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A nonrandomized controlled clinical pilot trial on 8 wk of intermittent fasting (24 h/wk)

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Introduction

Intermittent fasting (IF) has increasingly become a focal point for research. This is due to the fact that the benefits of constant caloric restriction (CR) can be achieved while reducing certain risks [1]. The fact that CR is always linked to a constant restriction of food causes a decreased acceptance of CR. So, IF seems to be a promising technique to achieve the known beneficial effects of CR [2,3]. *Intermittent fasting* is an umbrella term describing different kinds of regimens [4]. Currently, the most common methods include 5:2 fasting [5,6], the hypocaloric 2-d diet [5], the alternate-day fasting [7,8] or the every-other-day diet [9,10] as well as time-restricted feeding (e.g., with a 16/8 h rhythm) [11,12]. The nutritional definition of fasting days varies between moderate reduction of caloric intake (600–800 kcal), stricter reduction of energy intake (200–400 kcal), and zero-calorie fasting. Furthermore, there is increasing evidence supporting the use of fast-mimicking diets [13–15]. In Europe, particularly in German-speaking countries, the most popular tradition is the practice of block fasting (e.g., 7–14 d) with a maximum intake of 300 to 400 kcal of liquids as vegetable juice or broth, as prescribed by the Buchinger technique, formulated by Otto Buchinger and others [16].

A variety of animal studies have shown beneficial effects of different kinds of CR/IF [17,18]. The effects of IF on longevity were the same as in CR, but compared with IF, caloric-restricted mice had a higher body weight [19]. Other animal studies indicate that IF has a beneficial effect on breast [20], prostate [21], and pancreatic cancers [22]; cardiovascular and cerebrovascular diseases [23,24]; dementia [25]; other brain functions [26,27]; and type 2 diabetes [13]; which are at least equal to or better than the results of CR.

A range of possible mechanisms underlying the apparent benefits of IF has been proposed. These include increased efficiency of metabolic fuel usage, decreased systemic inflammation, reduced circulating insulin-like growth factor (IGF)-1 and increased cell survival via modulation of apoptosis and enhanced cytoprotection [13,24,28]. However, studies in humans and key molecular mechanisms are currently being investigated [29].

In present human studies, similar cardioprotective effects have been proved in obese women and thus confirm the results from animal studies [30]. A study with healthy, nonobese young adults indicates effects on expression of genes linked to aging and metabolism. The positive effect on glucose metabolism by lower insulin levels may have an antidiabetic effect [3,31]. On the one hand, IF reduces IGF-1, insulin, and glucose levels. On the other hand, it causes increased levels of IGF binding protein 1 and ketone bodies. The combination of both reduction and gain could build a protective environment that reduces DNA damage, cancerogenesis, and increases apoptosis of precancerous cells [32,33].

To our knowledge, this is the first study to examine the effects of a 1-d/wk IF on metabolic profile, psychometric measures, and quality of life.

Methods

Design

The present study was designed as a nonrandomized controlled clinical trial with two arms, involving healthy volunteers only. The study protocol was reviewed and approved by the Ethics Committee of the Charité-University Medical Center, Berlin, Germany. Patients were enrolled between September 12 and September 22, 2014; interventions and follow-up were completed by March 2015. Study procedures and data collection were carried out at the outpatient department of the Immanuel Hospital Berlin, Department of Internal and Complementary Medicine. The trial followed the Declaration of Helsinki and Good Clinical Practice guidelines for trial conduct. Participants provided written informed consent before taking part and were not reimbursed for participation.

Participants

Healthy volunteers of both sexes were eligible if they were between 18 and 65 y of age and had given written informed consent. We excluded individuals if they suffered from any chronic disease, eating disorders, were pregnant or breastfeeding, or if they participated in another clinical trial.

Interventions

Intervention group

All participants in the fasting group received a 60-min group training session about fasting in the 2 wk preceding the start of the IF by a board-certified nutritional counsellor. Participants were instructed to observe one fixed fasting day per week over a period of 8 wk, a fixed week day (e.g., Monday) was requested to facilitate adherence to the protocol (see later). Individual patient adherence was defined by fasting for $\geq$6 of the 8 d of fasting during the 8-wk intervention period (the maximum 2 missed fasting days could be any of the 8 scheduled fasting days). A fasting day was defined as abstinence from solid food for at least the period between 00:00 and 23:59 on the individually chosen weekly fasting day, and by a maximum intake of 300 kcal/d resulting from defined fasting beverages: standard fruit and/or vegetable juices (maximum 2 $\times$ 200 mL/d); clear vegetable broth (maximum 300 mL/d); $\geq$750 mL/d hot, unsweetened herbal teas; $\geq$1500 mL/d of non-sparkling, respectively tap water at room temperature. In case of intolerance to fruit or vegetable juices, grain-based liquids (linseed, rice, millet, and quinoa) were allowed for up to a maximum of 4 $\times$ 150 mL/d as alternatives to juices and broth; for better compliance cardamom, vanilla, and cinnamon were allowed in small quantities to enhance the taste of grain-based liquids. Unsweetened black tea, green tea, and black coffee were also allowed in small quantities (maximum two servings). Participants were instructed to prepare the vegetable broth by themselves, preferably by prolonged boiling of fresh organic vegetables ($\geq$1 h) or by using high-quality organic broth concentrates. Enrichment with fresh green herbs (e.g., basil leaves, parsley leaves), and mild seasoning with salt and pepper was also allowed. Thus, a sample fasting day could consist of 200 mL fruit or vegetable juice in the morning, 300 mL vegetable stock for lunch, 200 mL vegetable or fruit juice in the evening plus 2250 mL of tea and water distributed throughout the entire day. Laxative measures before, during, and after fasting days were not part of the protocol (e.g., standard polyethylenglycol solution, Glauber or Epsom salt). During the intervention, participants were asked to consume the vegetable stock on Mondays at lunch in a group setting and in the presence of a physician experienced with fasting patients. Here, any problems with the intervention could be counseled, while maximum adherence to the intervention was assured, particularly the adherence to a caloric intake of maximum 300 kcal per fasting day.

Control group

Participants in the control group received two group counseling sessions for a healthy diet according to current guidelines of the German Nutrition Society by a board-certified nutritional counselor. Based on this, the participants were instructed to follow a regular healthy diet over the 8-wk study period. Moreover, they were offered the opportunity to perform the IF intervention (as outlined previously) after the end of the 6-mo observational period (waiting-list control group design).

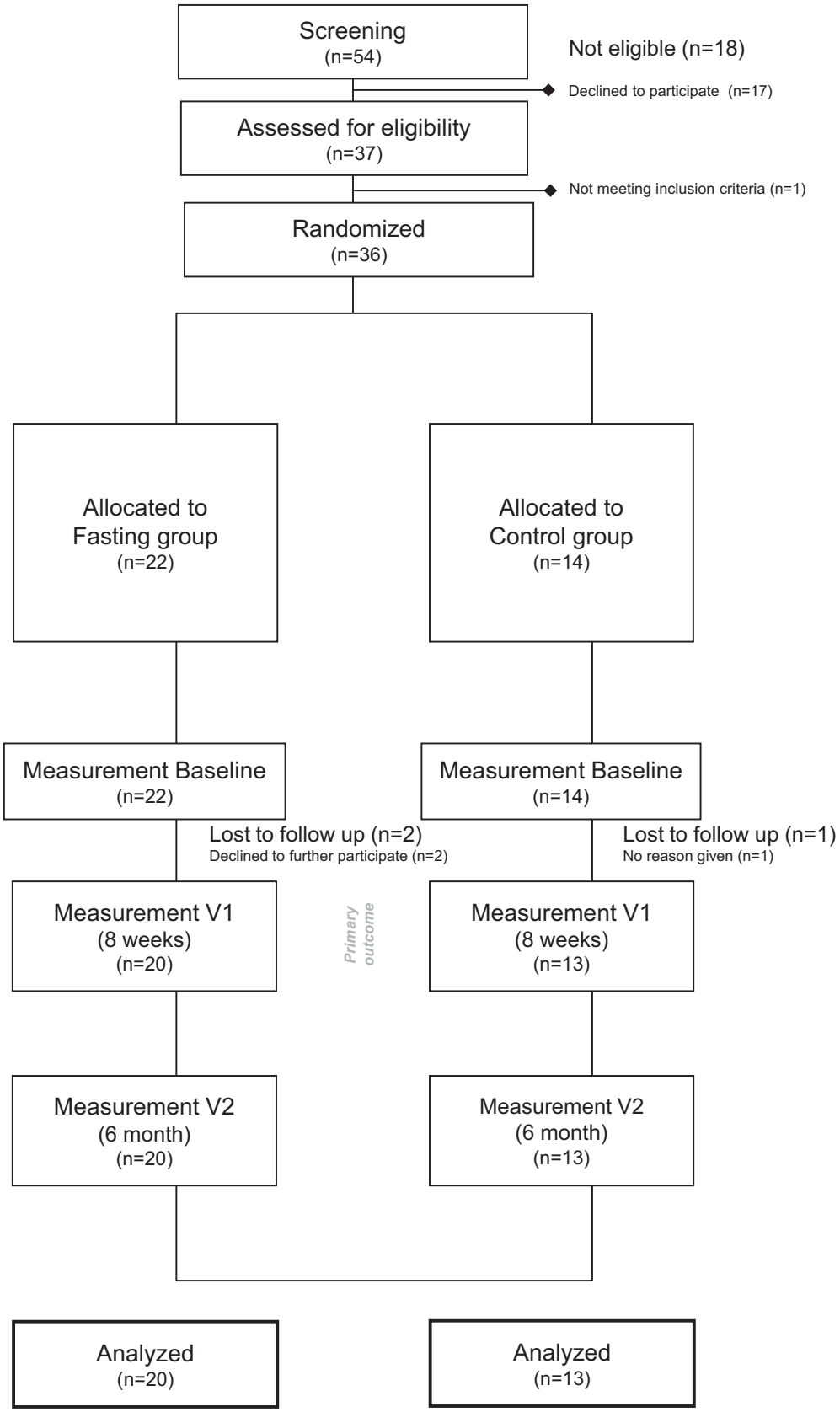

Fig. 1. Consort flowchart.

Table 1
Baseline characteristics

	Fasting group (n = 22)	Control group (n = 14)	*P* value
Age (y)	42.45 ± 10.82	41.36 ± 12.63	0.79
Women (%)	68.2	50	0.46
Weight (kg)	65.67 ± 12.42	67.53 ± 9.38	0.62
BMI (kg/m^2)	22.54 ± 2.74	21.85 ± 2.31	0.43
Systolic BP right (mm Hg)	115.91 ± 12.02	118.46 ± 8.51	0.47
Diastolic BP right (mm Hg)	73.86 ± 9.38	73.08 ± 7.23	0.78
Systolic BP left (mm Hg)	116.36 ± 11.57	116.92 ± 11.09	0.89
Diastolic BP left (mm Hg)	74.55 ± 7.85	75 ± 8.66	0.88
Hip circumference (cm)	96.68 ± 6.71	96.65 ± 6.29	0.99
Abdominal girth (cm)	85.82 ± 9.12	84.85 ± 7	0.73
BMI body fat mass (%)	26.25 ± 7.8	23.45 ± 10.84	0.42
BMI visceral fat mass (%)	5.27 ± 2.35	4.31 ± 1.7	0.17
BMI muscular mass (%)	31.91 ± 5.15	34.14 ± 7.28	0.34
Alkaline phosphatase (μkat/L)	1.12 ± 0.4	1.35 ± 0.26	0.05
GGT (μkat/L)	1.36 ± 5.06	0.29 ± 0.09	0.33
GPT (μkat/L)	0.32 ± 0.11	2.29 ± 7.13	0.34
Triacylglycerols (mmol/L)	1.15 ± 0.38	1.21 ± 0.67	0.78
Total cholesterol (mmol/L)	5.5 ± 1.13	5.75 ± 1.35	0.59
HDL cholesterol (mmol/L)	1.53 ± 0.35	1.36 ± 0.22	0.09
LDL cholesterol (mmol/L)	3.58 ± 0.94	3.94 ± 1.05	0.32
Quick (%)	93.32 ± 7.91	90.46 ± 7.74	0.31
INR	1.05 ± 0.07	1.08 ± 0.06	0.16
PTT (s)	30.45 ± 3.31	31.67 ± 3.2	0.31
Fasting insulin (mU/L)	4.81 ± 1.7	3.7 ± 1.55	0.06
Fasting glucose (mmol/L)	5.03 ± 0.42	5.01 ± 0.42	0.87
Plasma IGF-1 (ng/mL)	99.2 ± 38.2	91.8 ± 32.2	0.54
Serum BDNF (pg/mL)	39.5 ± 91	37.8 ± 8.7	0.57

BP, blood pressure; BDNF, brain-derived neutrophilic factor; BMI, body mass index; GGT, γ-glutamyl transpeptidase; GPT, glutamic/glutamate pyruvic transaminase; HDL, high-density lipoprotein; IGF, insulin-like growth factor; INR, international normalized ratio; LDL, low-density lipoprotein; PTT, partial thromboplastin time

Outcome measures

Outcome measures included changes in serum concentrations of important metabolic markers (insulin, glucose, homeostasis model assessment of insulin resistance [HOMA-IR], hemoglobin [Hb]A1c, total cholesterol [TC], low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], triacylglycerols [TGs]), liver enzymes (glutamic oxalic transaminase [GOT], glutamic/glutamate pyruvic transaminase [GPT], gamma glutamyl transferase [γ-GT], alkaline phosphatase [AP]), coagulation-markers (partial thromboplastin time [PTT], international normalized ratio [INR]), as well as peptides IGF-1 and brain-derived neurotrophic factor (BDNF), bioelectrical impedance analysis (BIA), body mass index (BMI), hip circumference and abdominal girth, systolic and diastolic blood pressures at rest, and the following questionnaires in the German validated version: quality of life (five-item World Health Organization Well-Being Index [WHO-5]), and mood and anxiety (Hospital Anxiety and Depression Scale [HADS], Profile of Mood States [POMS], Flourishing Scale [FSD], visual analog scales for overall health [VAS], and Likert scales). Outcome measures were assessed for all participants at baseline (1–4 d before start of the intervention), at visit 1 (7–11 d after the end of the 8-wk intervention period), and at visit 2 (6 mo after the end of the program). Blood samples were taken by a study nurse at the hospital and then sent to a cooperating local laboratory in Berlin by courier for all parameters other than IGF-1 and BDNF; blood samples for these two parameters were sent to a cooperating laboratory in Milan, Italy, on dry ice by courier. Study nurses also took the measurements mentioned above and handed out questionnaires that were filled out by the participants on site at the hospital.

Statistical analysis

This was an exploratory pilot study. Also, no data could be retrieved on any outcome parameter in a comparable intervention. Therefore, a sample size calculation did not seem possible. We intended to include a maximum of 40 patients. Baseline differences were calculated using two sample *t* tests wherever applicable. A per-protocol analysis was performed. Treatment effects were reported as group differences, *P* values were calculated for deltas (Δbaseline-V1 and Δbaseline-V2) separately. $P < 0.05$ was considered statistically significant. Wilcoxon rank sum test was used to compare differences from baseline between the groups without a null hypothesis. The main comparison was done between baseline and V1 (after 8 wk). The Wilcoxon signed rank test was used to compare within participants. For multiple comparisons (sensitivity analyses) Bonferroni correction was used. All statistical analyses were done within the statistical programming language R (Version 3.3.0).

Results

Fifty-four interested individuals contacted the study secretariat. Of these, 37 were screened, and 1 had to be excluded due to a coagulation disorder. Thirty-six healthy individuals fulfilled all entry criteria and were enrolled in the study. Of these, 22 allocated themselves to the intervention group and 14 to the control group. In all, 20 intervention and 13 control sets of full data could be included into the final per-protocol analysis (Fig. 1).

Baseline data

Participant's characteristics are provided in Table 1. Mean ± SD for each group are represented in Table 1. No significant between-group differences were observed at baseline. Baseline values for participants of both groups reflected a very healthy, middle-aged and predominantly female population, which is typically being observed in studies on complementary, nonmainstream medicine in Germany. Interestingly, despite normal baseline BMI, hip measurement, and abdominal girth values in both groups, the variance of individual participant values for BMI was large (Fig. 2). A similar distribution pattern was observed for IGF-1 baseline values (Fig. 3). Alkaline phosphatase was nonsignificantly higher in the control group.

Outcome measures

In the interventional fasting group, significant within-group differences from baseline to visit 1 (at 8 wk) were observed for

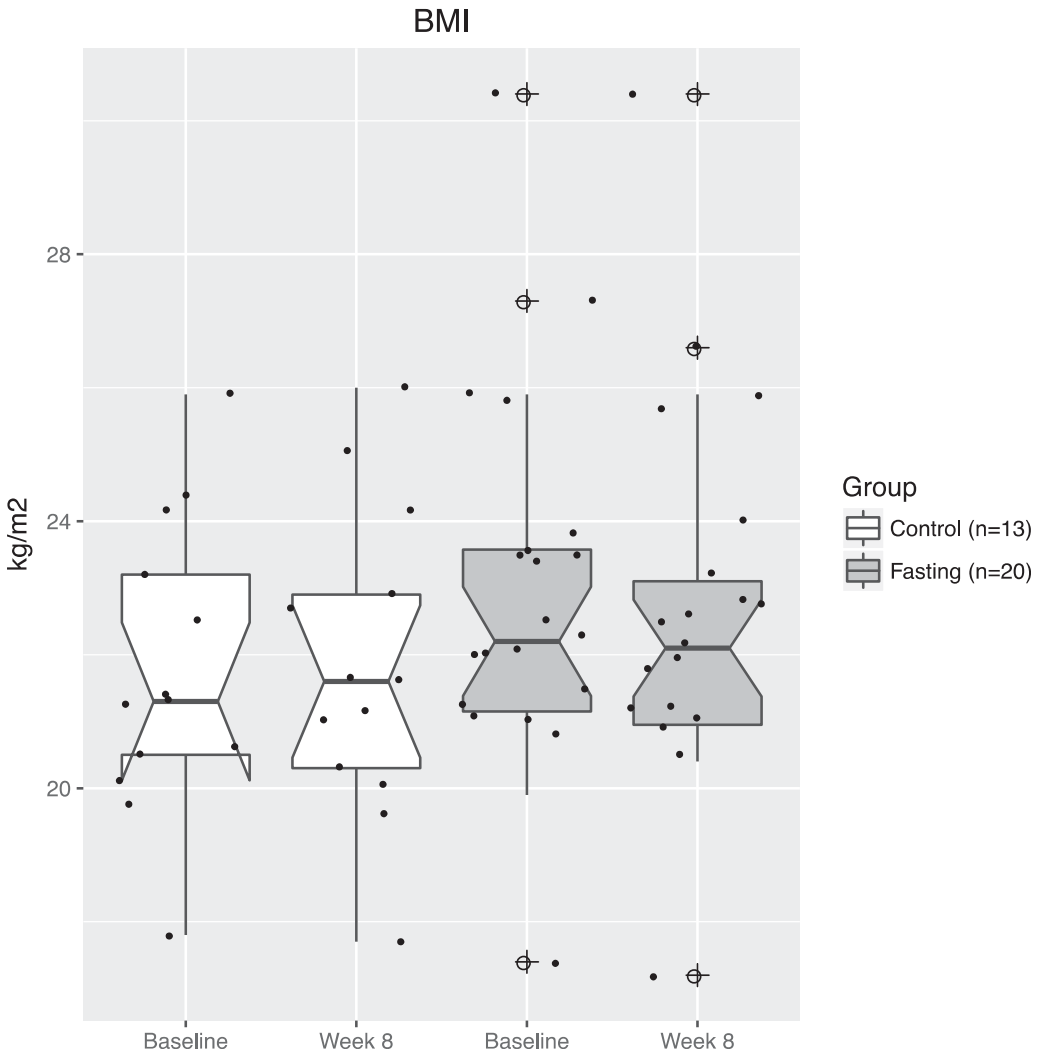

Fig. 2. Distribution pattern of BMI baseline values. BMI, body mass index.

diastolic blood pressure, overall body fat mass, muscle mass, and the HADS anxiety subscore (Fig. 4). Notably, significant within-group differences in the fasting group were observed after 6 mo for the HADS total score, and the HADS depression and anxiety subscales, the POMS total score (including subscales for positive mood and vigor).

In the conventional control group, significant within-group differences were observed for AP, GGT, fasting insulin, INR, HOMA-IR, the HADS total score and the HADS depression subscale at 8 wk. No further within-group differences of significance were observed in the control group for any endpoints at the 6-mo follow-up.

With the exception of a statistically significant difference of overall body fat mass in favor of the intervention group and a difference for AP values, no statistically significant between-group differences were found for any anthropometric outcome and laboratory work outcome at 8 wk. Also, sex subgroup analyses for IGF-I and BDNF did not reveal between-group differences. However, analysis of the questionnaires revealed significant between-group differences for the HADS and WHO-5 total scores in favor of the fasting group after 6 mo (Table 2 and 3; Fig. 4).

Of the 20 per-protocol participants in the intervention group, 9 completed six fasting cycles, 4 completed seven fasting cycles, and 7 completed eight fasting cycles. A sensitivity analysis including only patients with eight cycles revealed no significant differences for the evaluated outcomes. (Appendix Table 1 shows details of these findings.) Detailed results are provided in Tables 2 and 3.

Safety

In all, 86 adverse events (AEs) occurred, involving 29 study participants. AEs were observed in the intervention and control groups (n = 69 and 17, respectively). None of the AEs was classified as serious. Of the AEs in the fasting group, 76% (n = 59) were classified as related or possibly related to the fasting intervention; these included headache, migraine, nausea, ravenousness, circulatory disturbance, hunger, general feeling of weakness, tiredness, stomach ache, meteorism, heartburn, and cold sensations in the body. All AEs were resolved within the study period and none required specific therapies. Overall, the intervention was considered safe.

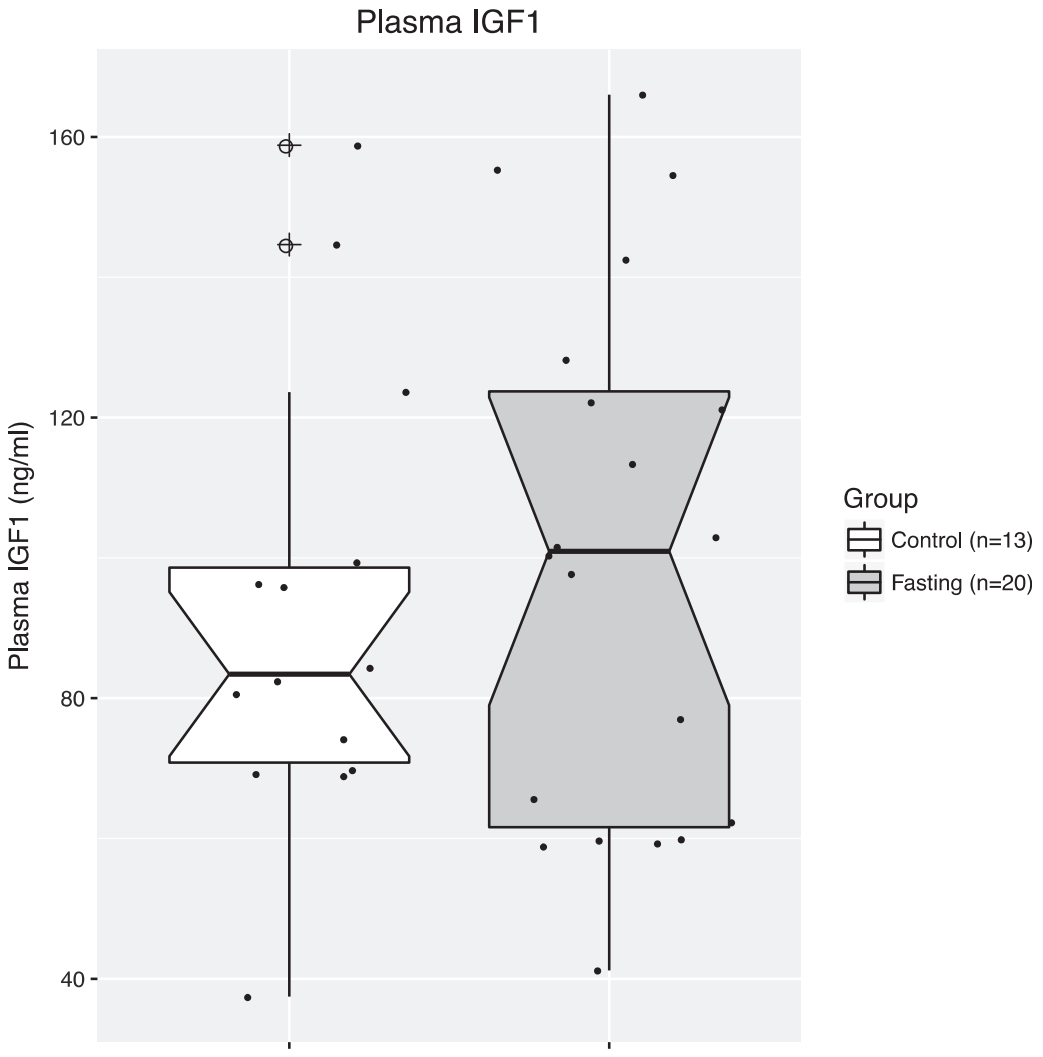

Fig. 3. Distribution pattern of IGF-1 baseline values. IGF, insulin-like growth factor.

Discussion

To the best of our knowledge, this is the first trial to investigate possible clinical effects of a repeatedly performed 1-d fast in healthy individuals. No significant between-group differences were observed at baseline between the two groups.

Although a number of within-group differences in the fasting group were observed, no clinically relevant between-group differences in the outcomes of the anthropometric as well as the metabolic parameters after 8 wk and at the 6-mo follow-up were found. This result seems to contradict the results of animal studies showing a number of positive changes mediated by IF [31,33]. Thus, it seems that there is little chance with healthy individuals to demonstrate possible health benefits on a metabolic level. It also might be important to consider that most human studies showing positive effects of IF investigated obese or diseased participants [7,20,23,25]. The present study failed to display changes in important metabolic signal proteins like IGF-1 or BDNF, confirming the results of other trials [5,6,34]. In contrast, different animal [35] and human studies [36] could show increased BDNF levels induced by IF.

The significant within-group differences for alkaline phosphatase, GGT, fasting insulin, INR, HOMA-IR, HADS total score and HADS depression subscale at week 8 in the conventional control group might be a result of the nutritional counseling sessions promoting a healthy diet or a statistical artifact due to the sample-size limitation of a pilot study.

Interestingly, both groups showed significant improvement in HADS score after 8 wk without a significant between-group difference. The significant between-group difference for HADS and WHO-5 total scores in favor of the fasting group after 6 mo is in line with former studies describing a positive effect on mood and depression [37–39]. Further investigations on patients diagnosed with manifest depression or anxiety could be of value as these individuals in the present study initially already scored well below scores that are valid to diagnose mild depression or anxiety disorders.

Although the results, particularly those relating to laboratory and anthropometric outcome parameters, might be surprising at first, it is important to reflect that only healthy individuals were included in this study, displaying optimum health levels at baseline. Looking at the baseline data of both groups it is debatable, whether hormesis effects can be triggered in the same

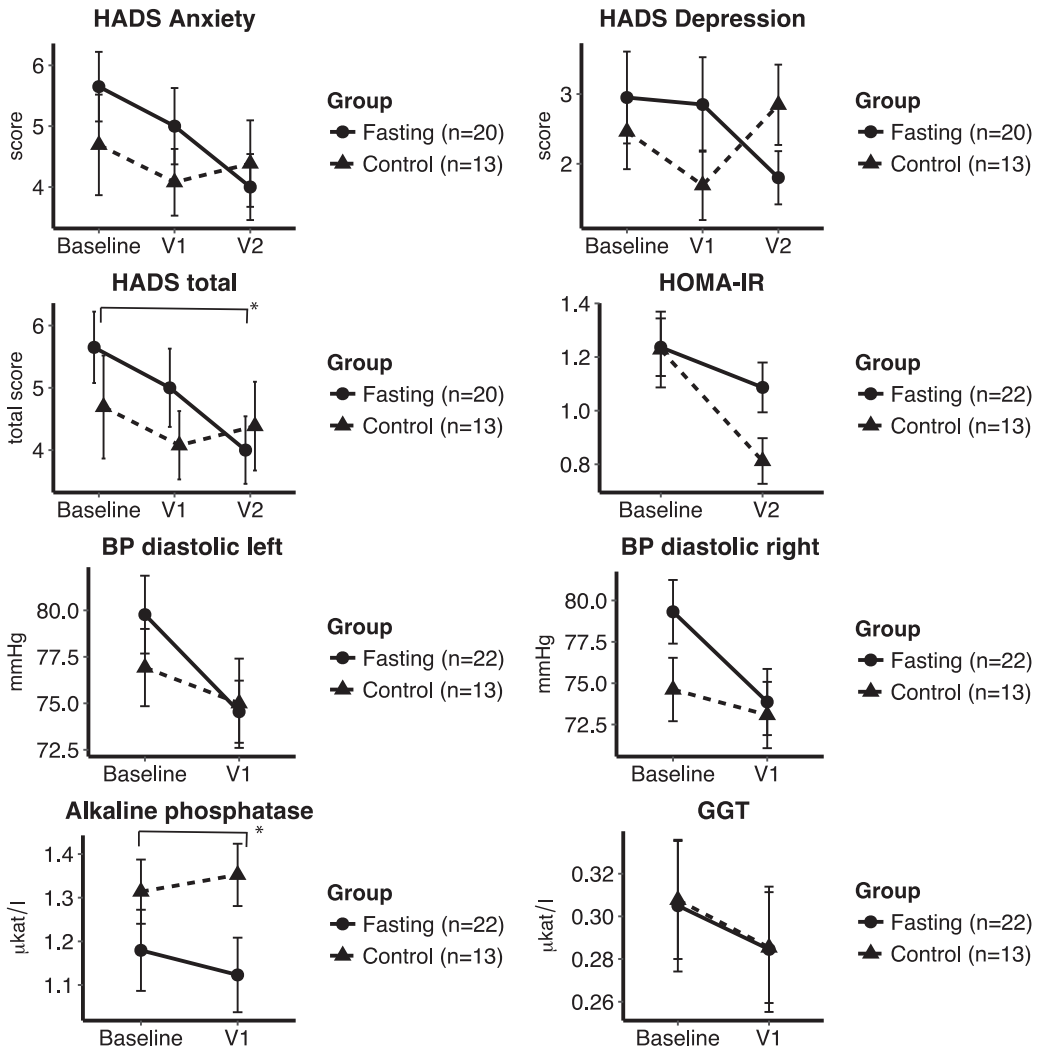

Fig. 4. Multiplot figure of relevant results. BP, blood pressure; HOMA-IR, momoeostasis model assessment of insulin resistance; HADS, Hospital Anxiety and Depression Scale; GGT, γ-glutamyl transpeptidase. $^{*}P < 0.05$ between-group baseline and follow-up.

magnitude for healthy individuals as for those with chronic conditions, such as diabetes or other metabolic syndrome entities.

Another aspect to be discussed in future studies is whether the inclusion of an IF intervention into regular working-day activities represents a potential confounder on fasting effects that might exert an additional stress factor.

Furthermore, the moderate intensity fasting intervention analyzed in this study may have been too weak compared to 5:2, time-restricted feeding, or other methods.

The main limitations of this trial are the small number of participants, the nonrandomized study design, and the lack of objective tracking of compliance (e.g., by including a fasting/nutritional diary). For instance, the fasting individuals might have overcompensated their caloric intake after starting to eat normal food again, whereas the dietary habits of both groups during the intervention might have been affected by the overall trial setting. Another limitation is the predominantly female population; however, this is a general shortcoming in the field of complementary and alternative medicine research. Well-planned, larger confirmatory randomized controlled trials might show beneficial effects of IF and are warranted for future research in this area.

Conclusion

The results of the present study did not find any clinically relevant in-between group differences in this controlled clinical pilot trial of 8 wk of IF with healthy volunteers. The only statistically significant between-group differences were observed for HADS and the WHO-5 total scores in favor of the fasting group at the 6-mo follow-up. Further clinical research in this field is warranted to analyze the mechanisms and effects of IF, both in healthy and diseased individuals.

Acknowledgments

The authors acknowledge the work of all participating medical personnel. Most importantly, however, the authors acknowledge the volunteers for participating.

Table 2
Mean change within groups (per-protocol analysis)

	Fasting group (n = 20)			Control group (n = 13)			*P* value between groups Δ baseline – after 8 wk†
	Baseline	Baseline – after 8 wk	*P* value*	Baseline	Baseline – after 8 wk	*P* value*	
Weight (kg)	66.4 ± 12.7	−0.72 ± 1.89	0.13	67.25 ± 9.25	0.28 ± 0.84	0.33	0.15
BMI (kg/m^2)	22.8 ± 2.8	−0.25 ± 0.68	0.10	21.8 ± 2.2	0.08 ± 0.29	0.33	0.09
Systolic BP right (mm Hg)	117.5 ± 12.98	−1.59 ± 10.05	0.61	121.54 ± 11.79	−3.08 ± 9.02	0.2	0.69
Diastolic BP right (mm Hg)	79.32 ± 9.04	−5.45 ± 9.25	0.01	74.62 ± 6.91	−1.54 ± 8.75	0.62	0.14
Systolic BP left (mm Hg)	119.55 ± 14.22	−3.18 ± 11.08	0.14	118.08 ± 13	−1.15 ± 6.5	0.58	0.65
Diastolic BP left (mm Hg)	79.77 ± 9.82	−5.23 ± 8.66	0.01	76.92 ± 7.51	−1.92 ± 8.79	0.53	0.25
Hip circumference (cm)	96.96 ± 7.43	−0.28 ± 2.31	0.63	95.65 ± 6.13	0.99 ± 2.09	0.13	0.14
Abdominal girth (cm)	85.48 ± 10.25	0.34 ± 4.37	0.71	85.15 ± 7.64	−0.31 ± 3.73	0.43	0.51
BMI body fat mass (%)	28.04 ± 9	−1.79 ± 3.77	<0.001	23.58 ± 9.93	−0.13 ± 2.34	1	0.03
BMI visceral fat mass (%)	5.18 ± 2.36	0.09 ± 0.68	0.53	4.69 ± 2.29	−0.38 ± 1.19	0.28	0.34
BMI muscle mass (%)	30.86 ± 6.05	1.05 ± 3.36	0.01	33.12 ± 7.3	1.02 ± 2.9	0.55	0.18
Alkaline phosphatase (μkat/L)	1.18 ± 0.44	−0.06 ± 0.19	0.16	1.31 ± 0.27	0.04 ± 0.05	0.02	0.04
GGT (μkat/L)	0.3 ± 0.14	1.06 ± 5.06	0.27	0.31 ± 0.1	−0.02 ± 0.04	0.04	0.94
GPT (μkat/L)	0.29 ± 0.12	0.03 ± 0.09	0.26	0.31 ± 0.12	1.98 ± 7.13	0.65	0.69
Triacylglycerols (mmol/L)	1.28 ± 0.64	−0.13 ± 0.45	0.17	1.25 ± 0.66	−0.05 ± 0.43	0.57	0.9
Total cholesterol (mmol/L)	5.64 ± 1.27	−0.13 ± 0.53	0.29	5.65 ± 1.46	0.09 ± 0.48	0.48	0.23
HDL cholesterol (mmol/L)	1.58 ± 0.39	−0.05 ± 0.13	0.2	1.37 ± 0.21	−0.01 ± 0.14	0.68	0.6
LDL cholesterol (mmol/L)	3.7 ± 1.06	−0.12 ± 0.49	0.29	3.82 ± 1.15	0.12 ± 0.38	0.28	0.14
Quick (%)	92.86 ± 7.15	0.45 ± 6.36	0.95	93.46 ± 8.25	−3 ± 6.95	0.15	0.19
INR	1.05 ± 0.06	0 ± 0.06	0.83	1.04 ± 0.05	0.04 ± 0.05	0.03	0.08
PTT (s)	31.09 ± 2.84	−0.64 ± 1.84	0.14	32.17 ± 2.86	−0.5 ± 1.98	0.58	0.66
Fasting insulin (mU/L)	5.49 ± 2.12	−0.68 ± 1.92	0.1	5.32 ± 2.24	−1.62 ± 2.18	0.01	0.27
Fasting glucose (mmol/L)	5.09 ± 0.56	−0.05 ± 0.42	0.94	5.18 ± 0.3	−0.18 ± 0.29	0.05	0.2
HOMA-IR	1.24 ± 0.5	−0.15 ± 0.41	0.1	1.23 ± 0.51	−0.42 ± 0.53	<0.01	0.23
P-IGF-1 (ng/mL)	116.74 ± 67.53	−21.66 ± 74.34	0.44	91.48 ± 33.44	−2.72 ± 40.49	0.89	0.63
S-BDNF (pg/mL)	39.48 ± 9.12	−0.61 ± 19.8	0.92	38.11 ± 8.99	0.51 ± 13.8	0.79	0.75

BP, blood pressure; BMI, body mass index; GGT, γ-glutamyl transpeptidase; GPT, glutamic-pyruvic transaminase; HDL, high-density lipoprotein; HOMA-IR, homoeostasis model assessment of insulin resistance; INR, international normalized ratio; LDL, low-density lipoprotein; P-IGF, plasma insulin-like growth factor; PTT, partial thromboplastin time; S-BDNF, serum brain-derived neutrophic factor
Mean ± SD

* Wilcoxon signed-rank test.

† Wilcoxon rank-sum test.

Table 3
Mean change within groups for questionnaires (per-protocol analysis)

	Fasting group (n = 20)					Control group (n = 13)					*P* value between Groups Δ Baseline – after 8 wk†	*P* value between Groups Δ Baseline – after 6 mo†
	Baseline	Δ Baseline – after 8 wk	*P*-value*	Δ Baseline – after 6 mo	*P*-value*	Baseline	Δ Baseline – after 8 wk	*P*-value*	Δ Baseline – after 6 mo	*P* value*		
HADS total	8.59 ± 5	−0.82 ± 2.67	0.13	−2.8 ± 3.53	<0.001	7.15 ± 4.31	−1.93 ± 3.34	0.05	0.08 ± 3.38	0.89	0.39	0.03
HADS anxiety	5.68 ± 2.46	−0.77 ± 1.6	0.05	−1.67 ± 1.62	<0.001	4.86 ± 2.93	−1 ± 2.66	0.2	−0.31 ± 2.25	0.52	0.76	0.06
HADS depression	2.91 ± 2.84	−0.05 ± 1.7	0.96	−1.15 ± 2.62	0.05	2.64 ± 1.98	−0.93 ± 1.49	0.03	0.38 ± 1.85	0.5	0.19	0.07
WHO-5 total	15.91 ± 4.92	1.05 ± 4.01	0.29	1.25 ± 3.43	0.17	17.29 ± 3.95	−0.57 ± 6.21	0.39	−1.67 ± 3.5	0.1	0.14	0.04
FSD total	47.82 ± 5.77	1.05 ± 2.59	0.11	1.81 ± 4.19	0.08	49.77 ± 3.54	−0.08 ± 4.07	1	−0.15 ± 2.79	0.72	0.39	0.18
POMS total	46.19 ± 17.51	1.24 ± 16	0.77	−5.29 ± 11.13	0.05	49.5 ± 16.16	−4.58 ± 18.28	0.46	1.64 ± 14.21	0.72	0.29	0.18
Positive mood	30.14 ± 6.74	−1.86 ± 8.08	0.57	2.67 ± 5.54	0.02	29.79 ± 5.51	−1 ± 6.73	0.73	−0.45 ± 6.19	0.96	0.85	0.1
Vigor	17.86 ± 6.74	1.86 ± 8.08	0.57	−2.67 ± 5.54	0.02	18.21 ± 5.51	1 ± 6.73	0.73	0.45 ± 6.19	0.96	0.85	0.1
Depression	5.55 ± 3.42	0 ± 2.25	0.79	−0.81 ± 2.87	0.26	5.62 ± 3.15	−0.08 ± 3.9	0.84	1.31 ± 4.01	0.42	0.53	0.45
Tension	4.77 ± 3.64	−0.09 ± 2	0.76	−0.81 ± 2.6	0.17	4.86 ± 3.11	−0.86 ± 3.66	0.23	0.54 ± 3.13	0.53	0.39	0.21
Fatigue	12 ± 5.22	−0.48 ± 6.06	0.99	−1 ± 3.85	0.1	12.69 ± 4.05	−0.69 ± 5.06	0.57	0.32 ± 5.2	0.79	0.77	0.71
Anger	5.5 ± 3.43	−0.09 ± 3.46	0.86	0 ± 1.9	0.94	6.29 ± 3.6	−1.29 ± 4.55	0.29	0.74 ± 3.99	0.9	0.38	0.82

FSD, Flourishing Scale; HADS, Hospital Anxiety and Depression Scale; POMS, Profile of Mood States; WHO-5, 5-item World Health Organization Well-Being Index
Mean ± SD
* Wilcoxon signed rank test.
† Wilcoxon rank sum test.

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Appendix

Appendix table 1
Subgroup analysis regarding intervention-adherence with 8 individuals that adhered to all 8 fasting cycles

	Fasting group (n = 8)			Control group (n = 13)			*P*-value between Groups Δ baseline - after 8 weeks†
	Baseline	Baseline - after 8 weeks	*P*-value*	Baseline	Baseline - after 8 weeks	*P*-value*	
Systolic BP right (mmHg)	118.57 ± 14.35	−1.43 ± 14.06	0.89	121.54 ± 11.79	−3.08 ± 9.02	0.2	0.57
Diastolic BP right (mmHg)	80 ± 10.41	−6.43 ± 8.52	0.03	74.62 ± 6.91	−1.54 ± 8.75	0.62	0.29
Systolic BP left (mmHg)	120 ± 16.07	−2.86 ± 15.24	0.75	118.08 ± 13	−1.15 ± 6.5	0.58	1
Diastolic BP left (mmHg)	82.14 ± 10.35	−7.86 ± 11.5	0.08	76.92 ± 7.51	−1.92 ± 8.79	0.53	0.23
Hip circumference (cm)	99.36 ± 7.09	−1.07 ± 2.13	0.21	95.65 ± 6.13	0.99 ± 2.09	0.13	0.07
Systolic BP right (mmHg)	88.21 ± 11.22	−0.93 ± 2.95	0.25	85.15 ± 7.64	−0.31 ± 3.73	0.43	0.92
BIA Body Fat Mass (%)	28.54 ± 11.37	−1.7 ± 2.16	0.11	23.58 ± 9.93	−0.13 ± 2.34	1	0.13
BIA Visceral Fat Mass (%)	5.71 ± 2.69	0 ± 0.58	1	4.69 ± 2.29	−0.38 ± 1.19	0.28	0.74
BIA Muscular Mass (%)	30.89 ± 6.26	0.69 ± 1.03	0.11	33.12 ± 7.3	1.02 ± 2.9	0.55	0.43
Alk. Phosphatase (μkat/l)	0.98 ± 0.22	0.03 ± 0.15	0.69	1.31 ± 0.27	0.04 ± 0.05	0.02	0.63
GGT (μkat/l)	0.25 ± 0.08	0.01 ± 0.04	0.4	0.31 ± 0.1	−0.02 ± 0.04	0.04	0.16
GPT (μkat/l)	0.24 ± 0.09	0.06 ± 0.11	0.15	0.31 ± 0.12	1.98 ± 7.13	0.65	0.34
Triglycerides (mmol/l)	1.03 ± 0.5	−0.06 ± 0.24	0.68	1.25 ± 0.66	−0.05 ± 0.43	0.57	0.68
Total cholesterol (mmol/l)	5.39 ± 1.51	−0.24 ± 0.61	0.35	5.65 ± 1.46	0.09 ± 0.48	0.48	0.3
HDL-cholesterol (mmol/l)	1.59 ± 0.3	−0.03 ± 0.13	0.58	1.37 ± 0.21	−0.01 ± 0.14	0.68	0.74
LDL-cholesterol (mmol/l)	3.55 ± 1.21	−0.27 ± 0.56	0.25	3.82 ± 1.15	0.12 ± 0.38	0.28	0.13
Quick (%)	87.43 ± 5.32	1.29 ± 7.65	0.61	93.46 ± 8.25	−3 ± 6.95	0.15	0.25
INR	1.09 ± 0.04	0 ± 0.08	0.71	1.04 ± 0.05	0.04 ± 0.05	0.03	0.26
PTT (sec)	32.14 ± 3.02	−1 ± 2	0.29	32.17 ± 2.86	−0.5 ± 1.98	0.58	0.32
Fasting Insulin (mU/l)	4.93 ± 2.55	−0.41 ± 1.03	0.3	5.32 ± 2.24	−1.62 ± 2.18	0.01	0.25
Fasting Glucose (mmol/l)	5.3 ± 0.54	−0.17 ± 0.39	0.23	5.18 ± 0.3	−0.18 ± 0.29	0.05	0.95
S-BDNF (pg/ml)	42.26 ± 8.53	−11.31 ± 17.44	0.16	38.11 ± 8.99	0.51 ± 13.8	0.79	0.13
P-IGF-1 (ng/ml)	166.71 ± 96.12	−81.67 ± 95.47	0.08	91.48 ± 33.44	−2.72 ± 40.49	0.89	0.04

BIA, Body impendence analysis; BDNF, Brain-derived neutrophic factor; IGF-1, Insulin-like growth factor 1
Mean ± SD

* Wilcoxon signed rank test.

† Wilcoxon rank sum test (adjusted alpha = 0.025 (correction for multiple comparisons, Bonferroni)).

Table 3
Results Questionnaires - Sensitivity

	Fasting group (n = 8)					Control group (n = 13)					*P*-value between Groups Δ baseline - after 8 weeks†	*P*-value between Groups Δ baseline - after 6 months†
	Baseline	Baseline - after 8 weeks	*P*-value*	Baseline - after 6 months	*P*-value*	Baseline	Baseline - after 8 weeks	*P*-value*	Baseline - after 6 month weeks	*P*-value*		
HADS total	8.29 ± 7.25	−0.29 ± 1.38	0.71	−3.71 ± 4.82	0.06	7.5 ± 4.31	−1.93 ± 3.34	0.05	0.08 ± 3.38	0.89	0.19	0.08
HADS anxiety	5.29 ± 2.93	−0.86 ± 0.69	0.03	−2 ± 1.41	0.03	4.86 ± 2.93	−1 ± 2.66	0.2	−0.31 ± 2.25	0.52	0.84	0.1
HADS depression	3 ± 4.51	0.57 ± 1.4	0.33	−1.71 ± 3.95	0.29	2.64 ± 1.98	−0.93 ± 1.49	0.03	0.38 ± 1.85	0.5	0.04	0.23
WHO-5 total	17.43 ± 6.16	0.43 ± 3.05	0.61	2.57 ± 3.74	0.11	17.29 ± 3.95	−0.57 ± 6.21	0.39	−1.67 ± 3.5	0.1	0.33	0.03
FSD total	46.14 ± 8.19	1.43 ± 2.82	0.2	3.57 ± 5.22	0.11	49.57 ± 3.48	−0.14 ± 3.92	0.89	−0.15 ± 2.79	0.72	0.36	0.08
POMS total	45 ± 24.82	6.5 ± 11.5	0.34	−8.86 ± 12.12	0.08	49.5 ± 16.16	−4.58 ± 18.28	0.46	1.64 ± 14.21	0.72	0.15	0.13
Positive mood	30.71 ± 8.36	−2.29 ± 7.27	0.75	4 ± 5.57	0.11	29.79 ± 5.51	−1 ± 6.73	0.73	−0.45 ± 6.19	0.96	0.78	0.13
Vigor	17.29 ± 8.36	2.29 ± 7.27	0.75	−4 ± 5.57	0.11	18.21 ± 5.51	1 ± 6.73	0.73	0.45 ± 6.19	0.96	0.78	0.13
Depression	5.71 ± 5.06	1.29 ± 1.8	0.07	−1.57 ± 3.74	0.29	5.62 ± 3.15	−0.08 ± 3.9	0.84	1.31 ± 4.01	0.42	0.16	0.49
Tension	5.57 ± 5.97	0.57 ± 1.51	0.32	−1.71 ± 3.73	0.18	4.86 ± 3.11	−0.86 ± 3.66	0.23	0.54 ± 3.13	0.53	0.2	0.16
Fatigue	9.33 ± 2.94	0.33 ± 2.5	0.68	−1.57 ± 2.15	0.11	12.69 ± 4.05	−0.69 ± 5.06	0.57	0.32 ± 5.2	0.79	0.62	0.63
Anger	5.29 ± 3.59	1.29 ± 2.56	0.1	0 ± 2	1	6.29 ± 3.6	−1.29 ± 4.55	0.29	0.74 ± 3.99	0.9	0.1	0.99

HADS, Hospital Anxiety and Depression Scale; WHO-5, WHO-5 Well-Being Index; HADS, Hospital Anxiety and Depression Scale; FSD, Flourishing Scale; POMS, Profile of Mood States
Mean ± SD

* Wilcoxon signed rank test.

† Wilcoxon rank sum test (adjusted alpha = 0.025 (correction for multiple comparisons, Bonferroni)).

Corrigendum to 'A nonrandomized controlled clinical pilot trial on 8 wk of intermittent fasting (24 h/wk)' Nutrition. 2018;46:143–152.e2.

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The authors regret a transmission error in the consort flowchart in box 3 (top down) of Fig. 1: "Randomized (n=36)" is of course incorrect; correct is "Allocated (n=36)". As clearly stated in title, abstract, methods, discussion and conclusion of the publication this was a nonrandomized controlled trial. The authors would like to apologise for any inconvenience caused.

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