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# Effects of Self-Conditioning Techniques (Self-Hypnosis) in Promoting Weight Loss in Patients with Severe Obesity: A Randomized Controlled Trial

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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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- 22 NCT02978105).

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

- 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 31

• Self-hypnosis added to a lifestyle intervention was effective in ameliorated satiety, quality of life, and inflammation

- Individuals who used more frequently self-hypnosis lost more weight and greatly reduced their caloric
   intake
- 34

• Self-hypnosis was safe and the obtained results were independent of the susceptibility to hypnosis

35 Abstract

Objectives: The usefulness of the rapid-induction techniques of hypnosis as adjunctive 36 weight-loss treatments is not defined. This randomized controlled trial evaluated whether self-37 conditioning techniques (self-hypnosis) added to lifestyle interventions were effective in 38 determining weight-loss, changes in metabolic/inflammatory variables, and quality-of-life 39 (QoL) improvement with respect to traditional lifestyle approaches in severe obesity. 40 *Methods*: Individuals (BMI=35-50kg/m<sup>2</sup>) without organic/psychiatric comorbidity were 41 randomly assigned to the intervention (n=60) or control arm (n=60). All received 42 exercise/behavioral recommendations and individualized diets. The intervention consisted of 3 43 hypnosis sessions, during which self-hypnosis was taught to increase self-control before 44 eating. Diet, exercise, satiety, QoL, anthropometric measurements, blood variables were 45 collected/measured at enrolment and at 1-year (trial-end). Results: Participants reduced their 46 caloric intake and lost weight, without significant between-group difference (-423.8kcal, -47 6.5kg intervention arm; -379.0kcal, -5.6kg controls). However, habitual self-hypnosis users 48 lost more weight (-9.6kg;  $\beta$ =-10.2; 95%CI -14.2 -6.18; p<0.001) and greatly reduced their 49 caloric intake (-682.5kcal;  $\beta$ =-643.6; -1064.0 -223.2; p=0.005) in linear regression models. At 50 51 trial-end, intervention group showed lower C-reactive protein values ( $\beta$ =-2.55; -3.80 -1.31; p<0.001), higher satiety ( $\beta=19.2$ ; 7.71 30.6; p=0.001) and better QoL ( $\beta=0.09$ ; 0.02 0.16; 52 p=0.01). Conclusions: In severe obesity, self-hypnosis ameliorated satiety, QoL, 53 inflammation, and determined greater weight loss in more frequent users. 54

#### 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

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

treatment with a therapist, and the successive utilization of audiotapes (7), to a combination of

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,

raging strengthening motivation towards change (9). Most of these treatments are long, demanding,

and difficult to be performed in clinical practice on a large number of patients. Moreover,

during the hypnotic sessions many researchers gave suggestions targeting aversion to specific

<sup>76</sup> high-calorie foods, persuading that overeating is a poison, or employing other techniques of

aversion (10-11), rather than purposeful messages or pleasant suggestions for heightening the

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.

We hypothesized that self-hypnosis could be applied before eating occasions or circumstances 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

techniques (self-hypnosis) added to traditional lifestyle approach (diet, exercise and

89 behavioral recommendations) were effective in determining weight loss, changes in metabolic

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/m<sup>2</sup>; 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

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

- 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
- Eating Scale (16). Only individuals who satisfied all the three scores (respectively < 8, < 17
- 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

techniques plus standard care) or the control arm (standard care, i.e. diet plus exercise plus

- 113 behavioral recommendations) (**Figure 1**).
- 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
- 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
- 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)
- 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
- 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

recommended (e.g. very-low-calorie diets, or highly unbalanced diets) were considered asdrop-outs.

130 Self-hypnosis

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

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

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

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

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/m<sup>2</sup>)
- 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 <u>http://www.epiclin.it</u>). 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

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

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
- -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).
- Body weight and waist circumference were measured at 3, 6, 9-months from randomization,too.
- 211 Participants from the intervention arm were asked about the frequency of self-hypnosis use;
- they were divided in individuals with low (0-1), medium (2-3), or high hypnotizability (4)
- according to the score obtained by the eyeroll Spiegel test.
- The physical activity level was calculated as the product of the duration and frequency of each
- activity (hours/week), weighted by an estimate of the metabolic equivalent (MET) of the
- activity and summed for the activities performed (20).
- Body weight was measured to the nearest 0.1kg, and height to the nearest 0.1cm by a
- stadiometer (SECA model 711, Hamburg, Germany), with the participants wearing light
- clothes and no shoes. Waist circumference was determined by a plastic meter at the highest
- 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

software.

- 223 Arterial blood pressure was measured by a mercury sphygmomanometer with appropriate cuff
- sizes (ERKA Perfect-Aneroid, Germany) in a sitting position after at least 10-min rest; the
- values reported were the mean of two measurements.
  - 9

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

The sample size was calculated in relation to the primary outcome. Available data on patients with clinical characteristics similar to those enrolled were used. With an effect size=0.67 and a 2-tailed  $\alpha$ -error=0.05, 48 patients per arm were needed to obtain a 90% power. This number 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

baseline to 12-months after randomization (deltas). Linear regression models were used to

compare deltas of the analyzed endpoints between-arms, adjusting for the baseline

measurement and the randomization stratification variables [gender, age (50; >50 years), BMI

237  $(40; >40 \text{ kg/m}^2)$ ].

An intention-to-treat analysis was performed including all the randomized patients by

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

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

to estimate the specific mean change from baseline for each arm at fixed times. To account for

the repeated measures on the same subject, mean changes from baseline were estimated

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*

At 12-months, there were 16/60 (26.7%) individuals lost at follow-up from the intervention

arm and 18/60 (30.0%) from the control arm. The main reasons for drop-outs are reported in

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
- intervention and control arms: 1470.6±281.1 and 1496.9±311.9kcal; p<0.001 for within-group
- difference in both groups). Mean differences were -423.8 and -379.0kcal respectively in the
- intervention and control arm (p=0.84). The composition in macronutrients did not
- 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
- 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
- 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
- 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
- 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
- the trial end (Table 2), with within-group significant differences (respectively, p=0.001,
- p<0.001 and p=0.002 for satiety, EuroQoL VAS, and EuroQoL health status). In the controls,
- these scores did not change significantly. The associations between being in the intervention
- arm and the scores were confirmed by linear regression (Table 2), and by the intention-to-treat
- analyses (Supplementary-Table 3).
- 290 Frequency of self-hypnosis use
- At the trial end, 16/44 (36.3%) declared to practice self-hypnosis regularly once/day, 7/44
- (15.9%) more frequently than once/day, 9/44 (20.5%) less frequently than once/day, i.e. with
- a weekly frequency, but 12/44 (27.3%) rarely or never. The corresponding values of delta
- weight were: -9.6kg (≥once/day), -7.5kg (<once/day), and +0.2 (rarely or none).
- 295 The frequency of hypnosis use was significantly associated with changes in weight, BMI,
- waist circumference, and energy intake, after adjusting for age, gender, and BMI
- 297 (Supplementary-Table 4). No significant association was evident with the other
- 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

individuals with low (43.2%), medium (52.3%), or high hypnotizability (4.5%) (19).

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

with any outcomes, either the anthropometric and laboratory variables or the scores of theanalyzed 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* 

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

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

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

335 The impact of hypnosis has been reported to increase over time, being more effective in the long-term, since it allows the establishment of a reinforcement in healthy behaviors that 336 337 continues beyond the training period (1,6,27). Weight maintenance requires continued motivation and engagement; the use of a reinforcement incentive tool, such as self-hypnosis, 338 might be a motivational successful strategy in promoting the maintenance of weight change. 339 340 Accordingly, a significant weight loss compared to baseline at 18-months (27) or a weight loss of 10kg at 2-years (6) was reported by the few studies evaluating the long-term effects of 341 342 hypnosis.

343 *Changes in quality of life and satiety score* 

Both quality of life and satiety increased in our intervention arm. These changes were notassociated with the frequency of self-hypnosis use.

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

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

364 *Change in CRP values* 

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

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

379 *Hypnotic susceptibility* 

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

Indeed, methods of evaluating the degree of susceptibility to hypnosis varied greatly, and its 384 385 assessment has been criticized, since correlations between hypnotizability and treatment outcome might be indicators of expectancy effects, rather than effects of some special 386 387 hypnotic process (1,5). Furthermore, other studies aimed at inducing deeper changes at the cognitive-behavioral level, with numerous long-lasting hypnosis sessions requiring a high 388 capacity for trance; therefore, hypnotic abilities can assume greater importance (10,40). 389 390 Contrariwise, our short-term sessions of self-hypnosis were aimed at obtaining a brief moment of relaxation, during which each participant could evoke the suggestion that he/she 391 would be able to control the amount of food subsequently eaten. Therefore, it is reasonable 392 thinking that the frequency of use of self-hypnosis was more important than the degree of 393 susceptibility in our patients. 394

Finally, we have chosen a very simple measure for pretesting for hypnotizability, since othercomplex 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 patient398 (39).

399 *Limitations* 

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

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

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

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

422 (	Conclusions	
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423	Self-hypi	nosis is a	non-invasive	intervention	free of side	effects.	which a	meliorated s	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

427

426

### 428 **References**

about its benefits could be drawn.

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	Intervention	Control arm	Total
	arm		
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 <sup>2</sup> )	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	$45.0\pm6.1$	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
Dietary intakes			
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

# Table 1. Baseline characteristics of the patients

Laboratory variables			
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)
Drugs			
Antihypertensive (%)	46.7	43.3	45.0
Hypoglycemic agents (%)	6.7	5.0	5.8
Lipid lowering (%)	13.3	11.7	12.5
Questionnaires			
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

 $\overline{Mean \pm SD}$ , median (interquartile range)

	Intervention arm		Control arm				
	End-of the trial	Mean	End-of the trial	Mean	Adjusted		
	value	delta	value	delta	mean		
					difference		
					on delta (β)*	95%CI	Р
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 <sup>2</sup> )	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	125.4±15.1	-4.0	129.6±17.5	-2.6	-3.11	-9.28; 3.07	0.32
(mmHg)							
Diastolic blood pressure	79.9±13.2	-2.3	80.7±8.2	-1.1	-1.03	-5.59; 3.53	0.65
(mmHg)							
Fasting glucose (mg/dL)	92.0±19.4	-2.3	91.5±18.3	+0.3	-1.17	-8.18; 5.84	0.74

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

Glycated hemoglobin	39.0±6.7	-2.7	38.4±6.7	-1.8	-0.33	-2.3; 1.64	0.74
(mmol/mol)							
Fasting insulin ( $\mu$ U/mL)	14.0 (10.2)	-3.7	15.3 (12.8)	-1.5	-1.50	-4.44; 1.43	0.31
HOMA-IR	3.3 (2.2)	-1.1	3.5 (2.6)	-0.4	-0.44	-1.26; 0.39	0.30
(mmol/l*µU/mL)							
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