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## MEMORY DEFICITS AMONG CHILDREN AND ADOLESCENTS WITH PAROXYSMAL CARDIAC ARRHYTHMIA

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### SUMMARY

#### Background:

The aim of this study was to assess memory functioning among children and adolescents with atrial-ventricular nodal re-entry tachycardia (AVNRT) and atrial-ventricular re-entry tachycardia (AVRT).

#### Material/ Methods:

A total of 113 pediatric cardiology clinic patients (62 F, 51 M), aged 9–18 years, who were scheduled for radiofrequency ablation due to AVRT or AVNRT underwent neuropsychological examination. Patients who had suffered a cardiac arrest, or had a congenital heart defect, neurological disorders or other diseases affecting cognitive or emotional development were excluded from the study. The control group consisted of 41 patients diagnosed at the same clinic who did not show any significant cardiovascular or nervous system disorders. Standardized tests were used to measure verbal and visual memory and visuo-spatial functions (Auditory-Verbal Learning Test, Benton Visual Retention Test and Rey's Complex Figure Test).

#### Results:

Cognitive disorders were found significantly more frequently in the study group (47.8%) than in the control group (22%;  $\chi^2=8.30$ ,  $p=0.004$ ). An early age at the onset of attacks, especially under the age of six, was an important factor that negatively affected cognitive functioning ( $\chi^2=3.87$ ,  $p=0.04$ ).

#### Conclusions:

AVNRT and AVRT in childhood have adverse effects on cognitive and emotional development.

**Key words:** memory disorders, AVNRT, AVRT

## **INTRODUCTION**

In adolescence, atrial-ventricular re-entry tachycardia (AVRT) and atrial-ventricular nodal re-entry tachycardia (AVNRT) are the most common forms of cardiac arrhythmia. AVRT is connected with Wolff-Parkinson-White Syndrome (WPW) and results from the presence of an accessory connection between the top atria and the bottom ventricles. AVNRT occurs when the reentry circuit forms within or just next to atrioventricular node; the circuit involves two anatomical pathways, which are both in the right atrium. The symptoms are due to loss of atrioventricular synchrony and rapid or irregular ventricular rates. The most frequent symptoms include palpitations, fatigue, and also dizziness, fainting and syncope, indicating hypoxia of the central nervous system. As far as AVRT is concerned, there is a serious risk of the transition of arrhythmia into ventricular tachycardia and sudden cardiac death.

In some children, symptoms occur in the first days or weeks, and in others they appear later in life, often in their twenties (Porter, Morton, Denman et al. 2004; Tortoriello, Snyder, O'Brian et al. 2003). Tachycardia in children and adolescents is characterized by a faster rate compared to adults, but is relatively well tolerated, which delays examination, correct diagnosis and treatment (van Hare, 2008).

There is no research on the cognitive functioning of children and adolescents with paroxysmal arrhythmia. The present study was inspired by interviews with patients and their families, during which they indicated learning difficulties. Patients complained of subjective memory problems, and their educational attainment was unsatisfactory. The question arose whether paroxysmal tachycardia, which may involve temporary hypoxia of the central nervous system, disorganizes the everyday life of children and adolescents or affects their cognitive development. Among the consequences of prolonged hypoxia is often memory impairment (Caine & Watson, 2000; Garcia-Molina, Roig-Rovira, Enseñat-Cantallops et al. 2006; Peskine, Rosso & Picq, 2010), but there has been no research on the effects of short-term, recurrent hypoxia.

The aim of our study was thus to assess chosen cognitive functions neuropsychologically, particularly memory, in children and adolescents with tachycardia attacks. In this study, we focused on those aspects of memory which most strongly affect academic performance: word memory, verbal learning, and visuospatial memory.

## **MATERIAL AND METHODS**

The study group consisted of 113 pediatric cardiology patients (62 girls and 51 boys), within the age bracket of 9–18, who were scheduled for radiofrequency ablation due to symptomatic AVNRT or AVRT arrhythmia. Patients with congenital heart defects, born prematurely, with neurological or other diseases that may have affected cognitive development, and those who had suffered a cardiac arrest were excluded from the study.

The control group consisted of 41 patients hospitalized at the same clinic who were being examined in relation to the suspicion of Marfan syndrome or in connection with the presence of palpitations or faintness, who did not show any symptoms of cardiovascular or neurological diseases. During hospitalization in the Cardiac Clinic, the patients and their carers were asked to give their permission for the participation of the child in neuropsychological research. Those patients who gave their permission were examined by a neuropsychologist. Both groups were examined under similar conditions by the same persons. Table 1 presents the demographic data from the two groups.

In the study group, 50 patients suffered from AVNRT (44%) and 63 (56%) from AVRT. Young female patients were equally affected by both forms of tachycardia, which each affected 31 females (50%), while AVRT was more prevalent in young males - in 32 patients, i.e. 62.7% (the difference did not reach statistical significance:  $\text{Chi}^2=1.84$ ,  $p=0.17$ ). The relationship between gender and the type of tachycardia was similar to that of other studies (Porter, Morton, Denman et al. 2004; Liu, Yuan, Hertervig, Kongstad & Olsson, 2001).

The age at which the first symptoms occurred varied among individual patients. In 11% of patients the first tachycardia attacks occurred in infancy, while half of the patients experienced symptoms after the age of 10. In the study group there was a relationship between gender and tachycardia at young ages – in the first year of life tachycardia affected 18% of young males and only 5% of young females ( $\text{Chi}^2=3.78$ ;  $p=0.05$ ), but by the end of the sixth year of life attacks affected as many as 40% of males and 16% of females ( $\text{Chi}^2=6.85$ ;  $p=0.009$ ). However, with the onset of adolescence, cases of tachycardia in females start to outnumber those in males. This reflects the fact that AVNRT is more frequent in young females, and that in this type of arrhythmia attacks occur later than in patients with AVRT. The average age of onset of AVRT is 8, while that for AVNRT is 11 ( $t=3.42$ ;  $p=0.0008$ ). In 15.9% of patients suffering from AVRT, attacks occurred in infancy, and in 41.3% they occurred up to the age of six (2.0% and 12.0% in AVNRT respectively,  $\text{Chi}^2=6.10$ ,  $p=0.01$  and  $\text{Chi}^2=11.76$ ,  $p=0.0006$ ).

The frequency of occurrence of arrhythmia attacks in the study group also varied among individual patients. In 31% of patients arrhythmia attacks occurred once or twice a year, in 46.4% they were more frequent – from a few to a dozen

Table 1. Comparison of the study and control group

	Examined group	Control group	p
<b>Sex</b> Girls Boys	62 (55 %) 51 (45 %)	22 (54 %) 19 (46 %)	0.89*
<b>Mean age</b>	15.2	15.3	0.79^

\* - Chi2 test; ^ - Student's t-test.

or so a year (22.6% experienced recurrent attacks several times a month). The patients who suffered from AVRNT arrhythmia experienced attacks more frequently than patients with AVRT ( $\text{Chi}^2=4.59$ ;  $p=0.20$ ). However, the patients with AVRT had to be hospitalized more often in order to restore sinus rhythm.

In one third of patients (31.7%) arrhythmia episodes were accompanied by fainting – more frequently in patients with AVRT (37.5%) than in patients with AVNRT (24.0%) ( $\text{Chi}^2=1.96$ ,  $p=0.16$ ).

Standardized neuropsychological tests were used to identify deficits in memory functioning: the Auditory–Verbal Learning Test (AVLT), the Benton Visual Retention Test (BVRT), the Rey's Complex Figure Test (RCFT copy trail and memory trail) and the Digit Span .

The results of the individual patients were compared with population norms for the appropriate age.

The comparison of results with norms allows the actual occurrence of possible deficits in the studied functions to be assessed. A critical result indicating the possibility of a disorder was defined for each test:

- for the AVLT and Digit Span this was a scale score of  $\leq 7$ ;
- for RCFT a result of 1, which is found in 10% of the lowest results in the normative population;
- for BVRT two indicators were adopted: the number of correct reconstructions (at least three less) and the number of errors (at least three more) compared to the results expected for the given age.

Patients who obtained a result indicating deficits in the examined functions in at least two tests, in accordance with their rules of interpretation listed above, were diagnosed as having memory disorders.

Statistical analysis was performed using the STATISTICA program. Individual relationships were determined using the appropriate nonparametric (Mann Whitney's U,  $\text{Chi}^2$ ) and parametric (Student's t) statistical tests.

## **RESULTS**

Table 2 shows the results obtained in individual tests by the patients in the study group and the control group.

In almost every test the average result was lower in the study group than in the controls; however, the differences did not reach statistical significance.

It should be noted that the group of arrhythmia patients obtained results indicating a significant decrease in the efficiency of a given function in all tasks (Fig.1).

As a result, many more respondents from the study group were eligible for a clinical examination for memory disorders, i.e. obtained an abnormal result in at least two tests. In the study group, 47.8% of patients were diagnosed as having disorders, while in the control group only 22% received this diagnosis ( $\text{Chi}^2=8.30$ ,  $p=0.004$ ).

Table 2. Results of neuropsychological tests

	AVNRT/AVRT Mean	Control group Mean	p
AVLT	8.14	9.0	0.33*
Digit Span	10.07	10.61	0.29*
BVRT - correct	-0.7	-0.7	0.99^
BVRT – errors	1.04	0.87	0.68^
RCFT - copy	3.05	3.21	0.42*
RCFT - memory	2.10	2.69	0.005*

\* U Mann – Whitney test ; ^ t-Student test

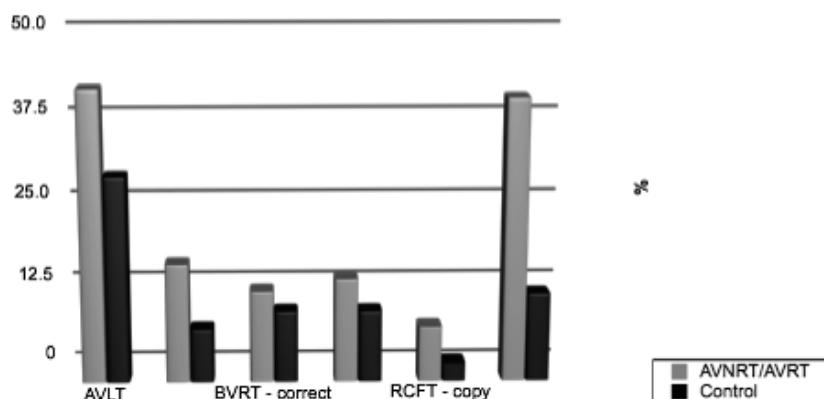


Fig. 1. Percentage of results indicating deficits.

The age at the first arrhythmia attack was related to memory deficits: the average age at which the first symptoms occurred was significantly lower in the group with disorders than in the group without disorders (8.3 years and 10.2 years, respectively; Student's  $t=2.15$ ,  $p=0.03$ ). Patients who experienced their first symptoms before the age of six were more often diagnosed with disorders (62%) than those who were affected by arrhythmia later in life (42%) ( $\chi^2=3.87$ ,  $p=0.04$ ).

## DISCUSSION

The research we carried out shows that children and adolescents with paroxysmal AVNRT and AVRT are at risk for significant deficits in memory functioning. There have been no other studies on cognitive functioning in children and adolescents with paroxysmal tachycardia. The focus has been on adults with heart failure and atrial fibrillation. In such patients cognitive deficits were primarily related to complications in the cerebral circulation and strokes of various extent (Vogels, Scheltens, Schroeder-Tanka & Weinstein, 2007; Pullicino, Wadley, Mc-

Clure et al. 2008; Gillian, Mead & Keir, 2001; Jozwiak, Guzik, Mathew, Wykretowicz & Wysocki, 2006; Wozakowska-Kaplon, Opolski & Kosior, 2009). Patients in adolescence have been analyzed from the perspective of congenital heart defects and the results of cardiac arrest. Examination confirmed the risk of serious dysfunctions in cognitive development (Hovels-Gurich, Seghaye, Schnitker et al. 2002; Uzark, Lincoln, Lamberti et al. 1998; Karl, Hall, Ford, et al. 2004; Maryniak, Bielwaska, Walczak et al. 2008). However, it appears that paroxysmal tachycardia in children may be an important risk factor for the development of memory deficits, especially when symptoms appear in the first years of life.

The mechanisms that lead to the development of memory disorders in this group remain unknown. Various coexisting factors may influence cognitive functioning in children and adolescents with cardiac arrhythmia. The impact of hypoxia accompanying tachycardia attacks should be taken into consideration – the immature brain is susceptible to damage caused even by short-term hypoxia. The hippocampus, which plays a crucial role in memory processes, is particularly sensitive (Anderson, Northam, Hendy & Wrennall, 2001; Jennett, 1998; Allen, Tranel, Bruss & Damasio, 2006).

The central autonomic network concept points to anatomical and functional links between areas (cingulate cortex) associated on the one hand with regulation and perceived heart rhythm, and on the other hand with regulating complex behavior. (Benarroch, 1993; Vogt, 2009; Critchley, Mathias, Josephs et al. 2003; Matthews, Paulus, Simmons, Nelesen & Dimsdale, 2004). Maybe the incoherence stimulus appearing during paroxysmal tachycardia attacks (fast irregular rhythm not caused by exertion or emotion) have an improper affect on the development of the central regulation of cognitive processes.

In some cases arrhythmia and cognitive deficits could be symptoms of the same syndrome. Laloni (2009) describes four patients with electrocardiographic features of WPW syndrome, neurocognitive deficits and dysmorphic features, who were found to have various chromosomal deletions (Laloni, Thakuria, Cox et al. 2009).

Tachycardia attacks in the first years of a child's life can lead to a reduction in its activity, both physical and exploratory, which can also have a negative influence on cognitive development.

To our knowledge, this study is the first to analyze cognitive functioning in children and adolescents with AVRT and AVNRT.

## **CONCLUSIONS**

1. AVNRT and AVRT in childhood have adverse effects on cognitive and emotional development.
2. Further research should be carried out in order to confirm our findings, explain the mechanisms of the observed disorders and assess whether effective treatment of causes of arrhythmia can improve cognitive functioning in patients with existing cognitive deficits and whether, if applied early enough, such treatment could reduce the risk of their development.

## REFERENCES

- Allen, J.S., Tranel, D., Bruss, J. & Damasio, H. (2006). Correlations between regional brain volumes and memory performance in hypoxia. *Journal of Clinical & Experimental Neuropsychology*, 28, 457-76.
- Anderson, V., Northam, E., Hendy, J. & Wrennall, J. (2001). *Developmental Neuropsychology. A Clinical Approach*. Hove: Psychology Press.
- Benarroch, E.E. (1993). The central autonomic network – functional organization, dysfunction, and perspective. *Mayo Clinic Proceedings*, 68, 988-1001.
- Caine, D. & Watson, J.D.G. (2000). Neuropsychological and neuropathological sequelae of cerebral hypoxia: A critical review. *Journal of the International Neuropsychological Society*, 6, 86-99.
- Critchley, H.D., Mathias, C.J., Josephs, O., O'Doherty, J., Zanini, S. & Bonnie-Kate, D. (2003). Human cingulate cortex and autonomic control: converging neuroimaging and clinical evidence. *Brain*, 126, 2139-52.
- Garcia-Molina, A., Roig-Rovira, T., Enseñat-Cantallopis, A., Sanchez-Carrion, R., Pico-Azana, N., Bernabeu, M. & Tormos, J.M. (2006). Neuropsychological profile of persons with anoxic brain injury: differences regarding the physiopathological mechanism. *Brain Injury*, 20, 1139-45.
- Gillian, E., Mead, G.E. & Keir, S. (2001). Association between cognitive impairment and atrial fibrillation: a systematic review. *Journal of Stroke and Cerebrovascular Diseases*, 10, 35-43.
- Hovels-Gurich, H.H., Seghaye, M.C., Schnitker, R., Wiesner, M., Huber, W., Minkenberg, R., Kotlarek, F., Messmer, B.J. & von Bernuth, G. (2002). Long-term neurodevelopment outcomes in school-aged children after neonatal arterial switch operation. *Journal of Thoracic & Cardiovascular Surgery*, 124, 448-58.
- Jennett, B. (1998). Epidemiology, causes and prognosis of the vegetative state. Proceedings from the European Conference on Brain Injury Rehabilitation – Children and Adults. Copenhagen.
- Jozwiak, A., Guzik, P., Matheu, A., Wykretowicz, A. & Wysocki, H. (2006). Association of atrial fibrillation and focal neurologic deficits with impaired cognitive function in hospitalized patients >65 years of age. *American Journal of Cardiology*, 98, 1238–1241.
- Karl, T.R., Hall, S., Ford, G., Kelly, E.A., Brizard, C.P., Mee, R.B., Wientraub, R.G., Cochrane, A.D. & Glidden, D. (2004). Arterial switch with full-flow cardiopulmonary bypass and limited arrest: neurodevelopment outcome. *Journal of Thoracic and Cardiovascular Surgery*, 127, 213-22.
- Lalani, S.R., Thakuria, J.V., Cox, G.F., Wang, X., Bi, W., Bray, M.S., Shaw, C., Cheung, S.W., Chinault, A.C., Boggs, B.A., Ou, Z., Brundage, E.K., Lupski, J.R., Gentile, J., Waisbren, S., Pursley, A., Ma, L., Khajavi, M., Zapata, G., Friedman, R., Kim, J.J., Towbin, J.A., Stankiewicz, P., Schnittger, S., Hansmann, I., Ai, T., Sood, S., Wehrens, X.H., Martin, J.F., Belmont, J.W. & Potocki, L. (2009). 20p12.3 microdeletion predisposes to Wolff-Parkinson-White syndrome with variable neurocognitive deficits. *Journal of Medical Genetics*, 46, 168-175.
- Liu, S., Yuan, S., Hertervig, E., Kongstad, O. & Olsson, S.B. (2001). Gender and atrioventricular conduction properties of patients with symptomatic atrioventricular nodal reentrant tachycardia and Wolff-Parkinson-White syndrome. *Journal of Electrocardiology*, 34, 295-301.
- Maryniak, A., Bielawska, A., Walczak, F., Szymowski, L., Bieganowska, K., Rękawek, J., Paszke, M., Szymaniak E. & Knecht, M. (2008). Long-term cognitive outcome in teenage survivors of arrhythmic cardiac arrest. *Resuscitation*, 77, 46-50.
- Matthews, S.C., Paulus, M.P., Simmons, A.N., Nelesen, R.A. & Dimsdale, J.E. (2004). Functional subdivisions within anterior cingulate cortex and their relationship to autonomic nervous system function. *Neuroimage*, 22, 1151-56.
- Peskine, A., Rosso, C., Picq, C., Caron, E. & Pradat-Diehl, P. (2010). Neurological sequelae after cerebral hypoxia. *Brain Injury*, 24, 755-61.
- Porter, M.J., Morton, J.B., Denman, R., Lin, A.C., Tierney, S., Santucci, P.A., Cai, J.J., Madsen, N. & Wilber, D.J. (2004). Influence of age and gender on the mechanism of supraventricular tachycardia. *Heart Rhythm*, 4, 393-396.
- Pullicino, P.M., Wadley, V.G., McClure, L.A., Safford, M.M., Lazar, R.M., Klapholz, M., Ahmed, A., Howard, V.J. & Howard, G. (2008). Factors contributing to global cognitive impairment in heart failure: results from a population-based cohort. *Journal of Cardiac Failure*, 14, 290-295.

- Tortoriello, T.A., Snyder, C.S., O'Brian Smith, E., Fenrich, A.L., Friedman, R.A. & Kertesz, N.J. (2003). Frequency of recurrence among infants with supraventricular tachycardia and comparison of recurrence rates among those with and without preexcitation and among those with and without response to digoxin and/or propranolol therapy. *American Journal of Cardiology*, 92, 1045-1049.
- Uzark, K., Lincoln, A., Lamberti, J.J., Mainwarning, R.D., Spicer, R.L. & Moore, J.W. (1998). Neuropsychological outcomes in children with Fontan repair of functional single ventricle. *Pediatrics*, 101, 630-633.
- van Hare, G.F. (2008). Developmental aspects of atrioventricular node reentry tachycardia. *Journal of Electrocardiology*, 41, 480-482.
- Vogels, R.L., Scheltens, P., Schroeder-Tanka, J.M. & Weinstein, H.C. (2007). Cognitive impairment in heart failure: A systematic review of the literature. *European Journal of Heart Failure*, 9, 440-449.
- Vogt, B.A. (2009). Regions and subregions of the cingulate cortex. In: B.A.Vogt (ed.), *Cingulate neurobiology and disease* (pp. 3-30). Oxford & New York: Oxford University Press.
- Wozakowska-Kaplon, B., Opolski, G., Kosior, D., Jaskulska-Niedziela, E., Maroszynska-Dmoch, E. & Włosowicz, M. (2009). Cognitive disorders in elderly patients with permanent atrial fibrillation. *Kardiologia Polska*, 67, 487-93.

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