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Cardiac complexity and emotional dysregulation in children☆

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ABSTRACT

Objective: Sample entropy (SampEn) gives an estimate of signal complexity in cardiac time series and can give information beyond linear heart rate variability. Lower cardiac SampEn is associated with psychopathology in adults. Emotional dysregulation is widely present in adult psychopathology and a forerunner to later mental problems in children. Therefore, this study investigated whether SampEn relates to emotional dysregulation in children.
Methods: Participants were 32 children between 9 and 13 years with internalizing difficulties and 25 controls. Parents filled out the "Emotional Problems" subscale in the Strengths and Difficulties questionnaire and the "Lability/Negativity" scale in the Emotion Regulation Checklist. SampEn, root mean square of successive differences (RMSSD), normalized power of high frequency (HFnu) components of the cardiac signal and pre-ejection period (PEP) were computed at rest. The study investigated the predictive power of SampEn, RMSSD and HFnu on the measures of emotional dysregulation. It also tested whether RMSSD or PEP were related to SampEn.
Results: SampEn was a significant predictor of both measures of emotional dysregulation, while RMSSD and HFnu were not. RMSSD and PEP were both significant predictors of SampEn.
Conclusions: SampEn is a potential marker of dysregulation in the underlying neurovisceral processes vital for emotion regulation, and an important complementary measure to linear cardiac indices, explaining more of the variance in emotional dysregulation than RMSSD and HFnu in this study. Lower SampEn can also be linked to both higher vagal and sympathetic activation via RMSSD and PEP.

1. Introduction

Psychophysiological data can provide important complementary information about underlying processes important to mental health and guide research and treatment of mental illness. So far, much of research has focused on linear models of variability, but non-linear dynamical models can give further insight into underlying processes involved in pathology (Bystritsky et al., 2012; Glass and Mackey, 1988). This study investigates a non-linear cardiac measure, Sample Entropy (SampEn) (Richman and Moorman, 2000), alongside two linear measures of vagal cardiac influence, the root mean square of the successive differences (RMSSD) and High-Frequency Heart Rate Variability (HF-HRV) as predictors of emotional dysregulation, measured by the Emotional Problems (Goodman, 1997) and Lability/Negativity (Shields and Cicchetti, 1997b) scales.

Emotion regulation is a fundamental process important to adaptive functioning (Campos et al., 2004), and a failure to regulate emotion or affect is present in a significant portion of mental disorders (Jazaieri et al., 2013) and is also a risk factor for later mental difficulties (Berking and Wupperman, 2012). Emotion regulation is the ability to flexibly modulate the emotional response in concordance with relevant context information and situational demands through behavioral, mental and physiological processes (Gross, 1998), and is an omnipresent part of the emotional response (Campos et al., 2011). Thus, emotion regulation is dependent on the successful integration of cognitive, emotional, behavioral and contextual factors in flexible interaction with others and the environment.

The Neurovisceral Integration Model (Thayer and Lane, 2009) argues that this integration can be modeled in a dynamical systems framework, where successful regulation is dependent on a dynamical

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balance between negative and positive feedback loops within the neurocardiac system. Dynamical systems approaches are grounded in mathematical models of the evolution of a system over time in a state-space. Values that the system tend to evolve towards given a wide set of different starting conditions are attractors, while the regions of values around attractors are basins of attraction (see for instance Beer, 2000; Globus and Arpaia, 1994).

In this perspective emotion regulation can be modeled as being determined by the flow of activation within an imagined multi-dimensional space. Some points draw activation more often than others, and the areas surrounding these points are like currents, helping to direct the flow of activation (Globus and Arpaia, 1994; Thayer and Lane, 2000). Emotional dysregulation operates in a state space where cognitive and emotional attractors like "worry", "fear", "negative thoughts" or "sadness" attract more activation than they should, creating inflexible and rigid patterns of arousal, cognition and behavior (Friedman, 2007; Globus and Arpaia, 1994; Thayer and Lane, 2000). This inflexibility is also reflected in the output of the neurocardiac system, due to diminished vagal tone and dysregulated sympathetic activity (Friedman, 2007; Thayer et al., 2012). A regulatory system with a more balanced state space on the other hand would dynamically fluctuate between a wider selection of states allowing for more flexibility and complexity in its output (Glass and Mackey, 1988). Therefore, the degree of complexity in output should be negatively related to dysregulation with lower complexity predicting more dysregulation.

An estimation of the complexity of a system is accessible through analysis of its output signal complexity, which refers to the ease with which one may represent or compress the signal to a shorter, more compact form (Zvonkin and Levin, 1970). For instance, completely random noise would not be representable by anything but a full rendition of the noise itself, while a sine wave can be represented by a simple mathematical function of amplitude and period. There are many non-linear complexity measures available for psychophysiological research and cardiac analysis, including entropy-based measures (Voss et al., 2009).

SampEn (Richman and Moorman, 2000) looks at the complexity of the informational content in the data, specifically the ratio of longer to shorter matched patterns in the heart series, over a sliding window of calculation with new pattern templates making the basis for the comparison in each time window. In this way SampEn calculates the randomness or regularity in the signal over time, providing an index of non-linear cardiac complexity where higher complexity is marked by a higher entropy rate. On shorter time samples SampEn can give a valid and reliable measure of cardiac complexity at a chosen temporal resolution (Lake et al., 2002; Maestri et al., 2007; Richman and Moorman, 2000; Yentes et al., 2013). Because the entropic value of a signal can be influenced by non-complex randomness in the signal, such as noise, a multiscale entropy (MSE) analysis (Costa et al., 2002) can yield important information about the complexity on different time scales. However, performing a MSE-analysis requires a longer time sample. A modified multiscale entropy (MMSE) has been proposed for shorter datasets (Wu et al., 2013, 2014), but the validity of MMSE analysis is yet unresolved (Lin et al., 2017).

Lower cardiac entropy has been linked to major depression (Leistedt et al., 2011; de la Torre-Luque et al., 2016), bipolar disorder (Henry et al., 2010), schizophrenia (Chang et al., 2009; Schulz et al., 2015) and anxiety (Bornas et al., 2007; de la Torre-Luque et al., 2016). As cardiac entropy and its relation to emotional dysregulation and mental disorder is a complex area there is still a need for further research (de la Torre-Luque et al., 2016). The use of dynamical systems theory as a theoretical framework for psychological phenomena like emotion regulation also calls for more empirical data using appropriate methodology (Gelfand and Engelhart, 2012). Therefore, this study aims to test predictions derived from the Neurovisceral Integration Model in a group of children referred to treatment for internalizing symptomatology and a group of healthy controls using cardiac entropy.

The first aim of the study is to investigate whether lower complexity as indexed by SampEn is a predictor of emotional dysregulation. The second aim is to compare SampEn to two established linear measures of heart rate variability (HRV), RMSSD and the normalized power of HF (HFnu). Vagal influence on the cardiac signal has shown relevance in several studies of emotion regulation and dysregulation (Appelhans and Luecken, 2006) and RMSSD is considered a valid measure of vagal and high frequency components of the heart signal. RMSSD is easy to compute, often reported and is considered relatively free of sympathetic and respiratory influence (Laborde et al., 2017). To validate the results SampEn is also compared to HFnu, another measure of vagal cardiac influence that has been linked to emotional dysregulation, reflecting the relative power of high frequency variability in the heart signal (Beauchaine and Thayer, 2015).

The third aim of the study is to further the understanding of the underlying basis of SampEn, and its potential role as a marker of dysregulation. Therefore, we investigated whether vagal or sympathetic measures of activity were significant predictors of SampEn. Here RMSSD was chosen as a predominantly high frequency vagally mediated HF-HRV measure (Laborde et al., 2017), and pre ejection period (PEP) (Newlin and Levenson, 1979) was chosen as a sympathetic measure.

1.1. Hypotheses

We propose that non-linear cardiac complexity as indexed by SampEn can be used as an indicator of the dynamical interaction between the CNS-ANS-Cardiac systems as outlined in the Neurovisceral Model of Integration in Emotion Regulation and Dysregulation. Following the predictions of the Neurovisceral Model it is specifically hypothesized that lower levels of SampEn is an indicator of less complexity in the system and a significant predictor of emotional dysregulation as measured by the two behavioral rating scales "Emotional Problems" and "Lability/Negativity". It is also hypothesized that due to the dynamical nature of the systems involved SampEn may be a better predictor of emotional dysregulation than RMSSD or HFnu. We also hypothesize that SampEn is positively related to vagal activation and negatively related to sympathetic nervous system (SNS) activation, in line with the Neurovisceral Model.

2. Method

The project was part of a multicenter project in child psychotherapy taking place at the Norwegian University of Science and Technology in Trondheim, Norway, and at the A-hus University Hospital's Child and Adolescent Mental Health Clinic in Furuset, Oslo. Forty children between nine and thirteen years of age were referred to the project through family services, mental health clinics, school nurses, general practitioner doctors and parent referral. The study was in compliance with the Helsinki Declaration (World Medical Association, 2013) and was approved by the Norwegian Regional Committees for Medical and Health Research Ethics.

The children were selected based on scores on the Child Behavior Checklist (CBCL) 6-18 (Achenbach and Rescorla, 2001). To be included in the project the children had to have scores in the subclinical or clinical range in the internalizing spectrum (anxiety, depression or somatization). The CBCL operates with individualized cutoffs for assessing subclinical and clinical scores, taking age and gender into account, so every participant was judged against normdata appropriate for their age and gender. Thirty-six children met the inclusion criteria for the CBCL. Exclusion criteria were the use of medicine with potential CNS or ANS effects, preexisting or ongoing heart conditions, severe learning difficulties or severe comorbid psychiatric disorder outside of the internalizing spectrum. One child was excluded due to severe symptoms of prodromal psychosis, one due to congenital heart defects and two children due to medicine use. Thirty-two children (16 girls) were