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Sexual Dimorphism in Minor Physical Anomalies on the Waldrop Physical Anomaly Scale in Normal Population

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The aim of the study is to investigate the sexual dimorphism of minor physical anomalies in normal population. Eighty-two subjects (42 men and 40 women) were examined for minor physical anomalies using the Waldrop Physical Anomaly Scale. Sexual dimorphism is presented by a tendency to a higher prevalence of anomalies in men. This tendency is found for most of the examined body regions, the craniofacial region as a whole and the total minor physical anomaly score. Men have greater percentage than women of relatively more stigmatized with minor physical anomalies individuals. The data suggest greater ontogenetic disability of men than women. Men's higher stigmatization with MPAs, especially of the craniofacial region, implies greater vulnerability of the male fetus during the prenatal development, which coincides with sexual differences in the fetal sensitivity to endo/exogenous factors.

Key words: dysmorphic stigmatization, maldevelopment, extragenetic influence, gender effect.

Introduction

Minor physical anomalies (MPAs) provide a key to identifying an ontogenetic abnormality. MPAs are slight dysmorphic features that are considered to develop during the first or/and early second trimester of gestation [2, 11, 14]. Once formed, these anomalies persist into adult life and prove potentially valuable indices of disturbances in early development [6, 7]. An algorithmic approach to anomalies begins with a careful history and physical examination. However, a careful physical examination by a dysmorphologist differs too much from the routine examination by most physicians. Dysmorphologists have detected as many as a dozen morphogenic abnormalities in children and adults that had not been documented in their previous medical records [9]. The Waldrop Physical Anomaly Scale appears a convenient instrument for assessment of MPAs [13]. It is derived from a pediatric study for distinguishing schizophrenic from normal children and has some inherent limitations as low internal consistency, low sensitivity, and subjectivity [4, 5]. Nevertheless, it is presently the most widely used scale for assessment of dysmorphic features as an index of developmental origins of schizophrenia. However, few studies allow for anomaly prevalence in the normal population as well as gender and ethnic effects on the anomalies. Furthermore, because of the interaction between genetic and teratogenic factors, the nature of the adversities that have an effect on the origin of MPAs needs to be accurately defined for proper etiologic evaluation of the anomalies.

The findings presented in this article are part of a more extensive study aiming to develop a systematic approach to structural abnormalities as a key element of malformation syndrome diagnosis, in particular of schizophrenia. Being a component of this approach the sexual dimorphism of MPAs is studied in ethnically homogenous population of mentally healthy Bulgarians.

Material and Methods

Subjects

The subjects were 82 mentally healthy individuals (42 men, 40 women) with a mean age 39.24 years (SD=10.18, range 22-68) of Bulgarian origin; individuals were excluded if their parental or grandparental ethnic group was different from Bulgarian. The two gender groups were similar in their basic sociodemographic characteristics. Normality was defined as the absence of a major axis I or axis II disorder according to DSM-IV (American Psychiatric Association, 1994) [1]. Potential subjects were also excluded if they had an identifiable neurological disorder (e.g., seizure syndrome, multiple sclerosis etc.). In addition, potential normal controls were excluded if they had a first-degree relative with a history of a psychotic disorder, major affective disorder or suicide.

The study was approved by the local Ethics Committee and after complete description, written informed consent was obtained from the subjects.

Assessment of Minor Physical Anomalies

The subjects were examined with a slightly modified Waldrop Physical Anomaly Scale, the widely used standardized scoring system for the assessment of MPAs [13]. It assesses 19 morphological abnormalities (Table 1) of six body regions: head, eyes, ears, mouth, hands, and feet. Most of the abnormalities are scored qualitatively as present [1] or absent [0]. The items fine electric hair, head circumference, epicanthus, intercanthal distance, low seated ears, high/steepled palate and third toe ≥ second are scored in a graded manner — 1 or 2, according to severity. The following modifications were made: the categories adherent ear lobes and lower edges of the ears extend backward/upward (two grades of a single item in the original scale) were defined as separate items because of the high prevalence of the first and occasional finding of the second. The furrowed tongue was graded by scoring 1 randomly furrowed tongue (a normal variant) and scoring 2 transversely furrowed tongue (frequently observed in pathological conditions). In the original scale both types are scored 1. The head circumference and intercanthal distance were scored 1 if they differed from the same-sex mean by 1.5-2 SD and 2 — by more than 2 SD in both directions.

All examinations were performed by the same examiner (S.S., the study anatomist). Reliability studies were conducted, using a second assessor (Z.L.) who was not otherwise involved in the study. She co-examined 30 schizophrenic patients (15 men, 15

T a b l e 1. Prevalence of MPAs on the Waldrop scale in men and women

Topographic region and anomalies	Men (*n*=42)		Women (*n*=40)		Statistical significance		
	n	%	*n*	%	Value	df	*p*
Head							
Fine electric hair							1.000*
1. Doesn't comb down	5	11.9	4	10.0			
2. Awry soon after combing	0	0.0	0	0.0			
Hair whorls ≥ 2	14	33.3	4	10.0	5.22	1	.022**
Head circumference					.91	2	.634**
1. 1.5 SD-2SD	3	7.1	5	12.5			
2. 2SD	2	4.8	1	2.5			
Eyes							
Epicanthus							.494*
1. Partly covered	2	4.8	0	0.0			
2. Deeply covered	0	0.0	0	0.0			
Hyper(hypo)telorism					.61	2	.737**
1. 1.5 SD-2SD	5	11.9	6	15.0			
2. 2SD	1	2.4	2	5.0			
Ears							
Low seated ears							.488*
1. ≤ 0.5 cm below the outer corner of the eye	0	0.0	1	2.5			
2. > 0.5 cm below the outer corner of the eye	0	0.0	0	0.0			
Adherent ear lobes	17	40.5	12	30.0	.58	1	.447**
Lower edges extend back/upward	2	4.8	0	0.0			.494*
Malformed ears	1	2.4	0	0.0			1.000*
Asymmetrical ears	4	9.5	4	10.0			1.000*
Soft and pliable ears	19	45.2	20	50.0	.04	1	.833**
Mouth							
High/steepled palate					.30	2	.860**
1. Flat and narrow at the top	10	23.8	10	25.0			
2. Definitely steepled	2	4.8	1	2.5			
Furrowed tongue					3.30	2	.192**
1. Randomly furrowed	5	11.9	7	17.5			
2. Tansversely furrowed	3	7.1	0	0.0			
Tongue with smooth-rough spots	0	0.0	1	2.5			.488*
Hands							
Curved fifth finger	10	23.8	14	35.0	.76	1	.384**
Single transverse palmar crease	0	0.0	1	2.5			.488*
Feet							
Third toe					-	-	-
1.Equal to second	0	0.0	0	0.0			
2. Longer than second	0	0.0	0	0.0			
Partial syndactylia of II and III toes	1	2.4	0	0.0			1.000*
Big gap between I and II toes	7	16.7	0	0.0			.012*

* Fisher's Exact Test: two-tailed
**χ^2- test (in 2×2 table with Yates' correction for continuity)

women) and 20 normal controls (10 men, 10 women) of the current study groups. Except for one item, Cohen's k for concordance between categorical/ordinal scores were all >0.75 and intra-class correlation coefficients for continuous measures — > 0.78. Acceptable level of reliability was not reached for curved 5th finger (k<0.60) due to the lack of clear anomaly definition and hence high subjectivity in assessment. This necessitated another modification of the scale: curved 5th finger was scored only as present (1) or absent (0), while in the original scale its presence is weighted (1 or 2).

Statistical Analysis

Summary scores were calculated for each body region, for the craniofacial region (MPA-CF), the periphery (MPA-P) and the total scale (MPA-T). Anomalies distribution index (MPA-CF - MPA-P) / MPA-T) was also calculated.

The data were analyzed with SPSS 9.0 using descriptive statistics, graphics analysis, Independent Student's t-test: two-tailed for continuous data, χ^2- test (in 2×2 table with Yates' correction for continuity) or Fisher's Exact Probability Test: two-tailed for categorical data and Multivariate Analysis of Variance (MANOVA). Statistical significance was defined as $p<0.05$: two-tailed.

Results

Between-gender Differences in Minor Physical Anomalies

The prevalence of the specific MPAs in mentally healthy men and women is presented in Table 1. Of the 19 examined anomalies 6 anomalies (epicanthus, lower edges extend back/upward, malformed ears, third toe ≥ second, partial syndactylia of II and III toes, and big gap between I and II toes) and the second grades of other 3 anomalies (fine electric hair, furrowed tongue, and low seated ears) are not found in the women, while only 4 anomalies (low seated ears, tongue with smooth-rough spots, single transverse palmar crease, third toe ≥ second) are not present in the men. The men score higher than the women in the two variables with significant between-gender difference — two or more hair whorls ($p<.05$) and big gap between I and II toes ($p<.05$). It is interesting to note that the two sexes show opposite topographical pattern of the peripheral anomalies. The men score higher in MPAs of the feet, while the women - in MPAs of the hands.

The overall tendency toward a higher prevalence of MPAs in the men than in the women, which is discernible in Table 1, becomes more apparent when the individual MPAs are summarized and compared by topographic regions (Table 2).

T a b l e 2. Comparison of MPAs on Waldrop scale by topographic regions between men and women

	Men (N=42)		Women (N=40)		Statistical significance	
Topographic region	Mean	SD	Mean	SD	Value*	*p*
Head	.62	.79	.38	.67	1.50	.137
Eyes	.21	.47	.25	.54	.32	.751
Ears	1.02	.78	.93	.94	.52	.606
Mouth	.60	.96	.50	.60	.54	.591
Craniofacial region (MPA-CF)	2.45	1.61	2.05	1.41	1.20	.234
Hands	.24	.43	.38	.54	1.26	.210
Feet	.19	.40	.00	.00	3.11	.003
Periphery (MPA-P)	.43	.55	.38	.54	.45	.657
Total MPA (MPA-T)	2.88	1.68	2.42	1.41	1.32	.189
Index of distribution	.69	.45	.62	.60	.54	.592

* Independent Student's t-test: two-tailed

Between-gender Differences in Minor Physical Anomalies by Topographic Regions

The regional pattern of the anomalies (Table 2) shows a general tendency to a greater stigmatization of the men. The men score higher in MPAs in all craniofacial regions except the eyes. The whole craniofacial region is more dysmorphic in the men than in the women (2.45 vs. 2.05), although the difference fails to reach statistical significance ($p = 0.234$). The whole periphery is slightly more dysmorphic in the men (0.43 vs. 0.38, $p>0.05$). The men have significantly higher MPAs score for the feet ($p<0.05$), while the MPAs score of the hands is higher in the women, but falls short of statistical significance (.38 vs. .24, $p>0.05$). The men score higher in the total MPAs score than the women (2.88 vs. 2.42) with difference approaching statistical significance ($p = 0.189$).

In both sexes the index of anomaly distribution indicates a tendency to a relatively greater stigmatization of the craniofacial region than of the periphery. The men show higher index of distribution than the women do (0.69 vs. 0.62), but the difference does not reach statistical significance ($p>0.05$).

Multivariate Analysis of Variance (MANOVA) was further used to study the effect of sex on MPAs. In our MANOVA model the independent classification variable is gender and the set of multiple dependent variables — the scores of the 6 topographic regions. For this model the Pillai's trace, which is the most powerful and robust test statistics for evaluating multivariate differences, approaches statistical significance ($F = 1.84, p = 0.105$). This indicates a tendency for between-sex difference in the 6 MPAs topographic regions as a whole. The significance levels for the univariate statistics (not adjusted for the fact that several comparisons are being made and thus should be used with a certain amount of caution) indicate which topographic regions contribute mostly to the general between-gender difference in MPAs. The contribution is statistically significant for the feet ($F=7.74, p=.007$), approaches statistical significance for the hands and head ($F=2.96, p=.090$ and $F=2.93, p=.091$, respectively) and does not have statistical significance for the eyes ($F=.59, p=.447$), mouth ($F=.22, p=.642$) and ears ($F=.16, p=.695$).

Between-gender Differences in the Distribution of Total Minor Physical Anomalies Score

Some between-gender differences in the distribution of MPA-T scores are evident in Fig. 1 and Fig. 2.

Figure 1 shows that the men have relatively higher variability in MPA-T score. The median of MPA-T is greater in the men than in the women (3 vs. 2). Figure 2 shows that in both genders the distribution of MPA-T is positively skewed (to the right). The skewness is more prominent in the women (Skewness = 0.56, SE Skew = 0.37) than in the men (Skewness = 0.16, SE Skew = 0.37), indicating that the bulk of the women have MPA-T of 1, 2 and 3 and relatively few extend to 4, 5 and 6, while in the men MPA-T scores are more evenly distributed around 3.

The sexual dimorphism in dysmorphic stigmatization was additionally assessed by comparing the percentage of subjects with MPA-T≥3, i.e. scores greater than the both sexes common mean (common mean=2.66: men — 2.88, women — 2.43) (Table 3).

The men show greater percentage than the women do for all examined categories. MPA-T scores ≥3 and ≥4 best discriminate men from women, although the difference

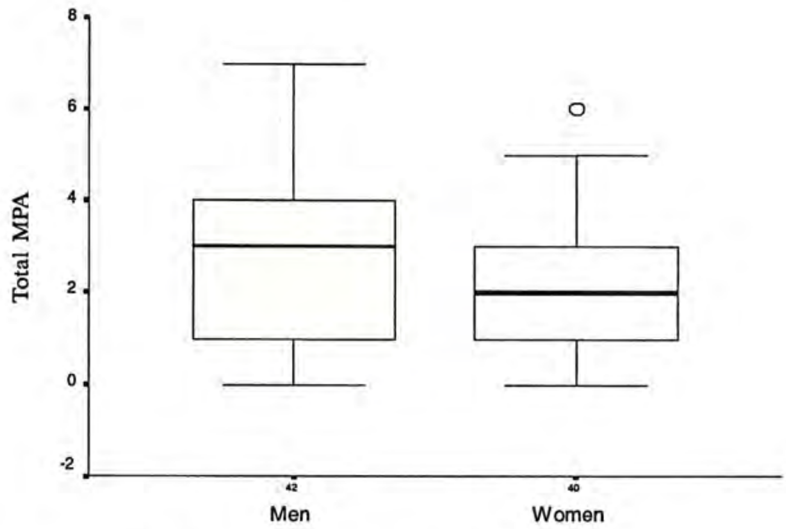

Fig. 1. Boxplots of MPA-T scores of men and women

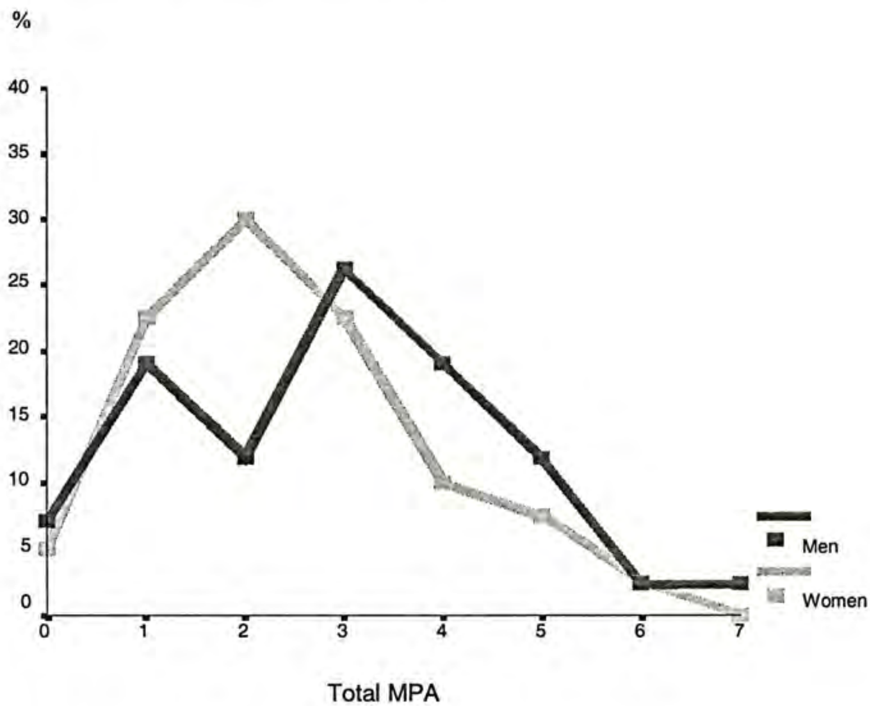

Fig. 2. Frequency distribution of MPA-T scores in men and women

T a b l e 3. Comparison of the percentage of subjects with MPA-T ≥3 between men and women

MPA-T	Men (N=42)		Women (N=40)		Statistical significance		
	n	%	n	%	Value	df	p
MPA-T≥3	26	61.9	17	42.5	2.36	1	.124*
MPA-T≥4	15	35.7	8	20.0	1.79	1	.181*
MPA-T≥5	2	4.8	1	2.5	.32	1	.575*
MPA-T≥6	1	2.4	0	0.0			1.000**

* χ^2 — test (2×2 table with Yates' correction for continuity)
** Fisher's Exact Test: two-tailed

fails to reach statistical significance (p = 0.12 and p = 0.18, respectively). The small number of cases with MPA-T scores ≥5 and ≥6 does not allow adequate comparison.

Discussion

The study reveals signs of sexual dimorphism in MPAs, indicated by the tendency to a higher prevalence of the anomalies in men. This tendency is present in most of the examined body regions, the craniofacial region as a whole and the total MPA score. Sexual dimorphism is also evident in the greater percentage of men with higher scores of MPAs.

Viewed in the context of extragenetic influence, the higher stigmatization of men with MPAs implies greater vulnerability of the male fetus during the prenatal development. Hence, the tendency to a more expressed craniofacial dysmorphism in men is not an illogical finding because of the complex processes of morphogenesis in this region. The analysis of the difference in the specific anomalies suggests sexual differences in the fetal sensitivity to endo/exogenous factors.

This "ontogenetic disability" of man is evident from studies of psychiatric patients (schizophrenics), which indicate lower resistance of the male brain to maldevelopmental processes than the female brain [8, 10]. G u a l t i e r i & H i c k s assert higher sensitivity to adversities of the ectodermal activity and more expressed relation of anomalies to neurodysontogenetic processes in the male fetus [3]. This statement is indirectly supported by the higher rate of MPAs, earlier onset of the disease, more expressed premorbid deficit, worse prognosis of the disease, and higher incidence of pregnancy complications in male schizophrenics [12].

To view anomalies only as a result of extragenetic events would be a shortsighted and incomplete approach. Apparently, prenatal events (for example, obstetric complications) have a particular role in dysmorphogenesis, which, however, can be further modulated by genetic factors. Clarification of the specific effect and interaction between genetic and extragenetic factors on the normal prenatal morphogenesis requires more extensive research including genealogical studies. Categorizing anomalies by character, region, severity etc. helps choosing the appropriate steps to diagnosis. Even without specific diagnosis, the nature of the defect may suggest the probable etiology and risk of recurrence in future offspring.

Conclusions

1. Minor physical anomalies show a tendency to sexual dimorphism in the normal population, presented with a higher prevalence of dysmorphic features in males

2. The greater craniofacial stigmatization of males and different pattern of the peripheral anomalies in sexes suggest greater vulnerability of the male fetus and different liability to developmental adversities in males and females.

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