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Electrocardiograms in school-aged healthy Polish children — an observational study

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WHAT'S NEW?

We performed an electrocardiographic examination (ECG) in healthy school-aged children. Compared with literature data, differences between Polish and other ethnic populations on ECG parameters exist. These findings are clinically importnt and suggest that diagnostic criteria for pediatric ECG should be revised to establish if they are justifiable for the entire population.

ABSTRACT

Background: Electrocardiographic (ECG) examination has long been used to assess cardiovascular function in clinical practice. Age-related ECG changes are observed as the cardiovascular system matures from the neonatal period to adolescence.

Aim: This study aimed to evaluate the effects of sex and age on ECG parameters in healthy schoolchildren.

Methods: The study included 336 healthy participants aged 5–12 years from Masovian voivodeship. Children were divided into age groups of 5–8 and 9–12 years. Values for heart

rate (HR), time intervals and amplitudes of P and QRS waves, and QRS axis for pediatric ECGs were estimated.
Results: Significant differences between boys and girls aged 5–8 years old were discovered for such parameters as PR interval, R-wave, and S-wave, R/S ratio. Age-related decline in HR, Q-wave in V5, and V6, R-wave in V1–V4, and increase in QRS duration were noted. Girls presented higher HR and shorter QRS than boys. HR, QRS axis, P wave amplitude in the II lead, and amplitude of R and S in the precordial leads were different in our population than previously reported.
Conclusions: Pediatric ECG tracings were estimated for the first time for school-aged Polish healthy children. Sex-related differences in selected ECG parameters in the younger age group were noticed. Several parameters differed from those previously reported in other ethnic populations. These findings are clinically significant and suggest that diagnostic criteria for pediatric ECG should be revised to establish if they are justifiable for the entire population.
Key words: ECG, healthy children, reference values

INTRODUCTION

Electrocardiographic (ECG) examination has been used in clinical practice for reliable assessment of cardiovascular and cardiopulmonary function [1, 2]. Measuring ECG recordings and interpreting them using reference values is commonplace for clinicians and researchers conducting studies in the field of cardiology. As the myocardium and cardiovascular system undergo maturation and change from the neonatal period to adolescence, age-related ECG changes are observed leading to challenges in interpreting the pediatric ECG [3–5]. It has been shown that selected ECG parameters may be influenced by sex due to cardiac and extracardiac factors [6]. Additionally, ethnic differences in ECG amplitudes were noticed [7].

For this reason, age- and sex-dependent ECG norms have been published for populations from Western Europe [8, 9], Africa [10], Asia [9, 11], and the Americas [8, 9, 12]. There are no studies on the characteristics of ECG parameters in children from Central-Eastern Europe. The most recent study, with the pediatric cohort to date and electronically recorded standardized leads, referred only to the USA and Canadian populations [13]. The only research based on Eastern European society presents the ECG standards performed in the Russian population [14]. Therefore, the study aimed to evaluate the effects of sex and age on ECG parameters in healthy Polish school children in comparison to the other published data of the rest ECG.

METHODS

Details and a description of the study group and the procedures performed before or during the ECG examinations have been published elsewhere [15]. The present study included 336 volunteer participants aged 5–12 years from Mazovian Voivodeship (Poland); the inclusion criteria were as follows: age between 5 and 12 years, absence of diseases and/or regular use of medications affecting the cardiopulmonary system, and not being an active athlete in any sports. The parents/legal guardians were interviewed about children's diseases and/or medications (the school health records concerning health status were additionally verified). During the initial analysis, twenty subjects with a history of a cardiovascular event, three children with a diagnosed chronic disease, two subjects with incomplete ECG data were excluded from the analysis. The final study sample included 316 children (152 boys). The body mass status was measured using body mass index (BMI) defined as body mass in kilograms divided by height in meters squared. All parents or guardians had received printed information about study protocol and aims of the research and gave their informed written consent. Ethical approval was obtained through the University Bioethical Committee (KB/74/2013).

ECG measurements

12-lead electrocardiogram was recorded using a PC with an integrated software system (Custo cardio 100; Custo med GmbH, Ottobrunn, Germany) at a sampling rate of 1000 Hz. The ECG recordings were performed at a 25 mm/s speed and 10 mV gain from 8 a.m. to 14 a.m. in the supine position in a quiet room (temperature between 22–28°C). Before the beginning of the ECG recording to familiarize with the study the children were in supine position for 5 minutes. During the recordings, each child was encouraged to breath normally and not to speak or move. Values of ECG parameters were calculated based on computerized analysis of the obtained set of ECGs recorded at high sampling rate. Before analysis, all ECGs were inspected by an experienced pediatric cardiologist. Corrected QT (QTc) intervals were obtained using the Bazett formula. In cases where artificially prolonged QTc values at increased heart rate (HR) were obtained, the value was individually corrected.

Data presentation

The study sample was divided into age groups 5–8 and 9–12 years. The median, 2^{nd,} and 98th percentile were presented in lead-independent ECG measurement. The median and 98th percentile were shown for P-, Q-, R-, and S-waves in all leads. Zero amplitude values indicating absent Q, R, or S waves, were excluded from the statistical analysis of the data. All procedures were performed to compare results with other authors that presented normal/reference pediatric ECG limits [1, 2].

Statistical analysis

The Kolmogorov–Smirnov test was used to assess the normality of the distribution for the boys and the girls for two age groups (5–8 and 9–12 years). To identify sex (marked in table using * in superscript) and age († in superscript) effects and their interaction (‡ in superscript) on ECG parameters, two-way analysis of variance (ANOVA) and Tukey HSD Test for unequal N were used. Due to skewed distributions of the data: P-wave (V1,V2), Q-wave (III, aVF,V5), R-wave (aVR, aVL), and S-wave (II, III, V5, V6) logarithmic transformation was carried out to perform two-way ANOVA. The threshold probability of $P < 0.05$ was taken as the significance level for all statistical analyses. Statistical calculations were performed using the software STATISTICA 10-StatSoft. Inc software (Tulsa, OK, US).

RESULTS

The anthropometric characteristics of the study group are presented in Table 1. There were no age and sex interactions. Main effect of age was observed for body mass ($F = 90.4$; $P < 0.001$), stature ($F = 200.1$; $P < 0.001$) and BMI ($F = 22.3$; $P < 0.001$). Body mass, stature, and BMI increased with age. Tables 2–7 contain results for lead-independent ECG measurements. There was a significant age and sex interaction for PR interval; R-wave II, aVF, V5, and V6; S-wave II, III, V1, V2, V5, and V6; R/S V2 and V6 (F between 4.0 and 11.7 for all; *P* between <0.001 and 0.45). Significant, independent age and sex effects were observed for HR (age: $F = 16.8$; $P < 0.001$; sex: $F = 7.2$; $P = 0.008$), QRS duration (age: $F = 7.5$; $P = 0.006$; sex: $F = 5.0$; $P = 0.026$) and R/S V1 (age: $F = 14.3$; $P < 0.001$; sex: $F = 7.6$; $P = 0.006$). A significant age effect was observed for QTc interval; Q-wave V5 and V6; R-wave V1–V4 (F between 4.2 and 47.9 for all; *P* between <0.001 and 0.042). Significant sex effect was observed for R-wave III and aVR; S-wave I, aVR, aVL, aVF, V3, V4; R/S V5 (F between 5.4 and 28.1 for all; *P* between <0.001 and 0.021). No age and sex interactions and no main effects were observed for the P axis and QRS axis; P-wave II, V1, and V2; Q-wave II, III, and aVF; R-wave I, aVL (*P* between 0.07 and 0.95).

DISCUSSION

Knowledge of circulatory system changes during its maturation in normal development is essential for interpreting ECG leads in different age groups of the pediatric population. We present values for ECG parameters of school children aged 5–12 years from Poland, Masovian voivodeship — sex-related differences in PR interval, R-wave, S-wave and R/S ratio were observed in the younger age group. We found differences between Polish and other societies — the most important relates to HR, the amplitude of the P wave, the electrical axis of the QRS, and QRS waves amplitude.

Previous studies determining normal thresholds for pediatric ECG were based on Western European, North American, Canadian, and Chinese populations. Mason et al. [8] collected data from various populations from the USA, and Europe and showed results in 10-year age cohorts from 0 to 99 years. Rijnbeek et al. [6] and Sun et al. [16] presented normal ECG thresholds for Dutch and Chinese children, respectively. The largest and most recent study (2020) of normative ECGs in pediatrics was conducted in the USA and Canada [13]. Even the generally accepted pediatric reference ranges for ECG parameters published in Poland [17] are based on the studies mentioned above from Western societies. Therefore, they do not consider the ethnic differences between Western and Central European populations detected in our study.

Heart rate is the most apparent manifestation of age and sex differences in pediatric ECG. It decreases with age and is higher in girls. The ethnic differences are also clear. In our population, the upper limits for HR were lower than in the other studies [6, 12, 13, 16]. For example, the 98^{th} percentile for boys reached 107 bpm, for girls 111 bpm in the age group of 5–8 years, while in the American/Canadian populations [13], the upper limits for similar age groups (6–7 years) were 119 bpm for boys and 128 bpm for girls.

Another difference between our data and those previously published is P wave amplitude. P wave is usually best studied in leads II or V1 and is a reflection of the size of the right atrium. In the recent study, the upper limit for the amplitude of P wave was up to 0.3 mV in the lead II and 0.2mV in the right precordial leads. In the literature, a P-wave amplitude greater than 0.25 mV in one of the leads is considered too high [16]. These results suggest that amplitude criterion should be lead-dependent in diagnosing right atrial enlargement and reconsidered at least for lead II.

Regarding PR interval, significant interactions between age and sex were found. Furthermore, it was estimated to be 170 ms for the 98^{th} percentile for the age group 9–12 years, while according to the Polish guidelines [17], the upper limit for these children is 190 ms. Although the differences were significant, they are irrelevant from a clinical point of view since prolongation of PR interval is usually benign. It is often observed in young, active individuals and relates to the so-called athlete's heart.

QRS duration increasing with age was broadly investigated [6, 18]. The far less known phenomenon is QRS width alteration with sex. It is broader in boys than in girls. Nevertheless, sex differences in QRS duration are relatively discreet and have no meaning in everyday practice. Maybe, the significance of these differences would be more apparent from a clinical point of view when analyzing long-term ECG monitoring [19].

Sex differences in QRS axis are observed nominally. They are more evident in our than in the other populations. In boys, the 98th percentile for QRS axis was 117° and was more shifted to the right than in girls (98°). Our population's upper limit for pathological right axis deviation was much lower than that of western societies [17]. According to them, it does not depend on gender and reaches 140°. Pathological right axis deviation in school children is primarily one of the indicators of right ventricular hypertrophy. Therefore, applying our criteria would increase the ECG sensitivity for the diagnosis of right ventricular pathology.

Age-related changes typical for the pediatric population must also be considered when analyzing the detailed morphology of QRS complex. After we take into account all the temporal and spatial variability of the waves during the depolarization of the ventricles, we obtain a wide range of different patterns of QRS shape, which are still within the scope of the norm. That makes ECG assessment challenging to evaluate in children.

The first example of this variability is Q wave. A pathological Q wave is an indicator of septal hypertrophy or myocardial necrosis. This usually occurs in II, III, aVF, V5, and V6. It is considered pathological if it takes more than 30 ms and above -0.50 mV. In our population, the amplitude of Q at the 98th level did not exceed –0.37 mV, so the upper limit is lower than previously assumed in the literature [3].

Furthermore, the rise of R wave amplitude in V5–V6 and decrease of R wave amplitude in V1–V4, as well as decrease of the R/S ratio in V1 with age, were noticed in our trial. All these changes are an expression of rising mass and electrical activity of the left ventricle free wall muscle during normal development of the circulatory system.

In the recent study, R and S waves amplitudes were lower than the corresponding values in children of the Netherland [6], USA, and Canada [4] for both age groups and sexes. These discrepancies could be explained in two ways.

Firstly, as a consequence of different ECG sampling rates [6, 12]. The higher the sampling rate, the higher the amplitude of the wave. Nevertheless, the sampling rate in Rijnbeek et al. [6] study was high, similar to our study (sampling rate 1000 Hz), but our data align more with the Davignon et al. [12] and Dickinson et al. [18], where the sampling rate was as low as 333 Hz.

Secondly, the suggested difference would come from the method of the data obtained. During the manual ECG assessment, the amplitudes of QRS waves are lower than during automatic attaining [12]. However, our tracings were analyzed automatically, as performed in the studies, where the amplitudes of R and S waves were higher than in the recent trial [6, 12]. In the light of these data, we can assume that our results could be explained by ethnic differences between Western Europe and Polish pediatric populations that affect ECG derivation.

The shape and amplitude of the QRS waves varied significantly between boys and girls in most leads, which is consistent with previous studies [6, 12]. This is most striking for the S wave in the left-sided precordial leads. For example, the upper limit of the S-wave in V6 is 0.47 mV and 0.18 mV for younger boys and girls, respectively. Considering these data, sex-dependent criteria may improve the sensitivity and specificity of the diagnosis of ventricular hypertrophy in ECG in the pediatric population.

On the contrary, the apparent gap between boys and girls aged 5–8 years old for R-wave, S-wave amplitudes, and R/S ratio in the precordial leads narrows in children aged 9–12 years. Presumably, these facts relate to non-lean body composition development during puberty. At the beginning of puberty in females, modest fat loss accompanied by muscle tissue enlargement is observed. These changes are more progressive in boys but occur 1–2 years later than in girls. Because of this gap in pubertal development, the differences in body composition between males and females seen up to the age of 8 start to be similar about the age of 9 years, which could be the reason for the narrowing gap of the ECG parameters. They begin to alter again later in adolescents when rapid development of the muscle tissue in males is seen [20].

To sum up, we ought to be aware that all the ECG tracings we observed can probably be the consequence of much more than the simple anatomical body composition of the chosen ethnic groups or sex. In the trials in animals, the physiologic hormonal differences between males and females are the reason for altered molecular ionic activity in the cardiac fibers. These may influence the currents responsible for the heart's electrical function. Besides, even such habits as daily physical activity need to be considered in the analysis regarding heart rhythm and function [21]. All these variables can drive the broad diversity of spatial and temporal picture of the ECG tracings even in the same age group of children and need further evaluation.

Limitations of the study

The sample size was relatively small; the children were only from Mazovian voivodeship and settled mainly in urban areas. Discrepancies with other studies could reflect ethnical differences but also demographic changes in highly developed societies during the last decades, e.g., the increase in body weight or the age of puberty. Comparison of the data with all published norms was difficult due to various age intervals used in the other trials.

CONCLUSIONS

Pediatric ECGs were estimated for school-aged Polish healthy children. We presented a sex-related gap in selected ECG parameters in the younger age group that partially narrow in older children. The values differed from previously reported in other ethnic populations. These findings are clinically significant and suggest that diagnostic criteria for pediatric ECG should be revised to establish if they are justifiable for the entire population.

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Table 1. Anthropometric characteristics for boys (upper row) and girls (lower row): median (2nd percentile–98th percentile)

Measure	Sex	5–8 (40♂, 35♀)	9–12 (112♂, 129♀)	5–12 (152♂, 164♀)	Effects direction and *P*
Body mass, kg†	**Boys**	24.6 (17.0–42.6)	35.8 (21.7–70.0)	32.3 (19.0–67.4)	↑ with age (*P* <0.001)
	Girls	23.3 (15.3–37.8)	37.1 (21.2–67.6)	33.2 (17.2–66.9)	
Stature, cm†	**Boys**	124.0 (107.0–142.0)	143.5 (127.0–168.0)	139.0 (111.0–166.0)	↑ with age (*P* <0.001)
	Girls	122.0 (107.0–141.0)	143.0 (122.0–168.0)	139.0 (114.0–166.0)	
Body mass index, kg/m^{2}†	**Boys**	16.4 (12.9–23.2)	17.8 (13.2–26.8)	17.2 (13.2–26.3)	↑ with age (*P* <0.001)
	Girls	15.8 (11.9–21.4)	17.7 (13.1–27.1)	17.1 (12.7–25.1)	

♂ boys; ♀ girls; † independent age effect; ↑ increase of values/higher values

Table 2. Lead-independent ECG measurement for boys and girls median (2nd percentile–98th percentile)

Lead	5-8		9–12		Effects direction and *P*
	Boys	**Girls**	**Boys**	**Girls**	
HR, beats/min†*	89 (66–107)	92 (64–111)	80 (61–104)	86 (62–111)	↓ with age (*P* <0.001), ↑ in ♀ (*P* = 0.008)
P axis (°)	62 (17–79)	55 (–2–83)	59 (–10–79)	57 (4–78)	*P* = 0.17
PR, ms‡	135(107–172)	123 (92–156)	137 (99–177)	135 (100–172)	Interaction (*P* = 0.014): 5–8 ♂ vs. ♀ (*P* = 0.026)
QRS axis (°)	83 (33–117)	82 (66–98)	81 (36–101)	82 (36–97)	*P* = 0.95
QRS, ms†*	87 (75–100)	85 (76–104)	89 (76–106)	87 (76–102)	↑ with age (*P* = 0.006), ↑ in ♂ (*P* = 0.026)
QTc, ms†	421(380–449)	420 (380–447)	414 (370–452)	413 (73–445)	↓ with age (*P* = 0.002)

*Independent sex effect; † independent age effect; ‡ interaction; ♂ boys; ♀ girls; ↓ decrease of values/lower values; ↑ an increase of values/higher values; QTc intervals obtained using Bazett formula, in cases where artificially prolonged QTc values at increased HR were obtained, the value was individually corrected by the pediatric cardiologist

Abbreviations: ECG, electrocardiogram; HR, heart rate

Table 3. P-wave amplitudes (mV) for boys and girls: median (98th percentile)

Lead	5-8		9-12		Effects direction and *P*
	Boys	Girls	Boys	Girls	
II	0.17 (0.29)	0.17 (0.28)	0.15 (0.28)	0.15 (0.30)	*P* = 0.34
V_1	0.10 (0.17)	0.09 (0.17)	0.09 (0.15)	0.09 (0.17)	*P* = 0.17
V_2	0.10 (0.18)	0.10 (0.25)	0.09 (0.17)	0.10 (0.19)	*P* = 0.71

Table 4. Q-wave amplitudes (mV) for boys and girls: median (98th percentile)

Lead	5-8		9-12		Effects direction and *P*
	Boys	Girls	Boys	Girls	
II	0.06 (0.20)	0.07 (0.27)	0.06 (0.23)	0.06 (0.19)	*P* = 0.43
III	0.11 (0.28)	0.11 (0.37)	0.08 (0.33)	0.10 (0.29)	*P* = 0.23
aVF	0.07 (0.22)	0.07 (0.30)	0.06 (0.26)	0.08 (0.21)	*P* = 0.62
V_5†	0.11 (0.29)	0.15 (0.24)	0.08 (0.36)	0.09 (0.30)	↓ with age (*P* = 0.009)
V_6†	0.10 (0.26)	0.15 (0.24)	0.08 (0.27)	0.09 (0.27)	↓ with age (*P* = 0.007)

†Independent age effect; ↓decrease of values/lower values

Table 5. R-wave amplitudes (mV) for boys and girls: median (98th percentile)

Lead	5–8		9–12		Effects direction and *P*
	Boys	Girls	Boys	Girls	
I	0.32 (0.68)	0.29 (0.73)	0.33 (0.75)	0.33 (0.86)	*P* = 0.82
II‡	1.09 (1.85)	1.41 (2.48)	1.14 (2.06)	1.32 (2.05)	Interaction (*P* = 0.012): 5–8 ♂ vs. ♀ (*P* <0.001)
III*	0.89 (1.93)	1.25 (2.30)	0.97 (1.93)	1.07 (1.94)	↑ in ♀ (*P* <0.001)
aVR*	0.06 (0.43)	0.05 (0.23)	0.06 (0.44)	0.05 (0.35)	↑ in ♂ (*P* = 0.012)
aVL	0.14 (0.36)	0.09 (0.34)	0.10 (0.47)	0.11 (0.47)	*P* = 0.07
aVF‡	0.95 (1.88)	1.34 (2.39)	1.03 (1.91)	1.20 (2.01)	Interaction (*P* = 0.019): 5–8 ♂ vs. ♀ (*P* <0.001)
V_1†	0.48 (0.97)	0.49 (0.92)	0.35 (0.76)	0.32 (0.84)	↓ with age (*P* <0.001)

V_2 †	1.03 (1.85)	0.89 (1.93)	0.69 (1.32)	0.65 (1.28)	↓ with age (*P* <0.001)
V_3 †	1.25 (2.67)	1.35 (2.57)	0.90 (1.95)	0.93 (2.11)	↓ with age (*P* <0.001)
V_4 †	1.80 (2.88)	2.29 (3.41)	1.91 (3.35)	1.92 (3.39)	↓ with age (*P* =0.042)
V_5 ‡	1.70 (2.96)	1.85 (3.18)	1.84 (3.18)	1.80 (3.32)	Interaction (*P* =0.045)
V_6 ‡	1.23 (2.16)	1.39 (2.45)	1.43 (2.23)	1.45 (2.29)	Interaction (*P* = 0.022): 5–8 ♂ vs. ♀ (*P* = 0.030), in ♂ ↑ with age (*P* = 0.009)

*Independent sex effect; †independent age effect; ‡interaction; ♂boys; ♀girls; ↓decrease of values/lower values; ↑increase of values/higher values

Table 6. S-wave amplitudes (mV) for boys and girls: median (98th percentile)

Lead	5-8		9-12		Effects direction and *P*
	Boys	**Girls**	**Boys**	**Girls**	
I*	0.21 (0.54)	0.10 (0.42)	0.17 (0.51)	0.15 (0.36)	↑ in ♂ (*P* <0.001)
II‡	0.28 (0.61)	0.11 (0.33)	0.21 (0.68)	0.14 (0.74)	Interaction (*P* = 0.003): 5–8 ♂ vs. ♀ (*P* = 0.002)
III‡	0.17 (0.43)	0.10 (0.26)	0.13 (0.58)	0.14 (1.09)	Interaction (*P* = 0.007)
aVR*	0.70 (1.00)	0.91 (1.43)	0.80 (1.29)	0.87 (1.28)	↑ in ♀ (*P* = 0.006)
aVL*	0.50 (1.09)	0.59 (1.07)	0.49 (1.08)	0.53 (1.01)	↑ in ♀ (*P* = 0.021)
aVF*	0.22 (0.50)	0.11 (0.28)	0.18 (0.59)	0.14 (0.75)	↑ in ♂ (*P* = 0.020)
V_1 ‡	0.68 (1.31)	1.06 (2.18)	0.90 (1.60)	0.92 (1.72)	Interaction (*P* <0.001): 5–8 ♂ vs. ♀ (*P* <0.001), in ♂ ↑ with age (*P* = 0.045)
V_2 ‡	1.52 (2.71)	1.84 (2.61)	1.71 (2.71)	1.59 (2.77)	Interaction (*P* <0.001): 5–8 ♂ vs. ♀ (*P* = 0.032)
V_3 *	1.36 (2.67)	1.03 (2.43)	1.16 (2.41)	0.92 (2.27)	↑ in ♂ (*P* <0.001)
V_4 *	0.78 (1.86)	0.44 (1.62)	0.63 (1.95)	0.46 (1.48)	↑ in ♂ (*P* <0.001)
V_5 ‡	0.41 (0.96)	0.15 (0.50)	0.32 (1.20)	0.22 (0.65)	Interaction (*P* = 0.011): 5–8 ♂ vs. ♀ (*P* <0.001), 9–12 ♂ vs. ♀ (*P* <0.001)
V_6 ‡	0.18 (0.47)	0.05 (0.18)	0.17 (1.13)	0.11 (0.34)	Interaction (*P* = 0.009): 5–8 ♂ vs. ♀ (*P* <0.001), 9–12 ♂ vs. ♀ (*P* = 0.003)

*Independent sex effects; ‡interaction; ♂boys; ♀girls; ↑increase of values/higher values

Table 7. R/S ratio for boys and girls: median (98th percentile)

Lead	5-8		9-12		Effects direction and *P*
	Boys	**Girls**	**Boys**	**Girls**	
V_1†*	0.66 (2.08)	0.43 (1.95)	0.43 (1.59)	0.37(1.67)	↓ with age (*P* <0.001), ↑ in ♂ (*P* = 0.006)
V_2‡	0.68 (2.14)	0.50 (1.52)	0.40 (0.98)	0.45(1.22)	Interaction (*P* = 0.002): 5–8 ♂ vs. ♀ (*P* = 0.017), in ♂ ↓ with age (*P* <0.001)
V_5*	4.23 (12.0)	11.1 (64.7)	5.42 (49.0)	7.39(100.5)	↑ in ♀ (*P* <0.001)
V_6‡	7.18 (69.5)	20.0 (131.0)	8.44 (121.0)	13.5(102.0)	Interaction (*P* = 0.006): 5–8 ♂ vs. ♀ (*P* = 0.007)

*Independent sex effect; †independent age effect; ‡interaction; ♂boys; ♀girls; ↓decrease of values/lower values; ↑increase of values/higher values