A controlled study of eight months of physical training and reduction of blood pressure in children: the Odense schoolchild study

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Abstract

Objective—**To examine the effect of physical training on physical fitness and blood pressure in children aged 9-11 years.**

Design—**Prospective randomised controlled intervention study of a sample of children drawn from a population survey of coronary risk factors in children.**

Setting—**Odense, Denmark.**

Subjects—**69 children with mean blood pressure ≥95th centile (hypertensive group) and 68 with mean blood pressure <95th centile (normotensive group), randomly selected from a population of 1369 children.**

Intervention—**67 children were randomised to receive three extra lessons a week of an ordinary school physical education programme for eight months.**

Main outcome measures—**Physical fitness assessed by calculation of maximum oxygen uptake and blood pressure recorded by one unblinded observer.**

Results—**After three months neither blood pressure nor physical fitness had changed significantly. After adjustment for values in weight, height, heart rate, and the variable in question before training physical fitness rose significantly at the end of eight months' training, by 3·7 mlO_2/kg/min (95% confidence interval 2·2 to 5·3) in the normotensive training subgroup and by 2·1 mlO_2/kg/min (0·1 to 4·2) in the hypertensive training subgroup compared with that in the controls. Systolic and diastolic blood pressures in the training subgroups fell significantly by 6·5 mm Hg (3·2 to 9·9) and 4·1 mm Hg (1·7 to 6·6) respectively in the normotensive group and by 4·9 mm Hg (0·7 to 9·2) and 3·8 mm Hg (0·9 to 6·6) respectively in the hypertensive group.**

Conclusions—**Physical training lowers blood pressure and improves physical fitness in children and might have implications for an important non-pharmacological approach to primary prevention of essential hypertension.**

Introduction

Regular exercise training generally is being recommended as a health measure for managing hypertension in adulthood.[1,2] A coincident reduction in blood pressure after exercise training in hypertensive subjects[3] and normotensive subjects[4] has been shown, but most reported studies suggest that the effect of training on blood pressure is non-existent or very small.[5-7] Most of the longitudinal training studies reviewed, however, must be interpreted with caution because of inadequate design, principally the absence of adequate and randomised control groups receiving the same care during the training period.[8-10] No study exists in which the controlled effect of physical training on blood pressure and physical fitness has been examined in a population based sample of children.

The purpose of this investigation was to examine the effect of three extra lessons a week of an ordinary school physical education programme for eight months on blood pressure and physical fitness in children aged 9-11 years by use of a randomised controlled design.

Subjects and methods

SELECTION OF SUBJECTS

The children for this study were drawn from a total of 1369 children (81·5% of the eligible population) aged 9-11 years who participated in the first phase of a prospective study (the Odense schoolchild study).[11]

We selected two groups of children: a hypertensive group (n=69) consisting of all children with a mean blood pressure (diastolic blood pressure plus a third (systolic blood pressure minus diastolic blood pressure)) at or above the 95th centile for the entire population and a normotensive group (n=68), comprising another 5%, selected randomly from children with a mean blood pressure below the 95th centile. Five children in the hypertensive group did not want to participate and neither did 17 children originally selected for the normotensive group, but they were all replaced with children from the population by a randomised reselection procedure. The study group then included 64 children in the hypertensive group and 68 children in the normotensive group. After giving informed consent each child was randomised to either a training subgroup (hypertensive training subgroup (n=32); normotensive training subgroup (n=35)) or a control subgroup (hypertensive control subgroup (n=32); normotensive control subgroup (n=33)).

The study was approved by the research ethics committee of the medical faculty of the University of Odense.

STUDY DESIGN

The study was a prospective controlled intervention study. All of the 132 participating children were examined immediately before training, at three months after the start of training, and at the end of eight months of training, according to the examination procedure reported previously.[11] All blood pressures were measured with the children sitting after at least five minutes' rest. A random zero sphygmomanometer (Hawksley) was used to reduce observer bias, and all of the measurements were taken by the same person (HSH). One measurement was performed at each examination. Blood pressures were recorded to the nearest 2 mm Hg. Korotkoff phase IV was used as the estimate of diastolic blood pressure.[7] Ratings of sexual maturity (range 1-5) were based on secondary sexual characteristics.[12] Physical fitness as assessed by maximum oxygen uptake was determined indirectly with a maximum progressive exercise test on a bicycle ergometer and by calculating maximum oxygen uptake from maximum mechanical power. Previously we showed that the standard error calculated for maximum oxygen consumption estimated with this method was less than 3·2%.[13]

EXERCISE TRAINING

The children in the training subgroup were divided into six different groups according to their place of

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residence within the municipality, and the groups followed the exercise training programme at these separate locations under the instruction of six different teachers. The programme consisted of extra lessons of an ordinary school physical education programme. Each training lesson was about 50 minutes long, including 10 minutes of warming up, and three lessons a week were scheduled for eight months. The content of the lessons did not differ from that of the regular schedule and included organised games, gymnastics, and exercises. The intensity of the lessons was evaluated alternately in six children by monitoring heart rate by telemetry (Sport tester PE-3000, Polar Electro, Finland) during a lesson. Both the training and the control subgroups continued their regular exercise schedule with two lessons weekly throughout the study period.

STATISTICAL ANALYSIS

Statistical analyses were performed on an intention to treat principle, so that children were treated statistically according to the experimental randomisation design throughout the study, even if their exercise training was discontinued. In each of the two groups the significance of the effects of state of training and sex were assessed from F ratios with a 2×2 (training$\times$sex level) analysis of variance with covariate adjustment for values before training of weight, height, heart rate, and either blood pressure or physical fitness, when appropriate. A repeated measures design was used for estimating trends with time.[14 15] The assumption of homogeneity of variances, which indicates that the variance-covariance matrices of the groups are equivalent, was assessed using Box's M statistic[16] and Bartlett's test.[17] All statistical analyses were carried out with the statistical package for the social sciences (SPSS) software. A probability value of less than 0·05 was considered significant. All statistical tests were two tailed.

TABLE I—*Physical characteristics of children before and after training. Values are means (SDs)*

	Before intervention		After intervention	
	Training subgroup (n=67)	Control subgroup (n=65)	Training subgroup (n=67)	Control subgroup (n=65)
Weight (kg)	37·4 (8·6)	39·3 (7·3)	40·6 (9·1)	42·1 (7·7)
Height (cm)	144·9 (7·4)	146·7 (5·6)	148·3 (8·0)	150·2 (5·8)
Triceps skinfold thickness (cm)	1·3 (0·5)	1·3 (0·5)	1·3 (0·6)	1·2 (0·6)
Quetelet's index (weight/height^2)	17·7 (2·8)	18·2 (2·8)	18·3 (2·9)	18·6 (2·7)
Heart rate (beats/min)	91·8* (11·4)	96·0 (12·0)	85·9 (11·5)	88·0 (12·5)

*p<0·05 compared with control group.

Results

PHYSICAL CHARACTERISTICS

Table I shows the effect of the physical training programme on selected physical characteristics of the children. Mean heart rate was significantly lower in the training group before the intervention period. None of the other characteristics differed significantly either before or after the intervention period. A change in Tanner score as a measure of the onset of sexual maturation during the training period was observed in 11 children in the control subgroups (10 girls and one boy) and in seven in the training subgroups (three girls and four boys).

COMPLIANCE

The average total number of exercise training lessons was 90 (range 86-91). A total of 51 (76%) of the 67 children who were randomised to training complied with the programme throughout and 48 (72%) participated in more than half of the lessons. The statistical analyses, however, were performed on an intention to treat principle.

The intensity of the training programme was assessed by monitoring heart rate. The mean individual maximum heart rate determined during the maximum exercise test on the bicycle ergometer was 200 (range 178-216) beats/min. A total of 127 measurements of heart rate during training lessons were performed. On average heart rates for each child exceeded the 70% value of the individual maximum value during 35 minutes of each 50 minute lesson.

PHYSICAL FITNESS

Table II shows the subgroup and sex specific mean values in physical fitness before training, at three months after the start of training, and at eight months of training. Before training physical fitness in the hypertensive training subgroup was significantly higher than that in the hypertensive control subgroup (F ratio 7·7). No increase in physical fitness was found after only three months of training. At the end of the eight months significant differences were observed between the training subgroup and the control subgroup in both the normotensive group (F ratio 23·3) and the hypertensive group (F ratio 5·1). During the eight months of training physical fitness increased significantly in boys and girls in both training subgroups. As the figure shows, the mean increase in physical fitness in the normotensive group was 3·7 mlO_2/kg/min (95% confidence interval 2·2 to 5·3)

TABLE II—*Mean (SD) values of physical fitness (mlO_2/kg/min) before exercise training, after three months, and after eight months*

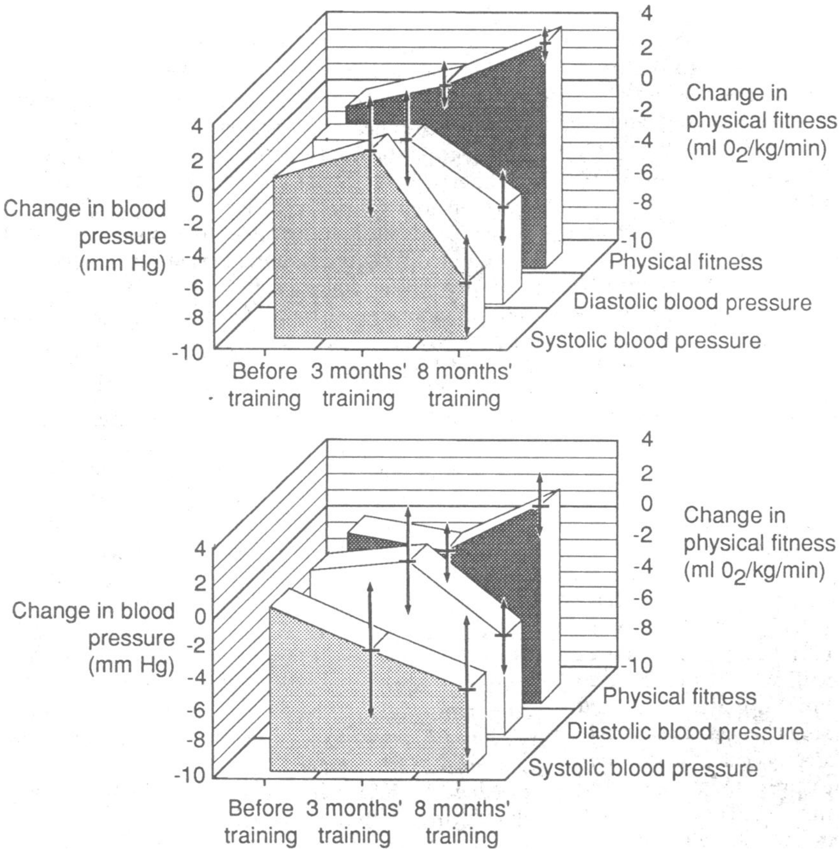
	Normotensive boys		Normotensive girls		F ratios*		Hypertensive boys		Hypertensive girls		F ratios*	
	Training subgroup (n=18)	Control subgroup (n=17)	Training subgroup (n=17)	Control subgroup (n=16)	Intervention; sex	Intervention-sex interaction	Training subgroup (n=17)	Control subgroup (n=16)	Training subgroup (n=15)	Control subgroup (n=16)	Intervention; sex	Intervention-sex interaction
Before training	51·0 (5·8)	53·1 (4·2)	48·9 (4·4)	46·9 (6·4)	1·1; 17·1†	2·6	52·3 (7·5)	48·1 (7·6)	45·6 (5·0)	41·8 (6·9)	7·7†; 35·3†	0·4
Three months	50·7 (6·4)	50·2 (5·7)	48·4 (4·2)	46·8 (6·8)	2·2; 1·0	3·0	51·5 (6·9)	48·4 (9·3)	44·9 (5·3)	41·4 (6·9)	1·3; 0·0	0·2
Eight months	55·3 (6·3)	52·5 (4·3)	51·3 (5·0)	46·6 (6·4)	23·3†; 3·8	0·9	54·4 (7·9)	48·6 (9·7)	47·2 (5·7)	41·2 (7·1)	5·1†; 1·8	0·1
F ratio (time)	25·6†	10·0†	8·7†	0·1			9·3†	0·2	5·0†	0·3		

*Adjusted for values before training in weight, height, and heart rate. Values at three and eight months, respectively, are also adjusted for value in physical fitness before training.
†p<0·05.

TABLE III—*Mean (SD) systolic blood pressure (mm Hg) before exercise training, after three months, and after eight months*

	Normotensive boys		Normotensive girls		F ratios*		Hypertensive boys		Hypertensive girls		F ratios*	
	Training subgroup (n=18)	Control subgroup (n=17)	Training subgroup (n=17)	Control subgroup (n=16)	Intervention; sex	Intervention-sex interaction	Training subgroup (n=17)	Control subgroup (n=16)	Training subgroup (n=15)	Control subgroup (n=16)	Intervention; sex	Intervention-sex interaction
Before training	101·3 (13·0)	108·0 (9·0)	101·5 (5·8)	105·8 (7·3)	4·1†; 0·3	0·3	113·4 (11·1)	114·3 (10·3)	115·9 (11·2)	114·4 (9·4)	2·2; 0·1	0·0
Three months	105·0 (11·0)	107·1 (9·7)	102·7 (9·1)	103·5 (6·6)	1·0; 1·5	0·0	113·1 (9·3)	115·5 (9·2)	113·2 (10·6)	116·3 (9·0)	1·4; 0·0	0·7
Eight months	96·9 (8·6)	108·8 (9·4)	98·2 (8·3)	105·1 (5·4)	15·0†; 0·1	1·3	107·2 (7·0)	116·3 (10·3)	115·2 (9·6)	114·0 (9·5)	5·8†; 1·9	4·8†
F ratio (time)	9·0†	0·4	2·8	0·5			6·2†	0·4	0·7	0·6		

*Adjusted for values before training in weight, height, and heart rate. Values at three and eight months, respectively, are also adjusted for value in systolic blood pressure before training.
†p<0·05.



Changes in blood pressure and physical fitness in 67 children after three and eight months of training compared with respective changes in 65 children randomised to no training. (a) Normotensive children, (b) hypertensive children. Values adjusted for values before training in weight, height, heart rate, and variable in question. Arrows indicate 95% confidence intervals; no significant change observed when arrow crosses zero

and in the hypertensive group was 2·1 mlO_2/kg/min (0·1 to 4·2).

BLOOD PRESSURE

Before training the normotensive training subgroup had a significantly lower systolic blood pressure than that of the normotensive control subgroup (F ratio 4·1) (table III), but all differences in values before training were controlled for by the analysis of variance model in the subsequent analyses. At three months systolic blood pressure did not differ significantly. Systolic blood pressure differed significantly between the training subgroup and the control subgroup after the training period in both the normotensive group (F ratio 15·0) and the hypertensive group (F ratio 5·8). The mean fall in systolic blood pressure (figure) was 6·5 mm Hg (3·2 to 9·9) in the normotensive training subgroup and 4·9 mm Hg (0·7 to 9·2) in the hypertensive training subgroup. No difference between the sexes was observed at the end of the training period (table III). Sex, however, had a significant effect in the hypertensive group, as shown by the significant interaction effect of intervention and sex. At the end of eight months of training systolic blood pressure had fallen significantly in boys in both training subgroups.

Diastolic blood pressure at three months of training was not significantly different (table IV). At the end of the eight month training period it was significantly lower in both training subgroups than in the control subgroups (mean fall 4·1 mm Hg (1·7 to 6·6 mm Hg) in the normotensive training subgroup and 3·8 mm Hg (0·9 to 6·6 mm Hg) in the hypertensive training subgroup; figure).

Discussion

No other published study has examined the controlled effect of physical training on blood pressure and physical fitness in a population based group of children. Our results therefore provide the first objective support for the effectiveness of physical training in increasing physical fitness and lowering blood pressure among populations of children.

Careful precautions were taken to ensure a highly accurate and precise estimate of the intra-arterial blood pressure, but some methodological problems might be inherent in the blood pressure recordings in that the observer was not blinded. All recordings, however, were made by the same experienced observer, all were measured to the nearest 2 mm Hg, and all were measured blindly with a random zero sphygmomanometer. Therefore if a bias was present we do not believe that it significantly interfered with the main outcome and the main conclusions of the study.

More than three quarters of the children who were randomised to the training programme complied with it throughout. The significance of any intervention study, however, carries the risk of bias due to nonresponders. This bias was ruled out by including children in the analyses who did not comply with the programme throughout, and these events may have contributed to an underestimation of the potential effect of the programme.

The apparent lack of effect on blood pressure and physical fitness of three months' physical training is remarkable and in agreement with the results of others.[18-20] The findings imply that the adaptive responses to physical training occur rather slowly over a prolonged period.

The study of the effectiveness of non-pharmacological health measures for primary prevention of coronary heart disease among populations of children is relatively new.[21] Attempts at educational intervention programmes that include recommendations on diet and physical activity alone[22-24] have not successfully controlled hypertension. A general approach combining dietary management and low levels of drug treatment significantly reduced blood pressure in hypertensive children after 30 months of observation.[25] Importantly, our study showed that the effect of blood pressure and physical fitness could be obtained across large numbers of children within the framework of ordinary school facilities and staff. There is, however, a real question of whether the beneficial effects of physical training can be maintained or enhanced in the long term, but recommendations should be offered for increasing participation in exercise and for improving

TABLE IV—*Mean (SD) diastolic blood pressure (mm Hg) before exercise training, after three months, and after eight months*

	Normotensive boys		Normotensive girls		F ratios*		Hypertensive boys		Hypertensive girls		F ratios*	
	Training subgroup (n=18)	Control subgroup (n=17)	Training subgroup (n=17)	Control subgroup (n=16)	Intervention; sex	Intervention-sex interaction	Training subgroup (n=17)	Control subgroup (n=16)	Training subgroup (n=15)	Control subgroup (n=16)	Intervention; sex	Intervention-sex interaction
Before training	67·8 (8·1)	72·7 (6·7)	66·0 (5·2)	68·0 (7·7)	2·8; 3·9	0·8	76·8 (7·4)	76·5 (7·2)	75·6 (10·0)	76·3 (10·2)	0·5; 0·4	0·1
Three months	70·7 (7·7)	72·5 (5·8)	67·9 (6·3)	69·1 (6·8)	0·0; 2·0	0·0	76·1 (7·7)	75·5 (8·2)	75·5 (8·9)	77·0 (5·2)	0·2; 0·1	1·0
Eight months	68·3 (7·1)	73·4 (5·0)	65·3 (6·0)	72·3 (5·3)	11·3†; 0·4	1·9	74·0 (6·7)	78·9 (6·1)	76·5 (5·6)	79·0 (7·0)	7·0†; 1·7	0·5
F ratio (time)	1·4	0·2	1·3	3·7†			1·8	2·3	0·3	1·5		

*Adjusted for values before training in weight, height, and heart rate. Values at three and eight months, respectively, are also adjusted for value in diastolic blood pressure before training.
†$p<0·05$.

children's attitudes toward physical activity within the school environment.[26]

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Fluoxetine and suicide: a meta-analysis of controlled trials of treatment for depression

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Abstract

Objective—A comprehensive meta-analysis of clinical trial data was performed to assess the possible association of fluoxetine and suicidality (suicidal acts and ideation).

Design—Retrospective analysis of pooled data from 17 double blind clinical trials in patients with major depressive disorder comparing fluoxetine (n=1765) with a tricyclic antidepressant (n=731) or placebo (n=569), or both.

Main outcome measures—Multiple data sources were searched to identify patients with suicidal acts. Suicidal ideation was assessed with item 3 of the Hamilton depression rating scale, which systematically rates suicidality. Emergence of substantial suicidal ideation was defined as a change in the rating of this item from 0 or 1 at baseline to 3 or 4 during double blind treatment; worsening was defined as any increase from baseline; improvement was defined as a decrease from baseline at the last visit during the treatment.

Results—Suicidal acts did not differ significantly in comparisons of fluoxetine with placebo (0·2% *v* 0·2%, p=0·494, Mantel-Haenszel adjusted incidence difference) and with tricyclic antidepressants (0·7% *v* 0·4%, p=0·419). The pooled incidence of suicidal acts was 0·3% for fluoxetine, 0·2% for placebo, and 0·4% for tricyclic antidepressants, and fluoxetine did not differ significantly from either placebo (p=0·533, Pearson's χ^2) or tricyclic antidepressants (p=0·789). Suicidal ideation emerged marginally significantly less often with fluoxetine than with placebo (0·9% *v* 2·6%, p=0·094) and numerically less often than with tricyclic antidepressants (1·7% *v* 3·6%, p=0·102). The pooled incidence of emergence of substantial suicidal ideation was 1·2% for fluoxetine, 2·6% for placebo, and 3·6% for tricyclic antidepressants. The incidence was significantly lower with fluoxetine than with placebo (p=0·042) and tricyclic antidepressants (p=0·001). Any degree of worsening of suicidal ideation was similar with fluoxetine and placebo (15·4% *v* 17·9%, p=0·196) and with fluoxetine and tricyclic antidepressants (15·6% *v* 16·3%, p=0·793). The pooled incidence of worsening of suicidal ideation was 15·3% for fluoxetine, 17·9% for placebo, and 16·3% for tricyclic antidepressants. The incidence did not differ significantly with fluoxetine and placebo (p=0·141) or tricyclic antidepressants (p=0·542). Suicidal ideation improved significantly more with fluoxetine than with placebo (72·0% *v* 54·8%, p<0·001) and was similar to the improvement with tricyclic antidepressants (72·5% *v* 69·8%, p=0·294). The pooled incidence of improvement of suicidal ideation was 72·2% for fluoxetine, 54·8% for placebo, and 69·8% for tricyclic antidepressants. The incidence with fluoxetine was significantly greater than with placebo (p<0·001) and did not differ from that with tricyclic antidepressants (p=0·296).

Conclusion—Data from these trials do not show that fluoxetine is associated with an increased risk of suicidal acts or emergence of substantial suicidal thoughts among depressed patients.

Introduction

Because depression is an important risk factor for suicide[1-3] there is a need to study the effects of