Increased augmentation index and central systolic arterial pressure are associated with lower school and motor performance in young adolescents

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Abstract
Objective: In adults, improper arterial function has been linked to cognitive impairment. The pulse wave velocity (PWV), augmentation index (AIx) and other vascular parameters are useful indicators of arterial health. In our study, we monitored arterial properties, body constitution, school success, and motor skills in young adolescents. We hypothesize that reduced cognitive and motor abilities have a vascular origin in children.

Methods: We analysed 81 healthy school children aged 11–16 years. Anthropometry central systolic arterial pressure, body mass index (BMI), standard deviation scores (SDS) BMI, general school performance grade, and eight motor tests were assessed. PWV, AIx, and central systolic arterial pressure (SBPao) were measured.

Results: AIx and SBPao correlated negatively with school performance grades. Extremely high AIx, PWV and SBPao values were observed in 5% of children and these children had average to low school performance. PWV correlated significantly with weight, height, and waist and hip circumference. AIx, PWV, school success, and BMI correlated strongly with certain motor functions.

Conclusions: Increased AIx and SBPao are associated with lower school and motor performance in children. PWV is influenced by the body's constitution.

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Introduction
Childhood obesity is a serious health issue in the developed world. Obesity affects almost all areas of a child’s life. Obese children are less successful in sport and social activities.\textsuperscript{1,2} However, a significant association between obesity and lower academic school performance has not been reported yet.\textsuperscript{3} A clear association between increased arterial stiffness and cognitive decline was found in adults individuals.\textsuperscript{4–6} Executive cognitive functions were more disturbed than memory functions.\textsuperscript{7} A possible pathophysiological mechanism for this cognitive decline may be impaired hemodynamic and microvascular function of the brain caused by atherosclerosis.\textsuperscript{8} An excessive accumulation of fat in visceral and other organs severely disturbs the metabolism, leading to metabolic syndrome and atherosclerosis.\textsuperscript{9,10} However, atherosclerosis can also be found in children and adults with a normal body constitution.\textsuperscript{11,12} Even minimal intima atherosclerotic damage changes the properties of arterial walls. Increased arterial stiffness can be measured by pulse wave velocity (PWV), but the augmentation index (AIx) and SBPao have also been recognised as indicators of arterial health.\textsuperscript{13–14} The aim of our study was to find children with subclinical changes in arterial function, like atherosclerosis, among the healthy school population. We tested whether underlying changes in arterial properties result in lower school and motor performance in children.

Materials and methods
Eighty-one healthy children aged 11–16 years who attended periodic health checks were recruited for our study. Approval was received from the ethical committee and written consent was obtained from the parents. We acquired information about family history and socioeconomic status from a short questionnaire presented to the participants and their parents. History of obesity, hypertension, hyperlipidaemia, diabetes, fatal cardiovascular disease (CVD) or stroke and malignancy in the first and second line of the family were recorded. The level of parent education and the employment status (employed, unemployed, farmer) was also noted. In addition, the number of daily meals and the number of sweet or salty snacks and fast food meals per week were documented. We measured the height, weight, waist and hip circumference (waist, hip) of participants in the morning, while they were in a fasting state and wearing light underwear. Height was measured using a stadiometer (SECA) to the nearest 1 cm. Body mass was recorded to the nearest 0.1 kg using a calibrated balance (SECA). The waist was measured at the narrowest point between the lower costal border and the iliac crest, to the nearest 1 cm. The hip was measured at the trochanteric region with a classic tape. Body mass index (BMI) and standard deviation scores (SDS) BMI were calculated according to the Manchester SDS BMI calculator. Puberty was checked according to the Tanner pubertal score. The time of menarche was recorded in girls. The general school performance grade was provided by the scholars, and the parents or guardians. The general school performance grade is an average of all subject grades obtained in one school year on a scale of 1–5, in which 5 is excellent and 1 is insufficient.
Arterial function assessment

Arterial function was assessed using the Arteriograph (Tensiomed, Budapest, Hungary), which is an easy-to-use, non-invasive occlusive oscillometric device for simultaneous measurement of arterial pressure (AP), AIx, PWV, mean arterial pressure, central systolic arterial pressure (SBPao), and other parameters such as ejection duration. A high fidelity pressure sensor within an upper-arm cuff records very small pressure changes during each cardiac cycle. At the beginning of systole, the blood ejected to the arterial system generates an early (direct) systolic wave (P1). A late systolic pressure wave (P2) is likely a result of rebounded pressure waves. In the case of normal arterial compliance, the direct P1 is higher than the reflected P2. If the arterial wall is stiff, e.g., because of atherosclerosis, a large part of the pressure wave is reflected from the aorta bifurcation and peripheral arteries, resulting in a high amplitude P2. All data received by the Arteriograph are wirelessly transmitted to a personal computer and analysed using the device’s proprietary software. The AIx was calculated from the amplitude of P1 and P2 and pulse pressure (PP) using the following formula: \[ \text{AIx} = \frac{(P2 - P1)}{PP} \times 100\% \]

AIx depends on the peripheral resistance and PWV and gives complex information about arterial wall properties. The PWV provides information about increased arterial stiffness and is less influenced by the peripheral resistance. PWV is automatically calculated from the return time, the time interval between the systolic waves (P1) and (P2), and the distance between the throat Jugulum-symphysis (termin used to describe an even more precise location and is also accepted with specialised literature) and the symphysis.\(^{15,16}\) Calculation of the PWV from the throat jugulum-symphysis distance is not recommended, and the gold standard approach is to measure the carotid-femoral distance.\(^{17}\) The aim of our study was to identify children with altered arterial function from a healthy population, which seems to be more effective when having reference values of investigated parameters. We used the Arteriograph because reference values for PWV, AIx and SBPao were available for our participant age group.\(^{18}\)

Motor skills measurement

SLOFIT is the national program for measuring the body fitness of school children in Slovenia. Every year in April all primary and secondary school children in Slovenia are tested by qualified sports teachers according to the official measurement protocol. The SLOFIT programme includes eight motor tests and three anthropometric measurements. We only used the motor test measurements: arm-plate tapping (APT), which tested the speed of alternate movement, standing long jump (SLJ), which tested explosive strength power, polygon backwards (PB), which tested the coordination of whole body movements, sit-ups (SU), which tested muscular endurance of the torso, standing reach touch (SRT), which tested flexibility, bent arm hang (BAH), which tested muscular endurance of the shoulder girdle and arms, 60-meter run (RUN 60), which tested sprint speed and 600-meter run (RUN 600), which tested general endurance.\(^{19}\)

Statistical analysis

The data were analysed with SPSS Statistics 22.0 software (IBM Inc., Armonk, New York) using the non-parametric Mann-Whitney U-Test and the non-parametric Spearman correlation after Shapiro-Wilk test of normality. A p value of \( \leq 0.05 \) was considered statistically significant.

Results

Characteristics of the total study population are listed in Table 1. Eighty-one children were tested, including 34 girls and 47 boys.
There were no significant differences in age, body weight (weight), waist circumference (waist), diastolic arterial pressure (AP diast), BMI, SDS BMI, AIx, PWV, and SBPao between the sexes. Boys were taller than girls (p < 0.01) and had a higher systolic arterial pressure (AP syst) (p < 0.05). There were no differences in school success and APT between girls and boys, but boys showed significantly better results in all other motor tests. All girls had already reached puberty and 30 (88.2%) had experienced menarche. On the Tanner scale for sexual maturity, 31 (91.3%) females reached grade 4 or 5 for breast development and 32 (94.2%) for pubic hair development. Three males (6.4%) had a Tanner scale of grade 1 (pre-pubertal), 16 (34.0%) were grade 2, 9 (19.2%) were grade 3, and 19 (40.4%) were grade 4.

No significant correlation was found between family burden and CVD, PWV, AIx, SBPao, or between school success and motor tests. Parent education level had a significant positive influence on their child’s school success. The employment status of the parents did not influence their children’s school success, but the children were significantly less successful at school if their father was a farmer. Eating habits, including the consumption of sweet or salty snacks and fast food did not correlate with PWV, AIx, SBPao, or any other parameters investigated. We found a statistically negative correlation of AIx with body height (p < 0.05). PWV correlated positively with body weight

### Table 1. Clinical characteristics of the study population according to sex and the whole group. Data are presented as mean values ± standard deviation. Statistical differences between genders were determined using the Mann-Whitney U-Test. Systolic arterial pressure (AP syst), diastolic arterial pressure (AP diast), augmentation index (AIx), pulse wave velocity (PWV), central systolic blood pressure (SBPao), arm-plate tapping (APT), standing long jump (SLJ), polygon backwards (PB), sit-ups (SU), standing reach touch (SRT), bent arm hang (BAH), 60-meter run (RUN 60) and 600-meter run (RUN 600).

| Parameter             | Total          | Girls          | Boys           | P   |
|-----------------------|----------------|----------------|----------------|-----|
| N                     | 81             | 34             | 47             |     |
| Age (years)           |                |                |                |     |
| Height (cm)           |                |                |                |     |
| Weight (kg)           |                |                |                |     |
| BMI (kg/m²)           |                |                |                |     |
| SDS BMI               |                |                |                |     |
| Waist (cm)            |                |                |                |     |
| AP syst (mmHg)        |                |                |                |     |
| AP diast (mmHg)       |                |                |                |     |
| AIx (%)               |                |                |                |     |
| PWV (m/s)             |                |                |                |     |
| SBPao (mmHg)          |                |                |                |     |
| School (1–5)          |                |                |                |     |
| APT (no. of repetitions) |            |                |                |     |
| SLJ (cm)              |                |                |                |     |
| PB (s)                |                |                |                |     |
| SU (no. of repetitions) |             |                |                |     |
| SRT (cm)              |                |                |                |     |
| BAH (s)               |                |                |                |     |
| RUN 60 (s)            |                |                |                |     |
| RUN 600 (s)           |                |                |                |     |

We found a statistically negative correlation of AIx with body height (p < 0.05). PWV correlated positively with body weight.
There was no correlation between body weight, BMI, SDS BMI, or waist circumference and school success.

Regarding arterial properties in connection with cognitive function, AIx (p < 0.05) and SBPao (p < 0.05) were negatively associated with school success. AIx was significantly associated with school success in boys (p < 0.05), but not in girls. In girls, SBPao associated significantly with school success (p < 0.05), while PWV did not affect school success. Results are listed in Table 2.

Motor performance was related to AIx, PWV, and school success. School success correlated significantly with APT (p < 0.05) and the SRT (p < 0.01). A negative correlation was found between school success and the time taken to complete the PB (p < 0.01). PWV correlated negatively with the length of SLJ (p < 0.05) and correlated positively with the 600 m run (p < 0.05). AIx correlated negatively with APT (p < 0.01). A strong correlation was found between BMI and all motor tests, except APT and the SRT. Results are presented in Table 3.

### Discussion

The most important discovery of our study was the negative correlation between AIx and SBPao and school performance grades. Less successful children have higher AIx and SBPao than children with excellent grades. Vascular cognitive impairment has been the

| Variable | APT | SLJ | PB | SU | SRT | BAH | RUN 60 | RUN 600 |
|----------|-----|-----|----|----|-----|-----|--------|---------|
| AIx (%)  | 0.333 | -0.138 | 0.155 | -0.180 | -0.147 | -0.079 | 0.208 | 0.172 |
| PWV (m/s) | 0.004 | 0.247 | 0.200 | 0.135 | 0.217 | 0.513 | 0.094 | 0.167 |
| School   | 0.264 | 0.210 | -0.326 | 0.180 | 0.397 | 0.013 | -0.110 | -0.081 |
| BMI      | -0.206 | -0.465 | 0.360 | -0.246 | -0.089 | -0.516 | 0.504 | 0.544 |

**Table 2.** Correlation coefficient (CC) and p values for correlations of school success and arterial properties, augmentation index (AIx), pulse wave velocity (PWV), central systolic arterial pressure (SBPao) for the total population and separated by sex. Correlations were determined using the non-parametric Spearman test.

| Variable | n | CC | p  | n | CC | P  | n | CC | p  |
|----------|---|----|----|---|----|----|---|----|----|
| AIx (%)  | 80 | -0.275 | 0.014 | 34 | -0.222 | 0.208 | 46 | -0.310 | 0.038 |
| PWV (m/s) | 80 | 0.022 | 0.844 | 34 | -0.247 | 0.159 | 46 | 0.222 | 0.144 |
| SBPao (mm/Hg) | 80 | -0.248 | 0.027 | 34 | -0.395 | 0.021 | 46 | -0.114 | 0.454 |

**Table 3.** Correlation coefficient (CC) and p values for correlations of augmentation index (AIx), pulse wave velocity (PWV), school success (School) and body mass index (BMI) to SLOFIT motor tests. Arm-plate tapping (APT), standing long jump (SLJ), polygon backwards (PB), sit-ups (SU), standing reach touch (SRT), bent arm hang (BAH), 60-meter run (RUN 60), 600-meter run (RUN 600). Statistical differences were determined using the non-parametric Spearman test.
subject of intensive research in adults.\textsuperscript{4–7,20} The aetiology of vascular cognitive impairment is multifactorial. Structural pathology and hemodynamic abnormalities, like cerebral hypoperfusion and impaired cerebral vasomotor reactivity, are the main causes of cognitive decline in patients with atherosclerosis or other vascular diseases.\textsuperscript{8}

Childhood obesity and metabolic syndrome are epidemic in modern society. There is a serious threat that the current generation of children will die before their parents.\textsuperscript{21} Increased arterial wall thickness\textsuperscript{22} and increased PWV\textsuperscript{23} have been reported in obese children, but increased arterial stiffness and cognitive function has not been reported in healthy young populations. Our results show that altered arterial properties affect academic achievement in children. In addition to the effects of AIX and SBPao on school success, we found high PWV, AIX, and SBPao values in 5% of our study population. This group of children had average to low academic attainment. Based on our findings, we conclude that the vascular origin of cognitive deficits can be diagnosed early in childhood. This may represent an important contribution to the improvement of health and educational care in children. The early prethrombotic stages of atherosclerosis can be completely reversed.\textsuperscript{10} Early diagnosis followed by effective prevention and treatment may improve cognitive function and prevent fatal CVD later in life. In adults with carotid atherosclerosis, cognitive execution but not memory function was impaired.\textsuperscript{7} Unfortunately, we did not obtain the grades from specific subjects and did not test specific cognitive functions, therefore we cannot comment whether this is true in children. Nonetheless, the correlations of school success, AIX, and PWV with SLOFIT motor tests in the present study were very interesting. Children with higher school grades tend to have a more flexible body and better coordination of the hands and entire body. Children with high AIX were not as successful at school and had slower alternating movement of the hands. In addition, children with high PWV values had lower explosive strength and general endurance. Based on our results, we conclude that subclinical vascular changes can affect some motor functions in children. Arm-plate tapping may be a useful test in screening for early vascular abnormalities leading to cognitive impairment, especially because it is not influenced by obesity.\textsuperscript{19}

Even though there is strong evidence that obesity and metabolic syndrome lead to structural brain damage,\textsuperscript{24} most epidemiologic studies have not found a direct connection between obesity and school performance.\textsuperscript{3} School performance was not correlated to BMI or other body measures in our study. Although obesity increases the risk of atherosclerosis and metabolic syndrome, 10%–20% of extremely obese people never progress to CVD, while people with normal or even low body weight can die of stroke or other fatal CVD.\textsuperscript{10,11}

Measurement of arterial function is a much more effective than anthropometry at uncovering early atherosclerotic changes and their consequences, such as cognitive deficits.\textsuperscript{13,14} Women have a higher risk for CVD than men.\textsuperscript{25} Increased arterial stiffness was found in pre-pubertal girls and post-menopausal women compared with men of the same age.\textsuperscript{26,27} There are some signs of sex-based differences in academic performance and CVD or stroke risk, with a stronger association in females.\textsuperscript{28,29} In our study, no gender differences were observed in general school performance, but the strong association between AIX and school success was only found in boys. On the other hand, SBPao was only related to school success in girls. Detailed analyses showed that all the females had already reached puberty. Female sex hormones have a strong influence on vascular compliance, which is significantly higher in post-pubertal than pre-pubertal girls.\textsuperscript{36} This means that discovering of altered arterial
properties are more effective in pre-pubertal or post-menopausal women. SBPao appears to be a more sensitive parameter than AIx for identifying arterial pathologies in women who have already reached menarche.

PWV was not correlated to school success; smoothed percentile curves showed a slight increase (about 1 m/s) between 3–18 years of age. In our study, PWV correlated significantly with body height, weight, waist, and hip measurements. The interpretation of PWV as a sign of vascular pathology in children is probably more complex. The body’s constitution appears to affect PWV values. However, the extremely high AIx, PWV, and SBPao values we found in 5% of our study population indicates a vascular pathology that should be investigated further.

Conclusions

Our study has shown that altered arterial properties may cause cognitive and motor impairment in young adolescents and that PWV is influenced by body constitution.

Strengths and limitations

The present study investigated general school performance and no other specific cognitive measures. Insight into grades for different subjects would give us a better insight into specific cognitive deficits.

For the interpretation of increased arterial stiffness, the pre-pubertal period in girls would be a better choice. Unfortunately, school success is evaluated with grades from the age of 8–10 years in Slovenia. In healthy girls, puberty normally starts around 8–12 years of age, therefore it was impossible to check school success in pre-pubertal scholars.

The PWV in our study did not correlate with school success, although values far above the published average were found in 5% of children with average to low school performance. PWV measured with the Arteriograph measures stiffness of the brachial artery and not the aorta. Calculating the PWV from the carotid–femoral distance may have given different results.

Declaration of Conflicting Interests

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