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Psychological predictors of the antihypertensive effects of music-guided slow breathing

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Background The possibility that daily sessions of music-guided slow breathing may reduce 24-h ambulatory blood pressure (ABP), and predictors of efficacy were explored in a randomized, placebo-controlled trial with parallel design.

Methods Age-matched and sex-matched hypertensive patients were randomized to music-guided slow breathing exercises (4–6 breaths/min; 1:2 ratio of inspiration:expiration duration) (Intervention; $n = 29$) or to control groups who were thought to relax while either listening to slow music (Control-M; $n = 26$) or reading a book (Control-R; $n = 31$). At baseline and at follow-up visits (1 week and 1, 3 and 6 months), ABP monitoring was performed.

Results At mixed model analysis, intervention was associated with a significant reduction of 24-h ($P = 0.001$) and night-time (0100–0600 h) ($P < 0.0001$) systolic ABP. The average reduction of systolic 24-h ABP at 6 months was 4.6 mmHg [confidence limits at 95% 1.93–7.35] and 4.1 mmHg (95% confidence limits 1.59–6.67) vs. Control-M and Control-R groups, respectively, ($P < 0.001$ for both). Antihypertensive treatment was selected as negative predictor of BP reduction at multivariate stepwise analysis. When antihypertensive treatment was inserted as covariate in a generalized linear model, psychological subscales assessed at baseline by the Mental Health Inventory questionnaire were found to affect systolic blood pressure reduction at 6-month follow-up (general positive affect $P < 0.001$; emotional ties, $P < 0.001$; loss of behavioral

control, $P = 0.035$). In particular, a level of general positive affect higher than the 75th percentiles was found to be significantly associated with low treatment efficacy (odds ratio 0.09; 95% confidence limits 0.01–0.93).

Conclusion Daily sessions of voluntary music-guided slow breathing significantly reduce 24-h systolic ABP, and psychological predictors of efficacy can be identified.

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Keywords: hypertension, music, nonpharmacologic treatment, respiratory exercise

Abbreviations: ABP, ambulatory blood pressure; ABPM, 24-h ambulatory blood pressure monitoring; ANOVA, analyses of variance; BP, blood pressure; DBP, diastolic blood pressure; MHI, Mental Health Inventory questionnaire; OR, odds ratio; QoL, quality of life; SBP, systolic blood pressure

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Introduction

Different behavioral techniques (yoga or meditation practice) were reported to reduce blood pressure (BP) and antihypertensive drug requirements [1–3], although conflicting results exist [4]. Methodological shortcomings [5] may have limited some of these studies, which, however, cannot be considered as a whole because of the relevant differences in tasks or stimuli used. These differences make impossible to identify the factor(s) responsible for antihypertensive effect, so in recent years

devices were developed to focus specially on breathing rate [6–9]. Electronic devices capable of driving the breathing rate by means of sounds were thus used in clinical studies performed with a preobservational and postobservational design [10,11], with a design similar to that of prospective matched case–control studies [12,13] and randomized controlled trials [14,15], all providing evidence in favor of a reduction of office and home BP after 2 months of daily sessions of slow-breathing exercises below 10 breaths/min. With these supports [16,17], device-guided slow breathing is now approved for use as an adjunct to lifestyle modifications and drug therapy in hypertensive patients. However, no information exists regarding predictors of success and compliance. To

The study was presented, in part, at the American Society of Hypertension's Twenty-Third Annual Scientific Meeting, New Orleans, Louisiana, 14 May 2008; and at the IXX European Meeting on Hypertension, Milan, Italy, 14 June 2009.

define which patients may really benefit from behavioral methods would be of great value to move this demanding nonpharmacologic treatment into the clinical practice.

An acute reduction in breathing rate and BP was also observed during listening to music with slow rhythm and tempo [18,19], and a possible entrainment of respiration rate to tempo (i.e. temporal patterning conveyed by tones' perception) was reported [8,19]. However, no studies investigated the antihypertensive effects of slow music listening and the relative contribution of specific voluntary breathing exercises.

Therefore, a randomized, placebo-controlled study with parallel design was performed to investigate, in hypertensive patients, the effect of voluntary music-guided breathing exercises on ambulatory BP and possible predictors of efficacy [20] and compliance.

Patients and methods

Participants

The study protocol was approved by the local ethics committee (Prot.n.2009/0004365), and all participants gave informed consent to participate in the study.

Inclusion criteria were outpatients aged 40–75 years with essential hypertension, untreated or constantly treated with the same doses of antihypertensive drugs for at least 3 months prior to the study. Exclusion criteria were chronic atrial fibrillation, angina, heart failure, cerebrovascular disease, diabetes mellitus, renal failure, asthma, chronic respiratory disease, pregnancy, neoplasia and altered night-time sleep because of shift work. Clinical characteristics of participants at enrolment are reported in Table 1. None of them had received formal musical training.

Study design and protocol

The study had a randomized, placebo-controlled, parallel design. The presumed role of stress in hypertension was preliminarily explained to all eligible participants, and

they were told that the study was designed to compare the effects of different approaches of relaxation therapy. If participants agreed, they were randomized into three groups. Participants allocated into the intervention group ($n=29$) were thought to perform the Buteyko and pranayama breathing technique (see following section) with breathing rate guided by music excerpts characterized by slow rhythm and tempo [19] (see the list at end of this paragraph). Participants allocated to control groups received no mention of breathing exercises and were thought to relax while either listening to slow music (see the list) (Control-M group; $n=26$) or reading a book or magazine (Control-R group; $n=31$). All participants were requested to repeat daily, at home for 6 months, the 30-min relaxation session at least 3 h after lunch. Follow-up visits were scheduled at 1 week, 1, 3 and 6 months. A further follow-up visit 6 months after the end of treatment was scheduled for the intervention group.

The excerpts of the classical music repertoire used included

- (1) Mozart WA: Violin Concerto No. 3 in G major–II (Adagio)
- (2) Mozart WA: Clarinet Concerto in A major II (Adagio)
- (3) Mozart WA: Piano Concerto No. 23 in A major–II (Adagio)
- (4) Mozart WA: Piano Concerto No. 21 in C Major–II (Andante)
- (5) Bach JS: Air from Suite No. 3 in D (transcribed for cello and piano by L. Rose)
- (6) Rachmaninov S: Vocalise, Op. 34, No.14 (transcribed for cello and piano by L. Rose)

The pieces of Celtic inspired music included four songs for harp and female voice:

- (1) Garella D: 'Paesaggio d'Autunno'
- (2) Garella D: 'Canto nel Vento'
- (3) Schroeder T: 'Mana Vu'
- (4) McKennitt L: 'Prospero's Speech'

Table 1 Characteristics of individuals at enrolment

Variables	Control-R (reading)	Control-M (music)	Intervention (music + respiration)	ANOVA (P)
Male/female (n/n)	20/11	16/10	16/13	0.594
Age (years)	61 (56–65)	58 (53–61)	58 (54–62)	0.406
Smokers (n)	1	1	2	0.796
BMI (kg/m ²)	26 (24–27)	25 (23–26)	25 (24–27)	0.744
Waist circumference (cm)	94 (89–99)	93 (82–103)	94 (88–99)	0.972
Systolic BP (mmHg)	130 (125–134)	131 (125–135)	131 (126–136)	0.876
Diastolic BP (mmHg)	77 (73–81)	79 (75–82)	79 (74–83)	0.827
Heart rate (bpm)	70 (65–74)	72 (67–77)	72 (67–77)	0.640
Blood glucose (mg/dl)	94 (88–101)	93 (85–101)	95 (87–103)	0.944
Total cholesterol (mg/dl)	197 (184–209)	201 (181–221)	203 (186–219)	0.819
HDL cholesterol (mg/dl)	57 (53–61)	60 (49–71)	59 (52–66)	0.768
LDL cholesterol (mg/dl)	115 (104–125)	117 (94–140)	118 (100–136)	0.943
Triglycerides (mg/dl)	102 (87–118)	98 (75–121)	100 (82–117)	0.936
Uric acid (mg/dl)	5.4 (4.8–5.9)	5.6 (4.1–7.1)	5.5 (4.7–6.2)	0.925
Creatinine (mg/dl)	0.88 (0.80–0.95)	0.85 (0.74–0.96)	0.87 (0.79–0.96)	0.898
Creatinine clearance (ml/min)	87 (79–96)	88 (70–106)	90 (78–102)	0.927

Mean (95% confidence limits). ANOVA, univariate analyses of variance; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

The Indian Raga music used included

- (1) Shantam: 'Heart rain' (composed on the Raga Megh scale – flauto bansuri and tampura)
- (2) Tapasya: 'Raga Bhairav' (Shiva mantra and tampura).

Care was taken that participants from the different groups did not meet or acquire extracurricular relaxation skills. At follow-up visits, all participants were seen individually by the same assistant who inquired about stressful periods and the influence of the daily rest on their general well-being. Participants kept diary cards to record home sessions and medication use. Quality of life (QoL) was assessed at randomization and at the 6-month follow-up visit using the Medical Outcome Study Short-form 36-Item Health Survey [21]. Participants allocated to the voluntary music-guided breathing exercises were requested to fill the Mental Health Inventory questionnaire (MHI) [20] at randomization. Psychological subscales (anxiety, depression, loss of behavioral and emotional control, general positive affect, emotional ties, satisfaction of life) were then calculated.

Training and intervention

Breathing technique was taught by a certified practitioner in a single 2-h session. After 20 min of quiet rest, listening of music characterized by homogeneous regular and slow rhythm and tempo (52 bits/min, Metronome Marking) (range: 40–60) (see the list in the previous section) [19] was started. During the first 10 min the patient was requested to synchronize his respiration to the slow musical rhythm, reaching 4–6 breaths/min (Buteyko method) [22], and then to maintain the same rate while performing 'abdominal' breathing with a 1 : 2 inspiration : expiration duration ratio (pranayama yoga) [22] for the other 20 min. The session with the therapist was repeated after 1 week, 1, 3 and 6 months from allocation.

Blood pressure measurements

Office BP measurements were taken at each visit (baseline and follow-up visits) with a validated instrument (M6, OMRON HEALTHCARE Co., Ltd., Kyoto, Japan) [23]. At each visit, 24-h ambulatory BP monitoring was also performed with a validated device (SpaceLabs 90207; Spacelabs Healthcare Co., Issaquah, Washington, USA) [24] programmed to take measurements at 15 and 20-min intervals over the day and the night, respectively [25]. No data editing was performed, and systolic and diastolic ambulatory BP and heart rate values were averaged over each hour, over the day (from 0800 to 2000 h), night (from 0100 to 0600 h) and over the entire 24-h period [25]. The definition of daytime and night-time based on narrow-fixed time interval was chosen because of previous demonstrations of its better reproducibility and relation with clinical outcomes, due to the exclusion of transition periods during which a great between-

participant variability in wakefulness and sleep times occurs [26].

Study endpoints

The primary efficacy endpoint was the change in ambulatory mean 24-h systolic BP (SBP). Secondary endpoints were changes in day-time or night-time BP, office BP, antihypertensive treatment and QoL. The effects of intervention on antihypertensive treatment were assessed by considering both the number of participants on antihypertensive treatment and the number of drugs assumed.

Statistical analysis

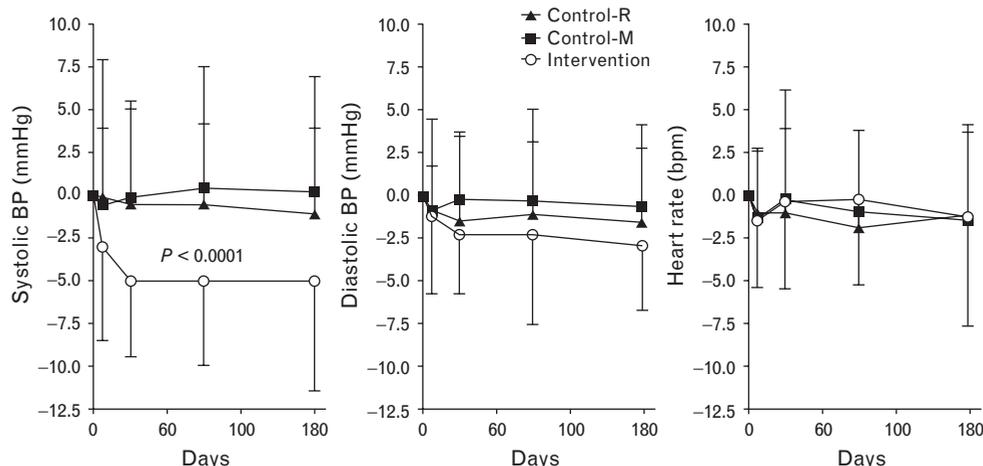
The predetermined sample size of groups was calculated for providing at least 80% power (β) with $P < 0.05$ (α) based on previous results with systolic home BP measurements [14,19], taking a 5-mmHg difference in population means with $\sigma = 5.5$ mmHg [27]. Categorical variables were compared with Fisher's exact test. Statistical analysis was conducted on derived variables given by the difference between each measurement and the baseline value within participant. A linear mixed-effect model was fitted by Restricted Maximum Likelihood [28]. Random effects were specified for repeated measurements within individual, whereas fixed effects were specified for experimental conditions. A linear time trend was also included in the model terms. A further model was fitted allowing interaction terms between time and experimental conditions. To explore variables affecting intervention efficacy stepwise multivariate analysis including age, sex, BMI, antihypertensive treatment (expressed as both treated participants and class of drugs assumed), and psychological subscales was preliminarily performed. Variables selected were then inserted as covariates in a generalized linear model to investigate the effect of psychological subscales. The odds ratio (OR) values of psychological subscale higher than the 75th percentiles on a fixed arbitrary threshold of 24-h SBP (the average reduction obtained at the 6-month follow-up) were then calculated. A value of $P < 0.05$ was taken as the minimum level of statistical significance throughout the article. Statistical analysis was performed using the SPSS (version 17.0; SPSS Inc., Chicago, Illinois, USA) and STATA (StataCorp LP, Lakeway Drive, Texas, USA) software packages.

Results

Patients population

Two patients in the Control-M group interrupted the follow-up because of the diagnosis of neoplasia and were excluded from data analysis. The therapist judged four and three participants unable to correctly perform breathing exercises at the end of the first and the second session, respectively (baseline, 1-week). At the following sessions (1, 3 and 6 months), all participants were found able to correctly perform the requested procedure. Throughout the follow-up period reported compliance with the study

Fig. 1



Changes of ambulatory systolic and diastolic blood pressure and heart rate at 6-month follow-up in the three groups of patients. In the intervention group daily session of music-guided slow breathing exercises significantly reduced mean 24-h systolic blood pressure at 6-month follow-up ($P < 0.001$ at mixed model analysis).

programme was comparable between groups. In particular, during all the study period patients assigned to the treatment group on average performed 5.1 sessions/week (out of the seven requested), for 22 min/day (out of 30 min requested). At 6-month follow-up the number of weekly treatment sessions were significantly reduced vs. baseline [mean reduction of 3.3 times/week, confidence limits at 95% 2.3–4.4; $P < 0.001$ at analyses of variance (ANOVA) test for repeated measurements].

Treatment efficacy

Blood pressure changes

In all participants the 24-h recordings were of good technical quality. Statistical analysis conducted on the difference between each ambulatory measurement and the baseline value within participant revealed a significant effect of intervention on SBP (Fig. 1 and Table 2). At mixed model analysis, intervention was found to be associated with a significant reduction of SBP values measured in the office ($P < 0.05$) and at ambulatory monitoring (mean 24-h, $P = 0.001$; night-time, $P < 0.0001$) (Table 2). In particular, the intervention group had on average a 24-h SBP 4.6 mmHg (95% confidence limits 1.93–7.35) and 4.1 mmHg (95% confidence limits 1.59–6.67) lower than that the Control-M and Control-R groups, respectively ($P < 0.001$ for both) (Table 2). It is worth noting that the effect of intervention on 24-h SBP was not significantly affected by time (Chi-squared 1.68; 2 DF; $P = 0.43$). After the first follow-up visit only a minor time-related further reduction was indeed observed in the intervention group (-0.1 mmHg/month 95% confidence limits -0.2 to 0.01), whereas the

control groups showed no significant changes. The effect of intervention on SBP was not significantly affected by time (Chi-squared 1.68; 2 DF; $P = 0.43$). After the first follow-up visit only a minor time-related further reduction was indeed observed in the intervention group (-0.1 mmHg/month 95% confidence limits -0.2 to 0.01), whereas the

Table 2 Mean changes (95% confidence limits) of mean ambulatory blood pressure (mmHg), and heart rate (bpm) at the end of follow-up (6-month visit) in controls and intervention groups

Variables	Control-R (n = 31)	Control-M (n = 24)	Intervention (n = 29)	P (mixed model)		
				Group (G)	Time (T)	G × T
Systolic BP (mmHg)						
Office	-1.3 (-3.2 to 1.8)	-1.3 (-3.6 to 2.1)	-7.4 (-7.9 to -2.6)	0.026	0.226	0.804
Mean 24-h	-1.0 (-2.2 to 1.2)	0.2 (-1.9 to 2.0)	-5.4 (-6.4 to -2.8)	0.001	0.733	0.595
Daytime	-1.0 (-3.2 to 1.3)	0.6 (-3.0 to 2.2)	-4.4 (-6.2 to -1.3)	0.120	0.152	0.749
Night-time	-2.1 (-3.2 to 1.0)	-0.8 (-1.7 to 3.0)	-7.5 (-8.7 to -4.3)	<0.0001	0.015	0.809
Diastolic BP (mmHg)						
Office	-0.8 (-2.8 to 1.3)	-1.4 (-3.4 to 1.0)	-3.9 (-4.8 to -0.6)	0.373	0.622	0.854
Mean 24-h	-1.5 (-2.5 to 0.1)	-0.6 (-2.0 to 1.0)	-2.9 (-3.5 to -0.6)	0.301	0.628	0.807
Daytime	-1.9 (-3.3 to 0.0)	-0.7 (-2.7 to 0.9)	-3.1 (-3.2 to 0.1)	0.775	0.379	0.414
Night-time	-1.1 (-2.2 to 1.0)	-0.2 (-1.6 to 2.1)	-4.3 (-4.4 to -0.9)	0.062	0.073	0.867
Heart rate (bpm)						
Office	0.6 (-3.1 to 2.4)	-0.5 (-3.0 to 3.2)	-0.6 (-3.0 to 2.7)	0.973	0.411	0.840
Mean 24-h	-1.2 (-2.7 to 0.2)	-1.5 (-2.6 to 0.6)	-1.3 (-2.4 to 0.6)	0.942	0.492	0.630
Daytime	-0.5 (-2.5 to 0.8)	-1.8 (-2.8 to 1.0)	-1.0 (-1.9 to 1.6)	0.825	0.126	0.414
Night-time	-1.6 (-2.9 to 0.2)	-0.8 (-2.7 to 0.8)	-0.9 (-2.8 to 0.4)	0.940	0.751	0.656

BP, blood pressure.

Table 3 Antihypertensive treatment (classes of drugs and participants on treatment) at baseline and at 6-month follow-up in controls and intervention groups

Variables	Control-R (<i>n</i> = 31)	Control-M (<i>n</i> = 24)	Intervention (<i>n</i> = 29)	<i>P</i> (mixed model)	
				Group (<i>G</i>)	<i>G</i> × Time
Classes of drugs (mean [95% CL])					
Baseline	1.8 (1.3–2.3)	1.8 (1.3–2.3)	1.5 (1.0–2.0)		
6-month follow-up	1.9 (1.3–2.4)	1.9 (1.3–2.3)	1.4 (0.9–1.9)	0.486	0.910
Treated participants (<i>n</i> [%])					
Baseline	26 (83.9%)	20 (83.3%)	21 (72.4%)		
6-month follow-up	26 (83.9%)	21 (87.5%)	22 (75.9%)	0.295	0.509

CL, confidence limits.

other two groups remained stable (0.1 mmHg/month, 95% confidence limits 0.02–0.24; 0.05 mmHg/month 95% confidence limits –0.07 to 0.18 for groups M and R, respectively). Between-group SBP differences were not affected by covariate analysis that considered age, BMI, medication status and sex. The 24-h diastolic BP (DBP) changes displayed a similar trend of reduction but did not reach statistical significance. The corresponding heart rate changes did not show any time-related change (Table 2).

Antihypertensive treatment

Antihypertensive treatment in the three groups was comparable at baseline (Table 3). Mixed model analysis did not reveal any significant effect of intervention on antihypertensive treatment. In particular, no between-group differences were observed in antihypertensive treatment when either the number of drug classes assumed per participant or the number of treated participants in each group was considered (Table 3).

Quality of life

At the 6-month visit no significant changes vs. basal evaluation and no significant differences between groups were observed on any multi-item dimensions analyzed in the SF-36 questionnaire.

Exploring heterogeneity of efficacy within the intervention group

Significant heterogeneity was observed in blood pressure (BP) reduction in the intervention group. All participants except one fulfilled psychological questionnaire at the beginning of the study. Preliminary multivariate stepwise analysis including age, sex, BMI, antihypertensive treatment (expressed as both the number of participant on antihypertensive treatment and the number of drugs assumed) and psychological variables selected antihypertensive treatment as the single significant negative predictor of mean 24-h SBP reduction at the 6-month follow-up (Table 4). In particular, average BP reduction was -9.02 ± 8.69 mmHg (95% confidence limits –16.29; –1.75) in untreated participants and -3.79 ± 4.52 mmHg (95% confidence limits –6.03; –1.54) in participants who were taking antihypertensive drugs. Antihypertensive treatment was then inserted as covariate in a generalized

linear model to investigate the effect of psychological subscales on changes of mean 24-h SBP at the 6-month follow-up visit. Three psychological subscales were then observed to affect the mean 24-h SBP reduction (general positive affect $P < 0.001$; emotional ties, $P < 0.001$; loss of behavioral control, $P = 0.035$) (Table 5).

In particular, when the average between-group difference of mean 24-h SBP at the 6-month follow-up (–4 mmHg) was considered as the threshold value, level of general positive affect higher than the 75th percentiles was found to be significantly associated with low treatment efficacy (OR 0.09; 95% CI 0.01–0.93; Fisher exact probability test, $P = 0.037$) (Fig. 2).

Table 4 Multivariate stepwise regression analysis between demographic, medical, psychological variables (Mental Health Inventory subscales) and changes of mean 24-h systolic ambulatory blood pressure at the 6-month visit

	β (B; 95% CL)	<i>P</i>
Antihypertensive treatment ^a	0.679 (9.76; 5.09–14.43)	<0.001
Number of drugs	–0.169	0.486
Age	0.269	0.131
Sex (male)	–0.105	0.521
BMI	0.015	0.930
Anxiety	–0.137	0.394
Depression	–0.124	0.454
Loss of behavioral and emotional control	–0.065	0.688
General positive affect	0.142	0.383
Emotional ties	0.023	0.898
Satisfaction of life	0.084	0.612

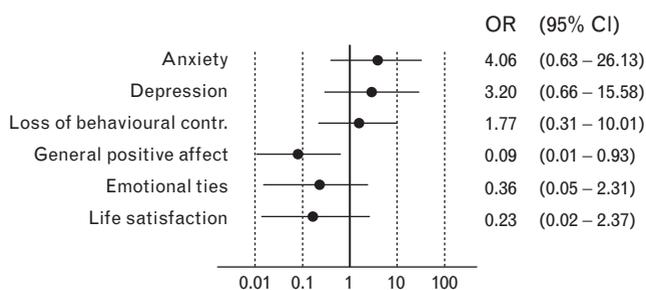
Multiple $r = 0.679$. CL, confidence limits. ^aSelected at stepwise multiple regression analysis.

Table 5 Effects of psychological subscales of Mental Health Inventory and antihypertensive treatment on changes of mean 24-h systolic blood pressure at 1 week, 1, 3 and 6-month visits vs. baseline

Variables	Generalized linear model (Time × Variable)	
	<i>P</i>	<i>P</i> ^a
Anxiety	0.229	0.154
Depression	0.498	0.152
Loss of behavioral and emotional control	0.176	0.035
General positive affect	0.041	0.001
Emotional ties	0.032	0.001
Satisfaction of life	0.225	0.070
Antihypertensive treatment	–	0.003

^aAntihypertensive treatment included in the model as covariate.

Fig. 2



Psychological subscales of Mental Health Inventory as predictors of treatment efficacy. Odds ratio of reaching the average between-groups difference of 24-h systolic blood pressure at the 6-month follow-up (-4 mmHg) for individuals belonging to the upper 75th percentiles of the different psychological subscales. A level of general positive affect higher than the 75th percentiles resulted to be significantly associated with low treatment efficacy. CL, confidence level; OR, odds ratio.

Blood pressure changes 6 months after interruption of study protocol

Ambulatory BP monitoring performed 6 months after the interruption of the study protocol in participants allocated to the intervention group revealed that 24-h systolic BP was still significantly reduced vs. baseline at multiple comparison test (-4.107 mmHg; 95% confidence limits -7.99 to -0.22 ; $P=0.031$). Likewise no significant differences were detected between mean 24-h SBP measured 6 months after the interruption of the study protocol and values measured at 1-week (-1.18 mmHg; 95% confidence limits -5.07 to 2.70 ; $P=0.951$), 1-month (0.67 mmHg; 95% confidence limits -3.21 to 4.55 ; $P=0.996$), 3-month (1.39 mmHg; 95% confidence limits -2.49 to 5.27 ; $P=0.907$) and at 6-month follow-up (1.29 mmHg; 95% confidence limits -2.70 to 5.28 ; $P=0.938$).

Discussion

According to the present findings daily sessions of voluntary music-guided slow breathing significantly reduces 24-h systolic BP, and a psychological profile affecting the antihypertensive response, can be identified.

The present study adopted the design of a randomized, controlled clinical trial with some peculiarities. Blinding of patients was mimicked by performing random allocation leaving participants unaware of competitor treatments thus limiting patient bias and personal expectations. Likewise the physician treating BP was not aware of group allocation and the therapist had no access to BP data. Two control groups were also specifically included because music, in addition to the known relaxing effect [29,30], may exert a tempo entrainment on respiration rate [19]. The lack of BP differences between the two control groups, however, suggests that music alone (at least at the tempo we selected) is not sufficient to give an antihypertensive effect in clinical practice. Participants in

the intervention group [5] listened to the same slow music given to participants in the active control group but were also taught respiration techniques. Thus, the selective BP reduction in the intervention group indicates voluntary breathing rate reduction as the active component in relaxing treatments [31–35].

Inconsistency of results of studies investigating the anti-hypertensive effects of different yoga procedures, posture exercises, Jacobson's method of progressive relaxation, autogenic training, simple meditation was mainly attributed to methodological shortcomings (small sample size, inconsistencies regarding baseline BP determinations, types of control group, confounding by multiple noncognitive cointerventions such as diet or exercise) [5]. However, the possibility also exists that some of the procedure used may have not reduced breathing rate to less than 10 breath/min during the exercise sessions. Although the value of this breathing threshold is now recognized on the basis of clinical studies [10–15], wherein daily sessions of device-guided slow breathing reduced office and home BP at 2-month follow-up, the present is the first study revealing that music-guided voluntary slow breathing may induce a significant reduction of 24-h ABP.

The mechanisms responsible for the BP reduction induced by slow breathing are multifold and still poorly understood. Certainly an important role is played by the modulation of autonomic cardiovascular regulation, characterized by an increased parasympathetic and a reduced sympathetic activity, as documented by an increase in the sensitivity of baroreflex heart rate modulation during and after a paced slow breathing exercise [7–9]. The present study was not designed to add information regarding the mechanisms. However, the observation that the antihypertensive effect may persist 6 months after the interruption of exercise sessions might suggest a possible persistent change of the reflex system. We cannot exclude that participants allocated to the intervention group may also have continued to perform slow-breathing exercises during their usual daily routine even if breathing rate measurements performed at follow-up visits revealed no significant between-group differences.

Information regarding predictors of efficacy is especially useful to move behavioral techniques into clinical practice. Probably due to the limited number of participants, the role of psychological predictors was masked by anti-hypertensive treatment, selected as the first-negative independent predictors of efficacy. However, when anti-hypertensive treatment is included in the model, the role of psychological profile comes into view. More precisely, the patients who appeared to benefit most from the behavioral intervention reported high score on the 'loss of behavioral/emotional control' scale and low ones on the 'general positive affect' and 'emotional ties' scale. On the

whole, such patients showed symptoms of psychological distress such as emotional instability, concern about losing personal control, depressive thinking. Even the psychological well-being appeared to be rather limited. The patients manifested lack of self-confidence and optimism, boredom, loneliness, unpleasant moods. Therefore, psychological distress and social isolation appeared to be positive psychological predictors of the treatment efficacy. It may be worth noting that Greenberg and Safran, [36] in their work on Emotion, found several studies in which negative affect was positively related to psychotherapy outcome.

The present study has different limitations. The sample size is relatively small and therefore we could not adjust for all potential confounders in the multivariable regression models. We do not provide any insight regarding the possible mechanism(s) linking behavioral pattern, that is slow breathing, with the antihypertensive effect. The sample used in the present study is quite heterogeneous and treated as well as nontreated hypertensive patients were included. However, these aspects might also represent the strength of the study reflecting 'the real world' of consecutive, unselected hypertensive outpatients seen in daily clinical practice.

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