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Family Resemblance in Cardio-Respiratory Traits*

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ABSTRACT

Family aggregation of cardio-respiratory traits in the population of Middle Dalmatian islands has been investigated on a random sample of adults. The similarity between first-degree relatives has been quantified by calculating Pearsons »product-moment« coefficient of correlation. The obtained results have been compared with the corresponding results of other authors, and discussed with respect to the possible influence of genetic and ecological factors on their formation. The highest correlation values within a family have been found in lung function parameters, whereas the lowest correlations have been found for resting pulse rate, and maximum oxygen uptake values. Exceptionally high correlations for lung function parameters among brothers and higher father-offspring correlations for those traits compared with other physiological traits, speak in favor of strong common family environmental influence on lung function traits, acting especially among male family members. The pattern of family correlations for systolic blood pressure resulting in a lesser resemblance in males and in intergenerational pairs, suggests either different environmental influence, either different sensibility – higher in males – to those influence. In contrast, the pattern of family correlations found for diastolic blood pressure, suggests that influences – whether they are primarily genetic or environmental – act on all family members with the same degree.

Introduction

The separation of genetic and environmental factors is one of the critical issues facing epidemiologists who investigate the etiological factors influencing common chronic diseases[1-3]. This issue is especially important in cardiovascular diseases where familial aggregation has been noted for the past two centuries. Family history of chronic diseases has been associated with the risk factors, but the independent contribution of genetic as opposed to environmental risk factors that aggregate within families is still unsettled[3-5]. Although the literature is seemingly abundant, the studies considering a relatively large number of physi-

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ological traits in the same population are very rare[5], which can partially be responsible for frequently controversial findings. Middle Dalmatian islands' populations, since relatively isolated and homogeneous in terms of environmental pressures, provide us with suitable material for proceeding those studies. In this study the results of family resemblance in lung functions, blood pressure, and maximum oxygen uptake values in population of Middle Dalmatian islands are presented, and considered with the objective of testing for presence and for the structure of familial aggregation.

Materials and methods

The physiological data and evidences of family relations used in this study are a subset of the extensive material collected since 1971 in the holistic anthropological research on population of the Dalmatian islands of Brač, Hvar, Korčula, and the Pelješac peninsula[6,7]. Therefore family members were selected independently and the final number of subjects was determined by the choice of inclusion in the family relation (from the original random sample) and by voluntary participation in physical function tests. Since sample sizes differ according to family relation as well as to investigated physiological trait, they are presented in Table 2 and Table 3.

Lung function testing was performed by recording maximum expiratory flow volume (MEFV) curves on a pneumotachographical open system with the BTPS conditions. Jaeger's »Pneumoscreen« (Wuertzburg, Germany) was used. Forced vital capacity (FVC), one second forced expiratory volume (FEV1), peak expiratory flow (PEF), and flow rates at 75%, 50% and 25% of the forced vital capacity (MEF 25%, MEF 50%, MEF 75%) were obtained from the best MEFV (maximum expiratory flow-volume) curve. At least three technically acceptable MEFV curves were recorded for each subject, and the best curve was taken. Systolic and diastolic blood pressure were measured by an auscultation method using mercury sphygmomanometer, on the left upper arm, in the sitting position, after 15 minutes rest. Maximal oxygen uptake (Vo2 max) was predicted from a submaximal bicycle ergometer work test employing heart rate response and the Astrand Ryhming nomogram. A belt-friction Bodyguard 990 bicycle ergometer was used. Heart rate was counted by the palpation method over the carotid artery. The nomogram-predicted value of Vo2 max was corrected for age according to Astrand.

Descriptive statistics and histograms were made for male and female scores and then all results exceeding ± 3 s.d. were excluded from the sample with the purpose of reducing variance, and increasing the accuracy of estimation[8]. Assuming that most of the traits change with age[9-13], the adjustment for age was performed by multiple linear regression and residual scores were used in further analyses. The adjustment was made for each within pair group separately. Pearson's product-moment correlation coefficients (r) between the members of various family pairs were calculated using the Pairwise method described by Donner[14]. In this procedure, all possible pairs for a specific type (parent-offspring, offspring-offspring) were formed, and Pearson correlations were computed over these pairs as if all pairs of values were independent. This is not exactly true, since parent – offspring pairs from a single family with more than one child are not independent, and therefore the results obtained from the usual formulae may be inaccurate. Differences between pairs are tested using Fisher's z-transformation of the correlation coefficients. Data processing was carried out on PC 386 using SPSS/PC+ software.

TABLE 1
SAMPLE SIZES (N), AVERAGE VALUES (X) AND STANDARD DEVIATIONS (SD) OF MEASURED PHYSIOLOGICAL FUNCTION PARAMETERS FOR FATHERS, MOTHERS, SONS AND DAUGHTERS

	FATHERS			MOTHERS			SONS			DAUGHTERS		
Variable	N	X	SD	N	X	SD	N	X	SD	N	X	SD
FVC	163	3.74	0.87	227	2.69	0.64	452	4.73	0.98	451	3.23	0.76
FEV1	164	2.97	0.80	227	2.23	0.53	452	3.88	0.89	452	2.69	0.65
PEF	161	7.42	2.09	221	5.16	1.38	396	8.78	2.24	415	5.62	1.35
MEF25	161	1.99	0.88	223	1.82	0.62	393	2.68	1.03	414	2.17	0.73
MEF50	161	4.35	1.66	223	3.68	1.02	396	5.55	1.73	415	4.09	1.06
MEF75	161	6.50	2.17	221	4.77	1.37	395	7.76	2.10	417	5.24	1.31
Systolic B.P.	167	146.71	18.21	242	150.99	22.98	458	138.93	16.27	471	138.71	20.78
Diastolic B.P.	168	90.18	12.32	244	91.45	11.43	460	87.49	10.89	472	86.09	11.42
Resting pulse	164	75.38	11.30	237	82.63	12.89	453	75.62	11.56	462	81.22	12.95
VO2 max (abs.)	54	2.18	0.58	58	1.62	0.44	313	2.58	0.66	227	1.86	0.40
VO2 max (rel.)	52	25.60	6.96	52	20.68	6.09	257	30.91	8.05	192	26.42	6.94

Results

Table 1 presents sample sizes, as well as means (M) and standard deviations (S.D.) of 11 physiological traits for fathers, mothers, sons, and daughters. Table 2 presents parent-offspring correlations for the same physiological traits. The correlation coefficients for Father-daughter pairs were significantly positive only for FVC ($r=0.280$, $P<0.05$). Negative, but nonsignificant correlations, fathers and daughters have for resting pulse rate and for absolute VO2 max value. For majority of traits, correlations between mothers and sons were significantly higher than zero. For FVC, FEV1, MEF25, MEF50, MEF75, and diastolic blood pressure, mothers and sons have highly significant ($P<0.001$) correlations, ranging from $r=0.389$ to $r=0.279$. Significant were also correlations for PEF, VO2 max (l/min) ($P<0.01$), and for resting pulse rate ($P<0.05$). This pair has nonsignificant, positive correlations only for systolic blood pressure, and for relative VO2 max value. Mothers and daughters were positively correlated in all physiological traits, with five correlations significantly differing from zero. Correlations are ranging from highest ($P<0.01$) for MEF75 ($r=0.256$) and for diastolic blood pressure ($r=0.242$), whereas correlations for FVC, PEF and systolic blood pressure have lower significance ($P<0.05$). Father-son pairs have four significant correlations (ranging from $r=0.315$ to $r=0.201$), with $P<0.01$ significance for FEV1, and with $P<0.05$ significance for FVC, MEF50 and MEF75.

Differences in correlations between parent-offspring pairs, tested by Fisher's z-transformation, show only two significant differences. In both, Mother-son pairs have higher values – than Mother-daughter pairs in FEV1, and than Father-daughter pairs in absolute value of VO2 max.

Offspring-offspring correlations are presented in Table 3. For all physiological parameters sisters have positive correlations, and among them seven significantly differ from zero. FVC ($r=0.343$), resting pulse rate ($r=0.361$) are on $P<0.001$ level, whereas FEV1, PEF, systolic and diastolic blood pressure, and relative VO2 max have $P<0.05$ significance. For all six parameters of lung function brothers have highly significant ($P<0.001$) correlations ranging from $r=0.589$ for FEV1, to $r=0.423$ for MEF25. In addition to lung function indicators, brothers have significant correlations ($P<0.01$) for absolute value of VO2 max. For resting pulse rate, brothers have

TABLE 2
CORRELATION COEFFICIENTS (r) FOR EXAMINED PHYSIOLOGICAL TRAITS IN PARENT-OFFSPRING PAIRS

Variable	r Father-daughter			r Mother-son			r Mother-daughter			r Father-son		
	n	r	p	n	r	p	n	r	p	n	r	p
FVC	83	0.280	*	156	0.325	***	107	0.210	*	97	0.201	*
FEV1	83	0.184		156	0.389	***	107	0.158		98	0.315	**
PEF	85	0.102		151	0.242	**	109	0.190	*	96	0.200	
MEF25	85	0.092		151	0.300	***	109	0.157		93	0.105	
MEF50	85	0.064		152	0.295	***	110	0.174		96	0.240	*
MEF75	85	0.058		150	0.299	***	109	0.256	**	96	0.219	*
Systolic B.P.	87	0.020		167	0.115		126	0.190	*	102	0.031	
Diastolic B.P.	86	0.127		168	0.279	***	126	0.242	**	102	0.180	
Resting pulse	87	-0.009		160	0.158	*	122	0.063		96	0.151	
VO2 max (abs.)	16	-0.192		37	0.505	**	18	0.249		28	0.373	
VO2 max (rel.)	16	0.099		31	0.014		18	0.229		28	0.250	

*** $P < 0.001$
** $P < 0.01$
* $P < 0.05$

negative (nonsignificant) value of correlation coefficient. Sister- brother pairs have significant correlations ($P<0.01$) for FVC, MEF25 and diastolic blood pressure. Negative, but nonsignificant correlations are found for absolute and relative maximum oxygen uptake values.

According to z-transformation test, brothers have significantly higher correlations for all lung function variables: than Sister-brother pairs for FVC and PEF; than Sister-sister pairs for MEF25; and than both other offspring pairs for FEV, MEF50 and MEF75. Sisters have significantly higher correlations for pulse rate values than Sister-brother and Brother-brother pairs. Sister-brother pairs have significantly lower correlations for maximum oxygen uptake in absolute values (l/min) than brothers, and in relative values (l/kg/min) than sisters. Among offsprings, no significant difference was found in correlations for systolic and diastolic blood pressure.

Discussion

Presented parent-offspring correlations in physiological traits show prominent differences in number of significant correlations. The majority of examined physiological traits significantly correlate in Mother-son pairs, in contrast to the only one significant correlation in Father-daughter pairs. Since Mother-son pairs have the biggest, and the Father-daughter the smallest sample among parent-offspring pairs, these prominent differences can at least partially be attributed to sample size differences. In contrast to parent-offspring pairs, in offspring generation, the same sex pairs correlate stronger than combined Sister-brother pairs. Since Sister-brother pairs have the biggest family sample and only three significantly correlated traits – the sample size difference as the cause for different family resemblance, is not applicable to offspring generation at least. Those different models of compared same sex and combined sex correlations in parent- offspring and offspring pairs should be tested by preforming family correlations on sex-adjusted data.

Differences found on same sex parent-offspring pairs, Mother-daughter and Father-son, which have comparable sample size, can be attributed to the real pattern. In a Father-son pairs all significant correlations are for lung function parameters, whereas mothers and daughters are

TABLE 3
CORRELATION COEFFICIENTS (r) FOR EXAMINED PHYSIOLOGICAL TRAITS IN OFFSPRING-OFFSPRING PAIRS

Variable	r Sister-sister			r Brother-brother			r Sister-brother		
	n	r	p	n	r	p	n	r	p
FVC	109	0.343	***	89	0.531	***	197	0.185	**
FEV1	110	0.229	*	89	0.589	***	198	0.102	
PEF	105	0.227	*	84	0.471	***	188	0.117	
MEF25	105	0.077		84	0.423	***	184	0.204	**
MEF50	105	0.032		84	0.463	***	188	0.110	
MEF75	107	0.164		84	0.494	***	189	0.135	
Systolic B.P.	123	0.216	*	94	0.175		207	0.121	
Diastolic B.P.	124	0.190	*	94	0.200		211	0.205	**
Resting pulse	118	0.361	***	90	-0.104		202	0.100	
VO2 max (abs.)	27	0.237		36	0.458	**	62	-0.144	
VO2 max (rel.)	24	0.489	*	31	0.312		54	-0.089	

*** P < 0.001
** P < 0.01
* P < 0.05

– in addition to three lung function parameters – significantly correlated in systolic and diastolic blood pressure values as well. It seems that in parent-offspring generation father-children pairs were correlated primarily in lung function parameters, since in the fathers and daughters, the only significant correlation is for FVC.

In offspring generation the substantial difference among sisters' and brothers' correlations according to type of physiological trait is found. Although both have comparable sample sizes and the equal numbers of significant correlations, brothers in addition to absolute Vo2 max value, significantly correlate exclusively in lung function parameters, whereas sisters have no recognizable pattern depending on the type of trait.

Although all family pairs show higher family resemblance in lung function parameters than in other physiological traits, the most prominent result refers to exceptionally and consistently high correlations among brothers for all lung function parameters. These values which exceed the level of correlations of all other family pairs, for any examined physiological trait considered in the context of ecostability of examined physiological traits suggest the following explanations. Differences among family correlations found for lung function parameters can be considered in the context of well-known higher ecolability of males[15,16], as well as of larger environmental differences between the two generations[17,18]. The fact that our findings are in accordance with both, supported by low genetic variance of lung function parameters estimated by other authors[19,20], speaks in favor of common environmental factors affecting lung function which influence especially the male family members.

Since family aggregation of lung function parameters can be the result of family aggregation of numerous environmental (e.g. work habits, nutrition, leisure) as well as biological factors (especially the height[5,19,20]), for identification of those factors, further analyses with the exclusion of the known covariates are necessary. The possibility that familial aggregation, particularly in lung function parameters, may be the result of the familial aggregation of cigarette smoking[5,19,21] should also be tested.

Our findings of higher correlations for systolic blood pressure in same-sex par-

ent-offspring pairs is in accordance with some other authors[22-24], only in our sample that difference in father-offspring pairs is not so outstanding. Parent-offspring pairs' correlations for blood pressure, show that for both, systolic and diastolic pressure, mothers and children are stronger correlated than fathers and children, which is in accordance with findings of Perusse[5] and Patterson[24]. The lowest family correlation for Father-daughter pair in systolic and diastolic blood pressure values is the finding shared with other authors[23,24].

Although in both, parent-offspring and offspring-offspring pairs the difference in correlations for blood pressure values were not significant, results show two very interesting patterns. Namely, average offspring correlation for systolic blood pressure (r=0.17) is higher than average correlation of parent-offspring pairs (r=0.09), whereas for diastolic blood pressure they are equal (rOO=0.20, rPO=0.21). Secondly, significance of correlations are evidently not randomly distributed among differently composed family pairs. Female pairs – mothers and daughters as well as sisters – have significant correlations for both, systolic and diastolic blood pressure which is exactly the same pattern Annest[25,26] found. Mixed pairs, however, Mother-son, and Sisther-brother (except Father-daughter pairs) have significant correlation for diastolic but not for systolic blood pressure, and male pairs, brothers, fathers and sons, including the Father-daughter pairs, do not have a significant correlation for either. These relations which do not follow either the pattern of differential sample size, or the absence of sex adjustment of data, show the specific pattern of family aggregation in blood pressure values.

Higher family resemblance for systolic blood pressure among female pairs and among offsprings than in parent-offsprings pairs, found in this population, suggest the following explanations. Lesser resemblance in systolic blood pressure values in intergenerational, especially male pairs can be attributed either to environmental factors which are not common to all family members and therefore have different impact on systolic blood pressure values in males and females, and on members of two generations, either to different susceptibility – higher in males[2,27] – to the same environmental pressures. In contrast, diastolic blood pressure values do not show differences in resemblance among various family pairs, neither in connection to sex, nor to generational differences. These findings suggest that genetic as well as environmental factors which have influence on diastolic blood pressure values – equally affect all family members.

Resting pulse rate values, with exception of Sister-sister pairs, and maximum oxygen uptake values generally show the lowest family resemblance. Among parent-offspring pairs, only the Mother-son pairs have a significant correlation for resting pulse rate ($P<0.05$), whereas Father-daughter, as well as Brother-brother pairs have negative (nonsignificant) values. Among parent-offspring pairs, significant was only the correlation for absolute value of VO2 max in Mother-son pairs – significantly higher than negative correlation in Father-daughter pairs. Sister-brother pairs have a negative value for absolute and relative value of VO2 max, both significantly lower than the same-sex offspring pairs. Low family resemblance in maximal aerobic power is in accordance with findings of Perusse[5], whereas Fagard[28] from twin data estimated high heritability of aerobic power, significantly higher than could be estimated from our data. Family correlations for maximum oxygen uptake and resting pulse rate values which are generally lower than for lung function parameters, do not show recognizable pattern which

would exceed sample size and same-sex pairs explanations.

Presented findings of generally higher correlations in sibling pairs than in parent-child pairs indicate that nongenetic – common familial – factors significantly contribute to the familial resemblance observed in all, but primarily in lung function parameters. Since proper identification of factors responsible for familial aggregation of physiological traits is of uttermost interest, further analyses aimed at exclusion of some environmental and biological covariates are necessary.

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OBITELJSKA SLIČNOST U OSOBINAMA KARDIO-RESPIRATORNOG SUSTAVA

SAŽETAK

U ovom je radu provedena analiza obiteljske povezanosti nekih parametara fiziološke funkcije kod odraslih članova obitelji populacije srednjodalmatinskih otoka. Međusobna sličnost srodnika prvog stupnja srodstva kvantificirana je izračunavanjem Pearsonovog »product-moment« koeficijenta korelacije, a rezultati su uspoređeni sa nalazima drugih autora i razmatrani u odnosu na moguće utjecaje genetskih i okolinskih čimbenika. Najviše vrijednosti obiteljskih korelacija zabilježene su kod parametara plućne funkcije, a najniže kod vrijednosti frekvencije srca u mirovanju, te maksimalne aerobne snage. Nalaz izuzetno visoke koreliranosti plućnih funkcija kod braće, te veće koreliranosti očeva i djece u parametrima plućne funkcije u odnosu na druge ispitivane fiziološke osobine, govori u prilog velikog utjecaja čimbenika zajedničkog obiteljskog okoliša na ova svojstva, posebice kod muških članova obitelji. Korelacije sistoličkog i dijastoličkog krvnog tlaka, upućuju na različite modele obiteljske povezanosti. Model obiteljskih korelacija koji nalazimo kod sistoličkog krvnog tlaka, a koji rezultira u manjoj sličnost muških članova obitelji, te manjoj međugeneracijskoj sličnost, sugerira ili prisustvo utjecaja različite okoline ili različitu, veću kod muškaraca, osjetljivost na te utjecaje. Nasuprot tome, uzorak obiteljske koreliranosti dijastoličkog tlaka, koji ne pokazuje spolne i generacijske razlike, ukazuje na ravnomjeran upliv genetskih i okolinskih čimbenika na sve članove obitelji.