual sessions of hypnosis, performed by trained
132 personnel (2 nurses, 1 medical doctor). To minimize the potential lack of fidelity, the health
133 care providers were assigned to the sessions by a scheduled rotation among sessions to ensure
134 a balanced intervention. Rapid-induction techniques were used, and the patient went into a
135 hypnotic condition in a few minutes (18).

136 Timing of the hypnosis sessions was after 2-weeks, 6-weeks, and 15-weeks from
137 randomization (13). The first session of the hypnotic procedure (lasting about 30-minutes)
138 was briefly introduced, and information about medical hypnosis and its potential application
139 as an amplification of personal resources to manage self-control were given. During this
140 phase, the degree of susceptibility to hypnosis was evaluated by the eyeroll test of Spiegel
141 (19). Thereafter, the rapid hypnotic induction was determined through a technique of attention
142 focusing (fixing a point or focusing the attention on a part of one's body) and ratification of
143 what was happening; the following were the phases of full-body relaxation, of slow breathing,
144 of imagining pleasant images and thoughts and creating an ideal "safe place" where the
145 subject could take refuge. In this imaginary place, the subject could feel stronger, more
146 determined, self-controlled, efficient, and able to sit at table aware of what he/she was about
147 eating, refraining from gorging. The last phase was the anchor phase, during which the
148 subject received a self-conditioning symbolic signal (i.e. joining the thumb with index or
149 making the fist with the thumb folded inside the hand) by which he/she could rapidly fall
150 under hypnosis in complete autonomy (self-hypnosis), also repeatedly during the day. The
151 anchor stage was then checked and if necessary the procedure was repeated a second and/or
152 third time by changing suggestions and/or the symbolic anchor signal. Finally, instructions

153 were given about self-hypnosis use before each meal or food-compulsion occasion for about
154 3-minutes (10-seconds to enter, 2-minutes of “safe place” thinking with muscle relaxation and
155 mental well-being, and 30-seconds to exit).

156 In the subsequent two sessions (“reinforcements sessions”) lasting 20-30-minutes, participants
157 reported difficulties, problems, barriers and benefits with self-hypnosis. The skill of going
158 into hypnosis was checked again. The same suggestions of the first session were employed,
159 and a new image was evoked to reinforce the skill to face difficulties (a metaphorical climb
160 on a mountain top by overcoming natural obstacles). Finally, suggestions for overcoming the
161 encountered barriers and problems were given.

162 The hypnotic sessions had a common core, but the way of hypnosis induction was
163 individualized based on the participants’ characteristics.

164 *Quality control*

165 The participants’ acquired skills were checked during each session by the hypnotists by the
166 evaluation of typical muscle changes (muscle inertia, levitation, catalepsy), characteristic
167 physical appearance (variation of facial expression, movements of eyelids/eyeballs,
168 swallowing, changes in respiratory rate, vasodilation), alteration of consciousness (partial
169 detachment from reality, time warp, realistic images and conceived situations). The hypnotic
170 condition achieved was considered satisfactory if all the above reported conditions were
171 present at the same time.

172 In the case of a low hypnotizability, the participant was still encouraged to run the procedure
173 before each meal and food compulsion attack.

174 *Outcomes*

175 The primary outcome was the between-arms weight change at 12-months after randomization.

176 Secondary outcomes were between-arms changes in waist circumference, arterial blood
177 pressure, metabolic/inflammatory variables, satiety, well-being, and eating and exercise
178 pattern.

179 *Randomization*

180 The list of randomization, stratified by age (50; >50 years), gender, and BMI (40; >40 kg/m²)
181 was generated by a variable-length block procedure, masked to researchers. The
182 randomization procedure was centrally run through an online procedure (available at:
183 <http://www.epiclin.it>). A unique code was assigned to each participant.

184 *Blinding*

185 Blinding participants and health professionals was not possible, owing to the nature of the
186 intervention. Indeed, the personnel who performed the laboratory analyses, the
187 anthropometric measurements, and collected questionnaire data was blinded to the arm
188 assignment.

189 *Safety*

190 Adverse events and compliance with the study protocol was monitored both during each visit
191 and between the visits (by phone calls). Participants were instructed to inform the researchers
192 if adverse effects occurred.

193 *Ethics*

194 The study protocol received ethical approval from the local ethics committee. All the
195 procedures were conducted according to the Helsinki Declaration. All patients provided their
196 written informed consent to participate.

197 *Measurements*

198 At enrolment and at 12-months (trial end), all the participants were submitted to the
199 following:

200 -3-day food record

201 -the Minnesota-Leisure-Time-Physical-Activity questionnaire (20)

202 -The Satiety Labeled Intensity Magnitude scale (21)

203 -The Satisfaction and well-being (EuroQol (EQ)-5 questionnaire [Index and Visual Analog
204 Scale (VAS)] (22)

205 -anthropometric and arterial blood pressure measurements

206 -blood sample collections after an overnight fast to measure glucose, insulin, glycated
207 hemoglobin (HbA1c), total and HDL-cholesterol, triglycerides, and high-sensitivity C-
208 reactive protein (CRP).

209 Body weight and waist circumference were measured at 3, 6, 9-months from randomization,
210 too.

211 Participants from the intervention arm were asked about the frequency of self-hypnosis use;
212 they were divided in individuals with low (0-1), medium (2-3), or high hypnotizability (4)
213 according to the score obtained by the eyeroll Spiegel test.

214 The physical activity level was calculated as the product of the duration and frequency of each
215 activity (hours/week), weighted by an estimate of the metabolic equivalent (MET) of the
216 activity and summed for the activities performed (20).

217 Body weight was measured to the nearest 0.1kg, and height to the nearest 0.1cm by a
218 stadiometer (SECA model 711, Hamburg, Germany), with the participants wearing light
219 clothes and no shoes. Waist circumference was determined by a plastic meter at the highest
220 point of the iliac crest. Body composition was assessed by Dual-energy X-ray absorptiometry
221 (DXA) (QDR-4500; Hologic, Bedford, MA, USA), using whole-body absorptiometry
222 software.

223 Arterial blood pressure was measured by a mercury sphygmomanometer with appropriate cuff
224 sizes (ERKA Perfect-Aneroid, Germany) in a sitting position after at least 10-min rest; the
225 values reported were the mean of two measurements.

226 Laboratory methods have been previously published (13). Homeostasis Model Assessment-
227 Insulin Resistance (HOMA-IR) was calculated according to the published algorithm (23).

228 *Statistical analyses*

229 The sample size was calculated in relation to the primary outcome. Available data on patients
230 with clinical characteristics similar to those enrolled were used. With an effect size=0.67 and
231 a 2-tailed α -error=0.05, 48 patients per arm were needed to obtain a 90% power. This number
232 was increased to 60, because of the possibility of drop-outs.

233 Endpoints analyses were based on the between-arms comparisons of the changes from
234 baseline to 12-months after randomization (deltas). Linear regression models were used to
235 compare deltas of the analyzed endpoints between-arms, adjusting for the baseline
236 measurement and the randomization stratification variables [gender, age (50; >50 years), BMI
237 (40; >40 kg/m²)].

238 An intention-to-treat analysis was performed including all the randomized patients by
239 multiple imputing missing 12-month variables, using the method of chained equations (24).

240 Combined estimates were obtained from 50 imputed datasets.

241 For each randomization arm, mean changes from baseline for weight, BMI and waist
242 circumference were estimated at 3, 6, 9 and 12-months using linear regression models for
243 repeated measures. Interaction terms between-arms and the time point variables were included
244 to estimate the specific mean change from baseline for each arm at fixed times. To account for
245 the repeated measures on the same subject, mean changes from baseline were estimated
246 controlling the standard errors with the Huber-White Sandwich Estimator (25).

247 The associations between hypnosis use frequencies (coded as dummy variables) and
248 anthropometric/laboratory variables, and questionnaire scores were evaluated by linear
249 regression models, adjusted for the randomization stratification variables.

250

251 **Results**

252 At 12-months, there were 16/60 (26.7%) individuals lost at follow-up from the intervention
253 arm and 18/60 (30.0%) from the control arm. The main reasons for drop-outs are reported in
254 Figure 1. No adverse event was recorded. During the trial, no death or hospitalization
255 occurred.

256 No significant difference was evident between individuals who completed the trial and those
257 who were lost, even if the latter tended to be younger and more frequently males
258 **(Supplementary-Table 1)**.

259 The clinical and laboratory characteristics at enrolment were very similar between the two
260 randomization arms **(Table 1)**.

261 *Changes in lifestyle habits and drug use*

262 Mean energy intakes significantly decreased in both groups at follow-up (respectively, in the
263 intervention and control arms: 1470.6 ± 281.1 and 1496.9 ± 311.9 kcal; $p < 0.001$ for within-group
264 difference in both groups). Mean differences were -423.8 and -379.0 kcal respectively in the
265 intervention and control arm ($p = 0.84$). The composition in macronutrients did not
266 significantly change from baseline to the trial end in both arms (data not shown).

267 Median (interquartile range) METs values at follow-up were 24.8 (27.2) and 30.5 (41.7)
268 h/week in the intervention and control arms respectively, without significant difference in
269 within and between-group analyses.

270 During follow-up, there were small variations in the therapy of the patients: hypoglycemic
271 drugs were added to 2 and 1 subjects respectively from the intervention and control arms,
272 lipid-lowering agents were added to 1 subject from both arms, antihypertensive drugs were
273 suspended to 1 subject from the intervention arm and added to 1 control.

274 *Changes in anthropometric and laboratory variables*

275 Individuals from the two arms significantly reduced their weight, BMI, and waist
276 circumference values from baseline to the trial end (**Supplementary-Table 2**). Within-group
277 variations were significantly different as early as 3-months after randomization.
278 Changes in anthropometric and laboratory variables are reported in **Table 2**. Deltas (end-of
279 the trial values – baseline values) did not differ between-arms, with the exception of delta
280 CRP values which significantly decreased in the intervention arm.
281 Intention-to treat analyses confirmed the significant reduction in CRP values in the
282 intervention arm (**Supplementary-Table 3**).

283 *Changes in satiety, and health status*

284 Participants from the intervention arm showed increased scores of satiety and quality of life at
285 the trial end (Table 2), with within-group significant differences (respectively, $p=0.001$,
286 $p<0.001$ and $p=0.002$ for satiety, EuroQoL VAS, and EuroQoL health status). In the controls,
287 these scores did not change significantly. The associations between being in the intervention
288 arm and the scores were confirmed by linear regression (Table 2), and by the intention-to-treat
289 analyses (Supplementary-Table 3).

290 *Frequency of self-hypnosis use*

291 At the trial end, 16/44 (36.3%) declared to practice self-hypnosis regularly once/day, 7/44
292 (15.9%) more frequently than once/day, 9/44 (20.5%) less frequently than once/day, i.e. with
293 a weekly frequency, but 12/44 (27.3%) rarely or never. The corresponding values of delta
294 weight were: -9.6kg ($\geq\text{once/day}$), -7.5kg ($<\text{once/day}$), and $+0.2$ (rarely or none).

295 The frequency of hypnosis use was significantly associated with changes in weight, BMI,
296 waist circumference, and energy intake, after adjusting for age, gender, and BMI
297 (**Supplementary-Table 4**). No significant association was evident with the other
298 anthropometric and laboratory variables, or questionnaire scores.

299 The frequency of self-hypnosis declined with time. The prevalence of individuals practicing
300 the procedure respectively \geq once/day, <once/day and rarely/none was 77.8%, 15.6%, 6.7% at
301 6 months and 72.7%, 15.9%, 11.4% at 9-months.

302 *Hypnotizability*

303 Participants in the intervention arm were divided according to the eyeroll test of Spiegel in
304 individuals with low (43.2%), medium (52.3%), or high hypnotizability (4.5%) (19).
305 No difference in the hypnotizability scores was evident between individuals who completed
306 or not the follow-up (Supplementary-Table 1). The susceptibility to hypnosis did not correlate
307 with any outcomes, either the anthropometric and laboratory variables or the scores of the
308 analyzed questionnaires.

309

310 *Discussion*

311 The use of self-hypnosis was associated with a significant between-group difference in the
312 quality of life, satiety score, and CRP values, but not with changes in the anthropometric
313 variables. In the intervention arm, however, the increased frequency of self-hypnosis use
314 correlated with increased reduction in body weight, and energy intakes.

315 *Changes in anthropometric variables*

316 Literature reports that hypnosis leads to variable weight loss at 6-months with a difference
317 ranging from 4 to 8 kg between the groups with and without hypnosis (2,6-7). Hypnosis has
318 been reported to be successful not by itself as a treatment for obesity, but as a facilitator of a
319 specific lifestyle intervention, by increasing the patient involvement in the therapeutic process
320 (6). Therefore, usually hypnosis has been combined with behavioral approaches, and most of
321 these treatments are long-lasting, complex, challenging, and, therefore, difficult to be
322 performed routinely (6-9).

323 Our hypnotic approach had the advantage to be rapid and our intervention was less
324 demanding and easier to be implemented in the clinical practice. However, we did not find
325 any significant differences between arms in the change of anthropometric variables.
326 Accordingly, a less-intensive hypnosis program, like ours, led to a lower difference in weight
327 loss between groups, i.e. <1kg difference (26). Nevertheless, our participants from the
328 intervention arm who used more frequently (\geq once/day) self-hypnosis showed a much greater
329 weight loss (with an adjusted mean difference of \sim 10kg), and reduction in energy intake when
330 compared to those practicing rarely or not at all.

331 We should take into consideration the fact that after 12-months, only 52% of the participants
332 practiced self-hypnosis \geq once/day, with a trend towards a progressive reduction of use with
333 time. Indeed, the reported average use of hypnosis programs in the medium term (>6 months)
334 was similar to ours (6).

335 The impact of hypnosis has been reported to increase over time, being more effective in the
336 long-term, since it allows the establishment of a reinforcement in healthy behaviors that
337 continues beyond the training period (1,6,27). Weight maintenance requires continued
338 motivation and engagement; the use of a reinforcement incentive tool, such as self-hypnosis,
339 might be a motivational successful strategy in promoting the maintenance of weight change.

340 Accordingly, a significant weight loss compared to baseline at 18-months (27) or a weight
341 loss of 10kg at 2-years (6) was reported by the few studies evaluating the long-term effects of
342 hypnosis.

343 *Changes in quality of life and satiety score*

344 Both quality of life and satiety increased in our intervention arm. These changes were not
345 associated with the frequency of self-hypnosis use.

346 Accordingly, satisfaction was reported to be greater in the hypnosis arms of the trials (6), and
347 only the hypnotherapy aimed at reducing stress, but not the one that induced a negative

348 attitude towards food, was effective in determining a significant weight loss with respect to
349 baseline (26). Differently from other studies which employed techniques inducing fear/hate
350 towards eating and showing some foods as a body poison (10-11,27), we referred to methods
351 of “ego strengthening” and esteem-enhancement suggestions, with the objective to reduce
352 stress, and possibly emotional eating, by increasing awareness of self-control and conscious
353 eating. Our results suggest that the improvement in patients' belief in their capacity of
354 controlling events might play adjunctive benefits. Furthermore, typical hypnotic inductions
355 closely resemble conventional relaxation training (1). Therefore, the finding of a better quality
356 of life in those who have been subjected to hypnosis is not unexpected. Furthermore, our
357 approach might have strengthened individual self-efficacy, whose increase correlates with
358 weight loss, and favorably modulates eating behavior and food compulsivity (28).
359 Finally, even if individuals from both arms similarly reduced their energy intakes, satiety was
360 significantly increased only in the intervention arm. This is in line with the known modulation
361 of appetite and satiation associated-peptides and hormones levels through psycho-neuro-
362 immuno- and psycho-neuro-endocrine mechanisms, even in the absence of substantial weight
363 loss (5,26).

364 *Change in CRP values*

365 Participants from our intervention arm showed a significant reduction in CRP values, the most
366 commonly used acute-phase reactant marker of inflammation. This finding is intriguing and
367 suggests a complicate relationship between the mind and the body. It is well known that
368 distress and quality of life are associated with inflammation and immunologic measures, and
369 chronic, systemic inflammation has been proposed as one mechanism underlying psychologic
370 and physical health problems (29-32). Higher levels of psychological distress have been
371 associated with increased circulating values of CRP and other inflammatory variables though
372 pathways including the sympathetic nervous system, and the hypothalamic-pituitary-adrenal

373 axis (32-34), and the associations between psychological distress and chronic age-related
374 diseases and mortality might be modulated at least in part by inflammation, as well as other
375 conditions, such as immunological factors, or dysregulated hormonal responses (35). Our
376 results could have clinical implications, owing to the chronic sub-clinic inflammatory state of
377 the individuals with obesity, and the predictive role of chronic inflammation towards
378 cardiovascular diseases, frailty, disability, and mortality (36-37).

379 *Hypnotic susceptibility*

380 Hypnotizability was not a significant predictor of weight loss or other outcomes in our
381 patients, in line with some studies and a recent meta-analysis (7,38-39), but differently from
382 others showing a significant relationship between hypnotic susceptibility and weight loss
383 outcomes (10,40-41).

384 Indeed, methods of evaluating the degree of susceptibility to hypnosis varied greatly, and its
385 assessment has been criticized, since correlations between hypnotizability and treatment
386 outcome might be indicators of expectancy effects, rather than effects of some special
387 hypnotic process (1,5). Furthermore, other studies aimed at inducing deeper changes at the
388 cognitive-behavioral level, with numerous long-lasting hypnosis sessions requiring a high
389 capacity for trance; therefore, hypnotic abilities can assume greater importance (10,40).

390 Contrariwise, our short-term sessions of self-hypnosis were aimed at obtaining a brief
391 moment of relaxation, during which each participant could evoke the suggestion that he/she
392 would be able to control the amount of food subsequently eaten. Therefore, it is reasonable
393 thinking that the frequency of use of self-hypnosis was more important than the degree of
394 susceptibility in our patients.

395 Finally, we have chosen a very simple measure for pretesting for hypnotizability, since other
396 complex and time-requiring tests have been considered even counterproductive, because such

397 methods could take more time than the therapy, creating concern or irritation in the patient
398 (39).

399 *Limitations*

400 The main limitation of this trial was the high percentage of drops-out (28%). Other hypnosis
401 studies reported higher drop-out rates (6,27,42), and >50% of patients with obesity, above all
402 the youngest, discontinued treatment in clinical practice (43). Furthermore, we took care of
403 performing an accurate intention-to-treat analysis with imputation of missing values, and
404 results did not change meaningfully.

405 The number of patients who completed the intervention was smaller than that originally
406 defined to obtain an adequate sample size. However, rather than to a reduced power, the lack
407 of statistical significance of some between-arm comparisons might be attributable to the effect
408 size found which was smaller than that expected.

409 We used a very simple approach with three sessions of about 30-minutes each, the last of
410 which was at 15-weeks after randomization. Therefore, the participants remained
411 approximately 8-months without receiving any reinforcement session. Accordingly, we
412 observed a decline in the use of self-hypnosis with time. We cannot exclude that a more
413 intensive intervention could have resulted in a greater between-arms difference in the
414 outcomes. However, our goal was to test a simple method, easily applicable to the largest
415 possible number of individuals in the clinical practice.

416 Assessments of the quality of life and satiety were highly subjective, and the knowledge of
417 the study arm might have influenced the participants' responses. However, there was
418 biological plausibility in the associations found. Furthermore, CRP, a variable associated with
419 overall distress and blindly measured, was found to be significantly associated with the
420 intervention arm. Finally, we failed to assess other aspects, such as attitude towards hypnosis
421 and sleep quality, which could represent potential confounding factors.

422 *Conclusions*

423 Self-hypnosis is a non-invasive intervention, free of side effects, which ameliorated satiety,
424 quality of life and CRP values after 12-months. Both the cost-benefit balance of this
425 procedure and further trials in larger samples should be performed, before final conclusions
426 about its benefits could be drawn.

427

428 *References*

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Table 1. Baseline characteristics of the patients

	Intervention arm	Control arm	Total
Number	60	60	120
Age (years)	49.0±12.7	49.0±13.0	49.0±12.8
Males (%)	33.3	30.0	31.7
Actual smokers (%)	20.0	21.7	20.8
METS (h/week)	24.5 (28.1)	28.3 (38.0)	25.6 (32.6)
Height (m)	1.64±10.2	1.63±9.6	1.63±9.9
Weight (Kg)	110.7±17.1	108.6±16.7	109.6±16.9
BMI (Kg/m ²)	41.2±4.7	41.0±3.8	41.1±4.3
Waist circumference (cm)	122.0±12.5	121.0±11.5	121.5±12.0
Percent body fat	45.3±4.6	45.0± 6.1	45.1±5.4
Systolic blood pressure (mmHg)	130.2±16.1	130.8±13.6	130.5±14.8
Diastolic blood pressure (mmHg)	81.5±10.6	81.5±8.3	81.5±9.5
<i>Dietary intakes</i>			
Energy (kcal)	1872.6±589.2	1875.1±466.7	1873.8±529.2
Carbohydrates (% total kcal)	48.8±7.0	47.7±8.1	48.3±7.5
Sugars (% total kcal)	12.1±3.9	11.3±5.1	11.7±4.5
Proteins (% total kcal)	16.6±2.7	16.5±3.0	16.5±2.9
Total fats (% total kcal)	33.5±5.4	34.7±7.0	34.1±6.3
Saturated fatty acids (% total kcal)	9.6±2.6	9.7±2.8	9.6±2.7
Polyunsaturated fats (% total kcal)	7.5±1.8	7.8±2.1	7.6±1.9
Fiber (g/day)	17.1±5.2	17.3±5.3	17.2±5.2

<i>Laboratory variables</i>			
Fasting glucose (mg/dL)	94.1±20.2	91.3±17.9	92.7±19.0
Glycated hemoglobin (mmol/mol)	41.4±8.9	40.2±6.8	40.8±7.9
Fasting insulin (μU/mL)	14.0 (6.7)	13.8 (11.4)	14.0 (8.5)
HOMA-IR (mmol/l*μU/mL)	3.1 (2.0)	3.4 (2.8)	3.2 (2.4)
CRP (mg/L)	5.3 (5.4)	5.4 (7.1)	5.3 (6.4)
Total cholesterol (mg/dL)	185.8±41.0	186.4±24.7	186.1±33.7
HDL-cholesterol (mg/dL)	49.8±13.4	47.1±12.2	48.4±12.8
Triglycerides (mg/dL)	105.5 (55.0)	111.5 (56.0)	96.5 (49.0)
<i>Drugs</i>			
Antihypertensive (%)	46.7	43.3	45.0
Hypoglycemic agents (%)	6.7	5.0	5.8
Lipid lowering (%)	13.3	11.7	12.5
<i>Questionnaires</i>			
Satiety score	50 (50)	50 (40)	50 (60)
EuroQoL VAS	61.8±16.3	64.2±17.3	63.0±16.8
EuroQoL health status	0.67±0.21	0.72±0.14	0.70±0.18

Mean ± SD, median (interquartile range)

Table 2. End-of the trial values of variables and comparisons between arms by a linear regression model

	Intervention arm		Control arm		Adjusted		
	End-of the trial value	Mean delta	End-of the trial value	Mean delta	mean difference on delta (β)*	95%CI	P
Weight (Kg)	102.9±16.3	-6.5	100.8±18.6	-5.6	-0.45	-3.78; 2.88	0.79
BMI (Kg/m ²)	38.7±5.0	-2.4	38.8±5.5	-2.1	-0.24	-1.49; 1.01	0.70
Waist circumference (cm)	115.2±14.7	-6.3	115.8±14.7	-4.9	-1.34	-5.06; 2.37	0.47
Percent body fat	42.5±5.5	-3.1	43.5±6.3	-1.5	-1.38	-2.91; 0.15	0.08
Systolic blood pressure (mmHg)	125.4±15.1	-4.0	129.6±17.5	-2.6	-3.11	-9.28; 3.07	0.32
Diastolic blood pressure (mmHg)	79.9±13.2	-2.3	80.7±8.2	-1.1	-1.03	-5.59; 3.53	0.65
Fasting glucose (mg/dL)	92.0±19.4	-2.3	91.5±18.3	+0.3	-1.17	-8.18; 5.84	0.74

Glycated hemoglobin (mmol/mol)	39.0±6.7	-2.7	38.4±6.7	-1.8	-0.33	-2.3; 1.64	0.74
Fasting insulin (μU/mL)	14.0 (10.2)	-3.7	15.3 (12.8)	-1.5	-1.50	-4.44; 1.43	0.31
HOMA-IR (mmol/l*μU/mL)	3.3 (2.2)	-1.1	3.5 (2.6)	-0.4	-0.44	-1.26; 0.39	0.30
CRP (mg/L)	2.2 (3.0)	-3.5	3.7 (6.0)	-0.7	-2.55	-3.80; -1.31	<0.001
Total cholesterol (mg/dL)	180.9±31.3	-5.3	182.7±33.5	-2.8	-2.07	-14.0; 9.81	0.73
HDL-cholesterol (mg/dL)	53.3±13.3	+4.0	50.9±15.6	+4.9	-0.48	-4.05; 3.09	0.79
Triglycerides (mg/dL)	94.5 (41.5)	-10.0	91.5 (32.0)	-21.6	9.14	-3.61; 21.9	0.16
Satiety score	80 (30)	+19.3	50 (60)	-1.4	19.2	7.71; 30.6	0.001
EuroQoL VAS	73.4±13.7	11.9	66.9±18.2	3.7	6.90	0.63; 13.2	0.03
EuroQoL health status	0.77±0.13	0.11	0.69±0.21	-0.02	0.09	0.02; 0.16	0.01

Mean ± SD, median (interquartile range)

Delta= end-of the trial value – baseline value

*Adjusted for stratification variables (age, gender, BMI) and the baseline value of the variable.

Figure legends

Figure 1

Flow of the study