**ABSTRACT:** I a а a а a a a . Ba a a (HRV) Н ECGa (ADHD) а a а a a a 1997. M  $: W \ a \ a$ HRV a a SDNN, MSSD a NN50 a а a 24 Н **ECG** 10.8 a ) ADHD( a а a a а (MPH). . R : C ADHDа а а a a а a **MPH** NN50 a RMSSD. NN50 a RMSSD a a a а а а

#### INTRODUCTION

Why are psychiatric disorders in children becoming more and more common? This question haunts us pediatricians as well as many teachers not forgetting the affected parents.

Epidemiologic data, such as the number of admitted children and adolescents with psychiatric disorders as reported by the Statistics Center of Baden Wuerttemberg, Germany or the prescriptions of the psycho-active drug Methylphenidate (MPH) through the public health system show that this is not a subjective impression (Figure 1). A

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of the HRV using the 24-hour ECG allows an interpretation of circadian changes of the autonomous nervous system, as opposed to the short-time measurement of HRV. pNN50 is defined as the percentage of consecutive NN-intervals which differ by more than 50 ms. The parameter SDNN indicates the standard deviation of all NN-intervals within a measured period. It is infuenced by both the sympathetic and the parasympathetic nervous system.

## INITIAL RESULTS OF A PILOT STUDY ON CHIL-DREN WITH ADHD

Children receiving methylphenidate (MPH) for ADHD are seen by pediatric cardiologists on a routine basis due to the potential risk of cardiac dysrhythmia. Since 2005, I added 24 hour ECG to the normal apparative diagnostics consisting of ECG, measurement of blood pressure and echocardiography. The systematic analysis of the heart rate variability of 12 patients before MPH therapy and 19 patients of the same age group under MPH treatment revealed in 2010 surprising unequivocal results 7: Compared to healthy control patients, children with ADHD with or without methyphenidate treatment have a higher mean heart rate (85  $\pm$  2/min versus 94  $\pm$  2 /min, p=0.0051 and 90  $\pm$  1 /min, p=0.035), a lower pNN50 value  $(10.3 \pm 1.0 \text{ versus } 3.4 \pm 0.3, p=<0.0001 \text{ and } 6.8 \pm 0.7, p=0.008)$ likewise the RMSSD value (44  $\pm$  2 versus 26  $\pm$  1, p=<0.0001 and  $37 \pm 2$ , p=0.008). The circadian analysis of the HRV showed an extensive reduction of nightly vagal activity measured as sNN50 in children with ADHD prior to MPH therapy (Figure 2). These results, if confrmed by prospective studies, are of major clinical and pathophysiological significance. They show that the HRV analysis in 24-hour ECG can be used as an objective bio marker for ADHD. Moreover, it may serve to monitor methylphenidate therapy.

Singer, McCraty et al., 1998) have a significantly higher risk of sudden cardiac death. The rMSSD values among children with ADHD in our study, due to the missing increase of the rMSSD, lie just slightly above this risk zone. It is below the value of 15 ms in a few children in our study. It should therefore be noted that children with ADHD seems to have an increased baseline risk of sudden cardiac death. This risk was attributed in the study on this topic by Gould (Gould, Walsh, Munfakh et al., 2009) to the therapy with methyphenidate.

This statement is nevertheless based on mere pathophysiological speculations which refer to widely accepted theories on how the autonomous nervous system relates to sudden cardiac death (Vaseghi & Shivkumar, 2008).

## COMPARISON OF HEART RATE VARIABILITY BE-TWEEN TWO GENERATIONS

On comparing the norm values of heart rate variability in childhood from the years 1995-1997 as collected by Massin (Massin & von Bernuth, 1997) with our values from the years 2010 – 2012 (De Bock, Jarczok, Hoffmann et al., 2013), it is remarkable that only the global HRV parameter SDNN lies within the normal distribution (Figure 4). In our control group it is however noticeable that

rMSSD values lie in the lower part of normal distribution. Should this trend be confrmed by a larger study, then it has come, within the last decade, to a general decrease of vagal activity in childhood years. If this loss of physiological, pre-pubertal vagal activity will - within the meaning of the polyvagal theory according to Porges - have consequences on the social and emotional development of the children this correlation may not just be coincidental but possibly causal.

# INTERNATIONAL COMPARISON OF HEART RATE VARIABILITY IN HEALTHY CHILDREN

There are a large number of publications with HRV data from healthy control groups from all over the world. Collecting some of these data as illustrated in fgure 4 we found a reduced vagus activity indicated by the rMSSD values in children from United States in 1998 (Umetani, Singer, McCraty et al., 1998) and 2010 (Zulfqar, Jurivich, Gao et al., 2010) and from Turkey published in 2004 (Unalacak, Aydin, Ermis et al., 2004), 2009 (Tascilar, Yokusoglu, Dundaroz et al., 2009) and 2011 (Akcaboy M, Atalay S, Ucar et al., 2011). Higher values as published from Germany 1997 (Massin & von Bernuth., 1997) were measured in Great Britain in 2011 (Birch, Duncan, & Franklin, 2012), France 1999 (Butera, Bonnet, Iserin et al., 1999) and China 2012 (Ma, Wang, Fu et al., 2011). The data from Italy published in 2001(Silvetti, Drago, & Ragonese, 2001) showed very high values in children with an age between four and twelve years. All these studies showed a comparable global heart rate variability indicated by SDNN.

### **FUTURE RESEARCH**

The attempt to explain fundamental changes in pediatric mental health with dysfunction of the autonomous nervous system is a bold hypothesis considering also that practical consequences are currently still unknown. Nevertheless, the chosen methodological approach offers the unique opport actqus t`ìì

- rate: relations to age and gender over nine decades. *Journal of the American College of Cardiology*, 31, 593-601.
- Unalacak, M., Aydin, M., Ermis, B., Ozeren, A., Sogut, A., Demirel, F., et al. (2004). Assessment of cardiac autonomic regulation in children with monosymptomatic nocturnal enuresis by analysis of heart rate variability. *The Tohoku Journal of Experimental Medicine*, 204, 63-9.
- Vaseghi, M., & Shivkumar, K. (2008). The role of the autonomic nervous system in sudden cardiac death. *Progress in Cardiovascular Diseases*, 50, 404-19.
- Zulfqar, U., Jurivich, D. A., Gao, W., & Singer, D. H. (2010). Relation of high heart rate variability to healthy longevity. *American Journal of Cardiology*, 105, 1181-5.