Title: Resting heart rate variability, attention and attention maintenance in young adults.

Short title: Heart rate variability, attention and attention maintenance.

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ABSTRACT

Heart rate variability (HRV) is a widely used measure that reflects autonomic (parasympathetic) control of the heart. HRV has been linked with attentional performance, but it is unclear to what extent resting HRV is associated with both attention and attentional maintenance. In order to address this, we calculated HRV in seventy-four young and healthy volunteers (43 men, age: 21.6±2.4), who completed the D2 Test of Attention (D2), which was used to calculate an index of Concentration Performance (CP) and a measure of attention maintenance, the coefficient of variation (CV). After accounting for the effects of sex and age on HRV, there was no significant association between HRV and CP (p = .2), but a significant relationship between HRV and CV (p = .03). Overall, our study demonstrates that attention maintenance, but not attentional performance, is associated with higher resting state HRV which suggests that attentional performance from D2 subtest-to-subtest may reflect HRV's facilitation of behaviour flexibility.

Introduction

Heart rate variability (HRV) reflects a variation in the time intervals between heartbeats and is a well-established index of the function of parasympathetic branch of the autonomic nervous system (ANS) (Eckberg 1983, Quintana and Heathers 2014). Because HRV is a non-invasive method based on electrocardiogram (ECG) data, it is widely used in the biomedical sciences (Laborde et al. 2017). It has been suggested that HRV reflects mental and physical wellbeing of an individual (Grippo 2017) and is typically assessed in resting conditions or in response to a stimulus. In the latter case, HRV values obtained at baseline are typically compared with HRV values obtained during the exposure to a stimulus, with the observed changes interpreted as the cardiac autonomic response to the given stimulus. For instance, we have previously shown that females exposed to the sounds of a crying baby demonstrated decreased parasympathetic activity, which is consistent with the assumption that crying triggers parasympathetic withdrawal, which promotes the caregiver's readiness to help (Tkaczyszyn et al. 2013). Similarly, other sounds, such as binaural musical stimulus, have been also shown to increase parasympathetic activity (Roy et al. 2012).

Because resting HRV indices exhibit a large inter-individual variation (Kuch et al. 2004), which is a relatively stable individual trait, it has been used in order to investigate individual differences in reactions towards particular situations occurring during everyday life (Mosley and Laborde 2015). For example, high resting state HRV values reflect the flexibility of the ANS, which is thought to help individuals cope with uncertain and changing environments (Beckers et al. 2006).

According to the Neurovisceral Integration Model (Thayer and Lane 2000), complex interrelations between the cortical and subcortical regions of a brain are important determinants of HRV. Therefore, high resting state HRV is thought to be related to efficient control of the structures responsible for higher neurological functions (e.g., the prefrontal cortex) over neighbouring brain areas associated with the ANS (e.g., the hypothalamus) (Gillie and Thayer 2014). Activities carried out consciously can be supported by the physiological processes mediated by the ANS and therefore individual differences in HRV serve as a reliable index of the interplay between voluntary activities and corresponding physiological events (Ahern et al. 2001, Lane et al. 2009, Thayer et al. 2014). Consequently, high resting state HRV reflects rapid and adequate autonomic physiological responses, such as contraction of the walls of the blood vessels accompanied by increased heart rate and breathing rate during the fight-or-flight response (Cannon 1915), that are matched to conscious behavioural responses (e.g., fleeing danger).

One of the extensions of this approach is the assumption that higher HRV is related to better cognitive performance (Shaffer et al. 2014). Indeed, several studies have shown that HRV is related to cognitive functions (Frewen et al. 2013), such as memory (Thayer and Lane 2000), cognitive control, (Thayer and Lane 2000, Williams et al., 2016) and attention (Kuch 2004). Attention is often defined as the ability to select relevant information and to ignore irrelevant, distracting stimuli (Gillie et al. 2014) and has been shown to be related to autonomic activity (Kuch 2004).

HRV changes in relation to the baseline values have been examined during various tasks that involve attention, taking into account the differences between specific types of tasks as well as the fitness level of the participants (Luque-Casado et al. 2016). There is also a large body of research on HRV and attention involving children (including those with attention-deficit hyperactivity disorder) (e.g. Griffiths et al. 2017, Koenig et al. 2017, Rukmani et al. 2016, Robe et al. 2019, Börger et al. 1999, Negrao et al. 2011, Tonhajzerova et al. 2009) or older people, in whom lower HRV accompanies lower cognitive performance (e.g. Kumral 2019). However, to the best of our knowledge, there has not been a single studies looking at the extent to which the resting pattern of HRV predicts the level of attention in healthy adult males and females during a simple attentional task free of any additional context.

It has been shown that inter-individual differences in HRV to a great extent determine the capacity to control attention while exposed to emotional stimuli; individuals with low levels of HRV demonstrated significantly worse performance in applied tasks when distracted by fearful faces (Ellis et al. 2006, Park et al. 2012). In other words, higher HRV characterised subjects who demonstrated greater resistance over the distractors (Park et al. 2013).

Here, we assessed the relationship between baseline HRV, reflecting cardiac autonomic activity, and attentional performance in a group of young and healthy males and females. We used a task that enabled the measurement of the relation between baseline HRV and attentional performance, along with changes in the level of attention during the task, which may reflect resistance over the distractors (attentional maintenance). Consequently, we predicted that *i*) higher resting HRV would be positively related to better attention (as indexed by attention test score) and that *ii*) higher resting HRV would be negatively related to the fluctuation across time in attentional performance (as indexed by attention test performance variability).

Methods

Study group and study protocol

The study was conducted at the Department of Physiology, Medical University in Wroclaw, Poland. The young and healthy volunteers (mostly medical students) were recruited on an opportunistic basis and took part voluntarily and anonymously, without any form of gratification (n=80, 60 men, age: 21.6±2.4). Exclusion criteria were: (I) self-reported history of any chronic illness and (II) self-reported acute illness on the day of the examination or during up to one month preceding the study.

The study protocol was approved by the ethics committee at Wroclaw Medical University (125/2015). All participants provided written informed consent. The study was conducted in accordance with the Helsinki Declaration. An *a priori* power analysis indicated that 84 participants would be required to detect a Pearson's correlation coefficient of 0.3, which is considered a medium effect size (Cohen 1992), with an alpha level of 0.05 and 80% statistical power. All participants were advised to avoid smoking cigarettes and consuming caffeine for at least 12 hours before the examination (Quintana and Heathers 2014). After giving the consent, each subject completed a short questionnaire related to his or her self-reported height and weight, the general health status (e.g. questions about the frequency of any health problems and/or taking medicines) and lifestyle (e.g. questions about diet and substance abuse). ECGs were collected between 9:00 am and 1:00 pm. The examination room was quiet, light-attenuated, and had a stable ambient temperature (22 degrees). After the collection of ECG data, each participant completed the D2 Test of Attention (D2).

The assessment of heart rate variability

HRV was calculated from the continuous, non-invasive, digital recording of ECG (sampling frequency of 1 kHz, 16-bit resolution) with at least 15-minutes duration. Data was stored and processed using a PowerLab 16/30 acquisition device (ADInstruments, Dunedin, New Zealand). For the calculation of HRV indices, we selected 5-minute fragments of each recording. The selection was based on the visual inspection of the technical quality of the raw 15-minute ECG recordings, using LabChart 7 software (ADInstruments, Dunedin, New Zealand). Considering that even a single artefact can influence the calculation of HRV (Berntson and Stowell 1998), we selected the first 5-minute ECG sample that was free from artefacts. The ECG samples were then imported into Kubios HRV analysis software (version 2.2) (Tarvainen et al. 2014) for the calculation of HRV indices. Artefact correction methods provided by Kubios software (Mika et al. 2018) include the threshold-based correction method. In this approach, each RR interval value is compared to a local average interval (obtained by median filtering the RR interval time series, which is not affected by single outliers). If an RR interval differs from the locale average more than a specified threshold value, the interval is identified as an artefact and is marked for correction. Application of this method for artefact detection confirmed the absence of artefacts within the selected fragments of ECG recordings (Mika et al. 2018). For the current analysis, we used RMSSD (defined as root-mean square differences of successive R-R intervals), as this measure is less affected by any changes in respiration rate than frequency domain measures (Penttilä et al. 2001, Saboul et al. 2013).

The assessment of attention

To assess attentional performance, we selected a widely used neuropsychological test: the D2 Test of Attention (D2). The D2 is a paper-and-pencil neuropsychological timed measure of selective and sustained attention. The original version of the test was created by Brickenkamp (Brickenkamp and Zillmer 1998); here we used a standardised and validated Polish version of the test (Brickenkamp et al. 2003). The standardized test, includes 14 lines, each comprised of 47 characters (in sum there are 658 items). The test items are composed of the characters ‘d’ and ‘p’ with one to four dashes, arranged around the letter (either individually or in pairs, above and below). The participant is asked to scan across each line to identify and cross out every ‘d’ with two dashes. The distractors are similar to the target stimulus (e.g., a ‘p’ with two dashes or a ‘d’ with one or three dashes). The participant has 20 seconds per line, thus in sum the whole test lasts up to 4 minutes and 40 seconds (Brickenkamp and Zillmer 1998, Brickenkamp et al. 2003). The D2 is characterised by a high level of reliability and validity (Brickenkamp and Zillmer 1998, Brickenkamp et al. 2003). The internal stability of test indices was shown to be very high ($r > 0.90$). In a series of test–retests, with intervals of up to 40 months, D2 test indices demonstrated satisfactory to good reliability (r > 0.70). Moreover, the validity of the test is documented by a large volume of research (e.g. Bates and Lemay 2004).

There are several indices that can be calculated from the D2 test (Brickenkamp and Zillmer 1998, Brickenkamp et al. 2003. Bates and Lemay 2004). For the present analysis, we used the index of Concentration Performance (CP), as this is the main index reflecting the participant's level of attention (Brickenkamp and Zillmer 1998, Brickenkamp et al. 2003. Bates and Lemay 2004, Spreen and Strauss, 1998). CP is calculated by subtracting the total number of errors (defined as overlooking the target stimuli and as crossing out the distractors) from the total number of processed letters (summed from all 14 lines). CP was shown to be significantly correlated with other complex measures of attention such as the Symbol Digit Modalities Test, Stroop Colour Word, and Trail Making Test Parts A and B (Brickenkamp and Zillmer 1998, Brickenkamp et al. 2003. Bates and Lemay 2004). Apart from CP, there are other indices which can be calculated based on completed D2 test. However, CP is the only measure that reflects performance over the entire test. Thus, selection of this index as a measure of overall level of attention seems to be relevant.

The assessment of attention maintenance

Notably, none of the commonly used measures (Brickenkamp and Zillmer 1998, Brickenkamp et al. 2003. Bates and Lemay 2004) derived from the D2 test can reflect whether test performance remained unchanged throughout the whole study. Such performance consistency could possibly serve as a measure of sustained attention (attention maintenance) during this ~5-minute test. In the view of the way how the D2 test is constructed and how the CP is calculated, we constructed an additional indicator of the variability of the results obtained in subsequent 14 D2 test rows. To determine attention test performance variability, we used the coefficient of variation (CV), a commonly used mathematical measure of data dispersion . CV is defined as the ratio of the standard deviation and the mean, hence it represents the extent of variability in relation to the mean of the set of 14 sub-results of the D2 attention test. We propose that CV may serve as an indicator of the consistency of the test, which can be interpreted as the measure of attention maintenance: lower value of CV means less variable (more similar) results in each of 14 sub-tests, which may reflect a better ability to maintain a stable level of attention throughout the whole D2 test. Therefore, for each participant we calculated two measures of attention: CP as an index of the overall level of attention and CV as an indicator of the attention maintenance.

D2 has been previously used as a reliable method in order to identify deficits in maintaining attention (Priller and Rickards 2016), as it lasts almost 5 minutes during which participants are required to stay focused on repetitive tasks. Given that the efficient maintenance of the attention is expected to be related to better overall task performance, it can be presumed that a high CP score (corresponding with better attention) should be obtained by those who achieved high scores in each subsequent row. On the other hand, one may expect that a person with a low CP score may also receive similarly low results in each row. Moreover, it is difficult to predict the value of CP in a person, who will solve subsequent sub-tasks in different ways (sometimes better, sometimes worse). Therefore, in order to confirm that lower variability (lower CV) corresponds with better attention (higher CP), we first analysed the relationship between CV and CP. To confirm our assumptions, CP should be significantly and negatively related to CV.

Statistical analysis

Statistical analysis was performed using the R statistical environment (version 3.6.0). Complete datasets were collected from 80 participants, which was less than the desired number of 84 due to resource constraints. Outliers for RMSSD and D2 score values (defined as values that are larger than the upper quartile by at least 1.5 times the interquartile range (IQR) or smaller than the lower quartile by at least 1.5 times the IQR) were removed from the sample (n = 6; all RMSSD values), leaving a total of 74 participants for analysis. RMSSD (T = 1.11; p < .001) and CV (T = 2.71; p < .001), but not CP (T = -.18; p = .49) distributions demonstrated skewness. CV (T = 15.11; p < .001), but not RMSSD (T = 3.75; p = .12) and CP (T = 3.11; p = .84) distributions demonstrated kurtosis. Thus, RMSSD and CV were log transformed to better adhere to parametric assumptions. Log transformation improved skewness for both RMSSD (T = -.4; p = .14) and CV (T = .31; p = .24). Log transformation reduced skewness for both RMSSD (T = -.4; p = .14) and CV distributions (T = .31; p = .24). Log transformation also reduced kurtosis for the CV distribution, however this was on the border of statistical significance (T = 4.22; p = .03).

After data cleaning and transformation, the correlation between D2 score and D2 CV score was calculated. Then, to assess the relationship between RMSSD and attentional performance and the variability of attentional performance, we compared two nested regression models: An alternative model, containing age, sex, and RMSSD, and a null model including only age and sex. The Akaike Information Criterion (AIC) was calculated and compared for each model, with a lower AIC suggesting a better model for a given dataset. Hierarchical regression was then used to compare the nested alternative and null models. A statistically significant result would suggest that RMSSD is associated with attentional performance over and above sex and gender effects. An alpha level of .05 was used for all statistical tests.

Results

Descriptive statistics (means and standard deviations, SD) of the sample are presented in Table 1. As expected, high CP was associated with low CV (r = 0.59; 95% CI(-.72, -.42); $p < 0.0001$; figure 1). Assuming that low CV may reflect better attention maintenance, this correlation confirms that attention maintenance is related to better overall task performance in the D2 attention test. There was no statistically significant relationship between BMI and RMSSD (r = 0.13; 95% CI(-.11, 0.34); $p = 0.31$)

For the prediction of CP, the null model (CP ~ sex + age) was a better model for the data than the alternative model (CP ~ sex + age + RMSSD), as it had a smaller AIC value than the alternative model (812.18 vs. 812.46; Table 1). However, there was no significant difference between the alternative and the null models ($F = 1.65$, $p = 0.2$).

For the prediction of the variability in CV, the alternative model (CV ~ sex + age + RMSSD) was a better model for the data than the null model (CV ~ sex + age), as it had a smaller AIC value than the alternative model (73.61 vs. 76.52; Table 2). There was a significant difference between the alternative and null models ($F = 4.8$, $p = 0.03$), suggesting that RMSSD positively predicted the variability in CV over and above any age or sex effects.

Discussion

We showed that attention maintenance, but not attentional performance, is associated with higher resting state HRV. Although we did not find any correlation between RMSSD and CP, we showed that RMSSD accurately predicts the variability in CV. The latter suggests that higher resting HRV is related to a greater variability of scores within subsequent D2 tasks. This is, to our knowledge, the first study in which a variability measure derived from the D2 attention test was used as an additional measure designed to reflect constant attentional maintenance during the attention test. Because attentional control in everyday life requires not only efficient attentional focus and control over attentional selectivity, but also sustained attention throughout prolonged activities, the results of our study suggest that attention maintenance is an important factor in activities involving a great deal of focus (Mirsky et al. 1991, Posner and Petersen 1990, Raz and Buhle 2006, Robertson and Garavan 2004).

As the D2 attention test is recommended as a tool for detection attentional maintenance deficits, we expected that a high level of attention (higher CP) would correlate with the low attention test performance variability (lower CV). Indeed, the results of our study show that CP and CV were negatively correlated with each other suggesting that individuals who solved successive rows in a similar way, obtained better overall results. This suggests that CV reflects attentional maintenance during the ~4 minutes of the D2 test.

It is difficult to directly compare our results to previous research as most of the studies associating HRV with attention used different methods in examining how HRV changes during the implementation of attentional tasks, in which respiration can be a considerable confound (Quintana and Heathers 2014). However, in light of the published literature (Kuch et al. 2004, Levin et al. 2013, Mirza and Stolerman 2000, Hahn 2015, Ellis et al. 2006, Park et al. 2013, Park et al. 2012), we proposed two hypotheses, suggesting that: (i) high resting values of HRV (reflecting the flexibility of the ANS) would correspond to better results in the attention test and consequently, we assumed that (ii) high HRV would correspond not only with a higher level of attention (higher CP score in D2) but also with lower variability of scores obtained within subsequent tasks (reflected by low CV). Our results supported the second but not the first hypothesis, as they suggest that higher resting state HRV is related to attention maintenance (low CV), but not attentional performance (higher CP score in D2). Thus, to some extent, the results of our study are inconsistent with the premises from the literature, especially in terms of the direction of the relationship with HRV and the level of attention. The majority of studies, for instance, suggests that higher HRV is related to better cognitive performance and better attentional performance should correspond to higher HRV. These apparent inconsistencies between previous studies and the results of our study may be related to substantial sex differences, which are typical for both HRV measures as well as performance on attentional tasks, especially in younger people (Saleem et al. 2012).

Luque-Casado and colleagues (Luque-Casado et al. 2016, Luque-Casado et al. 2013) analysed the extent to which indices of HRV undergo changes during tasks requiring involvement of sustained attention, temporal orienting of attention, and fine temporal discrimination in the context of participants' fitness level. Importantly, these studies did not report that higher values of HRV are related to better performance in all types of cognitive tasks. However, they showed that, in some participants, the longer the task, the greater the overall HRV decrease (Luque-Casado et al. 2016, Luque-Casado et al. 2013), which might reflect the relationship between attentional maintenance (which gets harder the longer the task proceeds) with autonomic function, consistent with the present results.

Park and colleagues (Ellis et al. 2006) interpret their findings in relation to the Neurovisceral Integration Model (Thayer and Lane 2000), according to which individual differences in HRV recorded at rest predicted inhibitory mechanisms involved in attentional perception. They showed that participants exhibiting lower HRV failed to correctly shift their attention during tasks with emotionally significant (i.e., fearful) stimuli, whereas those with higher HRV demonstrated similar reactions to fearful as well as neutral stimuli, which suggests that they were more effective in managing their attention (Ellis et al. 2006). It has been also shown that students characterised by lower HRV exhibited worse reactions towards fearful stimuli (operationalized as pictures of faces expressing fear) (Ellis et al. 2006) compared to the group of participants with higher HRV. In particular, the low HRV group was distracted by fearful faces and, as a result, were typically unable to keep their eyes focused on the fixation point located on the screen (Ellis et al. 2006). The authors concluded that stronger cardiac vagal activity reflected by higher resting HRV corresponds with better modulation of emotional attention.

In yet another study, the analysis of the relationship between HRV and selective attention included an additional aspect (i.e., the load of the task) along with fearful or neutral distractors (Park G, et al. 2013). Under lower load, HRV did not differentiate any aspects of task performance but the differences appeared while performing more complex tasks during which students with lower HRV needed more time to solve tasks with both fearful and neutral distractors. In this study, participants characterised by higher HRV demonstrated more efficient control of selective attention, which is critical for goal-directed behavior, and this relationship was stronger when fewer cognitive resources were available (Park G, et al. 2013). It can be suggested that the length of the task contributes to its overall load (reflecting how hard is the task), which affects the attentional performance. Perhaps the correlation between CP and RMSSD would appear in a similar task lasting much longer than 5 minutes, as it would create higher mental load for participants.

The studies by Hansen and colleagues were focused on the relation between vagal activity and cognitive tasks (including a sustained attention test) as well as the autonomic response to cognitive tasks. Participants (male sailors from the Royal Norwegian Navy) with higher HRV demonstrated better and faster responses as compared to low HRV group (Hansen et al. 2003).

A follow-up study demonstrated that the level of resting HRV was significantly related to performance on tasks that involved attention, which was independent of participant's physical fitness (Hansen et al. 2004) but unrelated to conditions of the experiment (Hansen et al. 2009). Once again, higher HRV predicted better performance in cognitive tasks, which was inconsistent with the present results.

The present study has some limitations which should be acknowledged. First, we did not measure the fitness level of our participants. The assumption that studied population is homogenous was based on their age, declare being healthy, and have similar lifestyle (they were mainly medicine students). As fitness level is a well-established determinant of resting HRV (Hansen et al. 2004), further analyses should include the assessment of fitness level of the studied subjects. Second, these results require replication in other samples to increase the confidence that these outcomes are generalisable to other populations.

In conclusion, by showing that cognitive functions in young and healthy individuals can be predicted by resting state HRV, our study fills the gap in research examining the interplay between attention and HRV. While we did not find a significant relationship between resting HRV and attention, we demonstrated that there is a clear relationship between HRV and attention maintenance. We argue that higher HRV facilitates greater flexibility in behaviour, which reflects the differences in attentional performance from subtest-to-subtest.

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Table 1. Baseline characteristics, resting heart rate variability and the results from the test of attention derived from the analysed group (n=74)

	Mean±SD	Min.	Max.
Age (years)	21.6±2.4	19	31
BMI (kg/m^2)	22.2±2.9	17.6	31.5
RMSSD	49.2±27.5	6.7	127.8
Log transformed RMSSD	3.8±0.6	1.9	4.9
CP	496.3±59.3	342	627
CV	0.10±0.05	0.04	0.36
Log transformed CV	-2.37±0.4	-3.22	-1.02

Data are presented as means with standard deviations (SD), as well as minimum and maximum values. BMI = body mass index; RMSSD = root mean square differences of successive R-R intervals; CP = index of concentration performance derived from D2 test; CV = coefficient of variation.

Table 2. Multiple regression models for the prediction of the D2 score (CP).

	B	*SE B*	*β*	*P*
Model 1				
Constant	569.81	61.930		< 0.001
Sex	-39.69	13.390	-0.33	.004
Age	-2.33	2.789	-0.09	0.4
Model 2				
Constant	629.76	77.350		< 0.001
Sex	-38.55	13.359	-0.32	.005
Age	-2.56	2.782	-0.1	.36
RMSSD	-14.89	11.603	-0.14	.2

B = Regression coefficient (unstandardized), *SE B* = Standard error of the regression coefficient (unstandardized), β = Standardized beta coefficient, P = p-value, CP = index of concentration performance derived from D2 test, RMSSD = root mean square differences of successive R-R intervals.

Table 3. Multiple regression models for the prediction of the coefficient of variation (CV).

	B	*SE B*	*β*	*P*
Model 1				
Constant	-2.41	0.43		< 0.001
Sex	0.06	0.09	0.08	.5
Age	< 0.001	0.02	< .001	0.99
Model 2				
Constant	-3.1	0.53		< 0.001
Sex	0.05	0.09	0.06	.59
Age	0.002	0.02	0.02	.89
RMSSD	0.17	0.08	0.25	.03

B = Regression coefficient (unstandardized), *SE B* = Standard error of the regression coefficient (unstandardized), β = Standardized beta coefficient, P = p-value, CV = coefficient of variation, RMSSD – root mean square differences of successive R-R intervals.

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Figure 1. Relationship between CP (reflecting the level of attention) and CV (reflecting attentional maintenance. A line of best fit with 95% confidence region was overlaid to illustrate the data trend.

Highlights:

-Heart rate variability (HRV) has been linked with attention

-It was unclear if resting state HRV is associated also with attentional maintenance.

-Attentional performance in the D2 attention test was not significantly related to resting state HRV.

-Attention maintenance was associated with higher resting state HRV.

-Results may reflect how HRV facilitates behaviour flexibility.

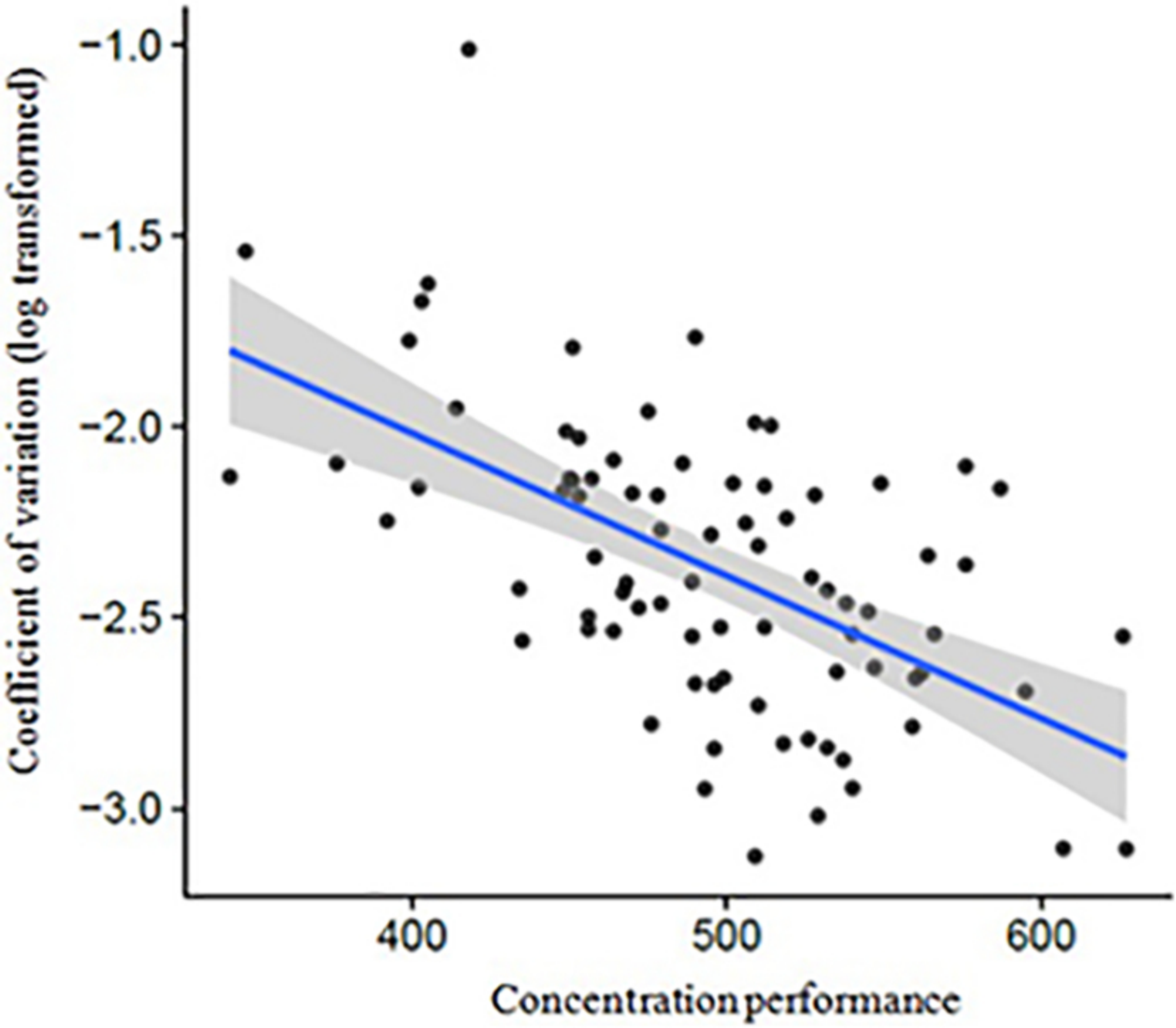
Coefficient of variation (log transformed)
−1.0
−1.5
−2.0
−2.5
−3.0
400
500
600
Concentration performance

Figure 1