# Is heart rate variability related to cognitive performance in visuospatial working memory?

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In the current study, we investigated the relation between cognitive performance and heart rate variability in visuospatial working memory. We used a visuospatial working memory paradigm involving simultaneous encoding, maintenance, active manipulation and retrieval to simulate routine daily activities. Subjects performed the visuospatial working memory paradigm which had 3 memory loads and simultaneous ECG recording was acquired for measuring heart rate variability. Based on the performance in the visuospatial working memory task, subjects were segregated into two groups: Good performers and poor performers. Two major findings emerged in this study. First, the heart rate variability decreased with an increase in the working memory load. Second, good performers had relatively higher heart rate variability compared to poor performers while performing the visuospatial working memory task. Our results highlighted the influence of cognitive performance on heart rate variability. In summary, the current study indicates that the heart rate variability during the visuospatial working memory task could predict the qualitative differences in the cognitive performance between the individuals.

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**Full Title: Is Heart Rate Variability Related to Cognitive Performance in Visuospatial Working Memory?**

**Short Title: Heart Rate Variability and Cognitive Performance**

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**Abstract**

Background: An integrative model of health and disease must incorporate cognitive, affective, behavioural and physiological factors that contribute to inter-individual differences. In the current study, we tried to link autonomic mediated heart rate variability to cortically mediated cognitive activity using a visuospatial working memory paradigm that simulates day to day routine activity.

Method: We used a visuospatial working memory paradigm involving simultaneous encoding, maintenance, active manipulation and retrieval to simulate routine daily activities. Subjects performed the visuospatial working memory paradigm which had 3 memory loads and simultaneous ECG recording was acquired for measuring heart rate variability. Based on the performance in the visuospatial working memory task, subjects were segregated into two groups: Good performers and poor performers.

Result: Two major findings emerged in this study. First, the heart rate variability decreased with an increase in the working memory load. Second, good performers had relatively higher heart rate variability compared to poor performers while performing the visuospatial working memory task. Our results highlighted the influence of cognitive performance on heart rate variability.

Conclusion: In summary, the current study indicates that the heart rate variability during the visuospatial working memory task could predict the qualitative differences in the cognitive performance between the individuals.

Keywords: Heart rate variability; Visuospatial working memory; Cognitive performance.

**Is Heart Rate Variability Related to Cognitive Performance in Visuospatial Working Memory?**

## 1. Introduction

An integrative model of health and disease must incorporate cognitive, affective, behavioural and physiological factors that contribute to inter-individual differences. There has been great body of work on the role of individual differences in the beat-to-beat variations of heart rate in health and disease. We have tried to link autonomic mediated heart rate variability (HRV) to cortically mediated cognition using a visuospatial working memory (VSWM) paradigm that simulates day to day routine activity.

Memory is a process which involves encoding, maintenance, manipulation and retrieval of selective information in the environment. Working memory is a cognitive component that maintains information temporarily which is no longer present in the environment or that was internally generated, and it supplies a work space for transforming and manipulating elements of perception and thinking. Working memory has two components, the phonological loop the one that stores verbal information and visuospatial sketchpad, which stores visuospatial information, controlled by central executive system (Baddeley, 1996). Baddeley also suggested that the neural processing of visual and verbal information is independent. As both these modalities are processed in parallel, simultaneous verbal processing does not limit the VSWM (Baddeley, 1996).

Visuospatial working memory (VSWM) refers to the cognitive ability that is essential to encode, maintain, manipulate and retrieve information in the visual space to facilitate the action of ongoing activity. Apart from being an essential cognitive component for routine activity, good VSWM is crucial for professions such as drivers, sailors, aviators and naval officers. Moreover, VSWM is affected in various disease states such as autistic spectrum disorders, Alzheimer's disease, Parkinson's disease and schizophrenia (Bradley et al., 1989; Fleming et al., 1997; Mammarella et al., 2014; Porges and Raskin, 1969; Quental et al., 2013). Hence, a convenient tool for predicting and assessing the VSWM performance in health and disease would be of great benefit in the future.

HRV was significantly reduced during sustained attention (Porges and Raskin, 1969) and it is also related to memory performance, mental workload and attention (Thayer et al., 2009)(Backs and Seljos, 1994; Ekberg et al., 1995; Middleton et al., 1999; Redondo and Del Valle-Inclán, 1992; Schellekens et al., 2000; Veltman and Gaillard, 1998; Vincent et al., 1996). Low HRV has been linked with poor cognition, where the autonomic system is less reactive to changes in the external environment and is therefore less adaptable (Phillips, 2011). Lower HRV values were observed during working memory task compared to executive and planning tasks (Backs and Seljos, 1994). These evidences suggest that HRV may potentially serve as a tool to predict and assess the cognitive function in health and disease. Though these studies have reported the relation between HRV and cognition, consensus has not been reached till date and needs further investigation.

Neural network studies in humans have reported increased activity in the prefrontal cortex during tasks involving executive function and working memory. Thayer et al. (2009) proposed that decrease in activation of prefrontal cortex disinhibit Central nucleus of the amygdala (CeA), in turn lead to disinhibition of sympathoexcitatory RVLM neurons and inhibition of parasympathoexcitatory neurons. Both would lead to an increase in heart rate and a concomitant decrease of vagally mediated HRV (Thayer et al., 2009). Recent meta-analysis report on the neuroimaging studies that investigated the relationship between HRV and regional cerebral blood flow, suggested that HRV may index the degree to which medial prefrontal cortex (mPFC) guided "core integration" system is integrated with the brainstem nuclei that directly regulate the heart (Thayer et al., 2012). Therefore the capacity of the organism to effectively function in a complex environment may be studied from an easily measurable HRV output.

The fundamental characteristic of working memory is to actively manipulate the incoming and the stored information, since it posses more demand on the cognitive resources than mere maintenance of information. Passive processes are recruited by the tasks that require recall of information in the same format as it was memorized, while active processes are recruited by tasks that require the information to be modified, transformed, integrated or otherwise manipulated. Task design of the paradigms used in the previous studies limited the active manipulation of the information. In the current study, we used VSWM task involving active manipulation of the encoded visuospatial information while simultaneously maintaining and retrieving the information for the execution of the task goal (Suriya-Prakash and Sharma, 2015).Though there are studies of HRV during cognitive function tasks, only a few of them have used working memory task involving passive maintenance. To the best of our knowledge, no previous study had investigated the effect of VSWM on HRV in healthy human adults. In this study we have tried to explore the effect of cognitive performance with an increase in the memory load on HRV measures using VSWM paradigm, involving active manipulation for the first time.

## 2. Materials and methods

### 2.1. Participants

24 healthy male volunteers (mean age 27.63 ± 3.004; range 21-34; all right handed) participated in this experiment after giving written informed consent. Participants recruited were the post-graduate students in the institute. The study was approved by the Institution Ethics Committee, All India Institute of Medical Sciences, New Delhi, India.

### 2.2. Task Design

This study has been designed with an objective to investigate the effect of cognitive performance and memory load using VSWM paradigm on HRV in healthy human subjects. We used a VSWM task involving simultaneous encoding, retention & retrieval, consisting of three memory loads (3 pairs, 6 pairs and 8 pairs of identical abstract pictures). Abstract pictures were used rather than real life objects to minimize the contribution of verbal working memory for performing the VSWM task. In each load, participants had to encode the picture for 10 seconds after which pictures were hidden in the array. The pictures in the hidden array turn unhidden on the mouse click. Matching trial starts with a mouse click to turn open a picture in the search array after which participant starts searching for the matching picture located elsewhere in the array. Then, the participant clicks on an open picture chosen as the matching picture. Successful matching trial makes the pair of abstract pictures to disappear from the array. All pairs of abstract pictures have to be matched correctly to complete the load. Memory load I, II and III had three, two and one blocks of trials, respectively making at least 8 trials in each memory load (Suriya-Prakash and Sharma, 2015).

## 2.3. Procedure

Lead II ECG has been recorded using polygraph input box (PIB; Electronic Geodesic Inc., Eugene, OR, USA). ECG recording was done in a silent electrically noise free room. Five minutes baseline ECG recording was taken followed by simultaneous ECG recording during VSWM paradigm. Data was acquired using Net Station 4.5.6.

## 2.4. Data Analysis

Data acquired were exported in MAT file format for further offline analysis in Matlab R2012b (The MathWorks, Inc., Natick, USA). HRV has been analysed using Kubios HRV software package (Tarvainen et al., 2009). Time and frequency domain analysis of HRV measures were performed. The time domain HRV measures include, AVNN (Average of all NN intervals), SDNN (Standard deviation of all NN intervals), rMSSD (Square root of the mean of the squares of differences between adjacent NN intervals), NN50 and pNN50 (Percentage of differences between adjacent NN intervals that are greater than 50 ms). Frequency domain measures include TOTPWR (Total spectral power of all NN intervals up to 0.04 Hz), LF (Total spectral power of all NN intervals between 0.04 and 0.15 Hz), HF (Total spectral power of all NN intervals between 0.15 and 0.4 Hz) and LF/HF (Ratio of low to high frequency power).

The SDNN is the standard deviation of the normal (NN) inter beat interval, i.e. the square root of variance measured in millisecond, which represents parasympathetically-mediated respiratory sinus arrhythmia (Shaffer et al., 2014). The RMSSD is the root mean square of successive differences between normal heartbeats. RMSSD is used to estimate the vagally mediated changes reflected in HRV (Shaffer et al., 2014). The NN50 is the adjacent NN intervals that differ from each other by more than 50 ms and pNN50 is the percentage of NN50. It is correlated with the RMSSD and HF power (Shaffer et al., 2014). The HF power reflects parasympathetic activity.

The LF power is assumed to represent sympathetic outflow. The LF/HF ratio is considered to represent sympatho-vagal balance (Electrophysiology, 1996).

### 2.5. Statistical Analysis

Statistical analysis was carried out using Statistical Package for Social Sciences version 20.0. As expected, the performance of the participants decreased as the error rate increased significantly in higher working memory loads (Load I = 0.29 ± 0.69, Load II = 1.79 ± 1.532, Load III = 6.63 ± 3.621). Mean (SD) of total error rate in all three loads = 8.71 (4.18), Median = 8.5 and 50th Percentile = 8.5. Based on the distribution of the total error rate, participants who committed ≤ 8 total errors were classified as good performers (n=12) and participants who committed ≥ 9 total errors were classified as poor performers (n=12). There was no significant difference in age between performance groups (Age-matched).

Baseline HRV measures were subtracted from the HRV measures during the memory load I, II and III of the VSWM paradigm. Two-way ANOVA measures were used to analyze the effect of two factors, working memory load (3 loads) and the performance groups (2 groups: good and poor performers) on the error rate (Number of errors committed by the subjects in each load). Multivariate analysis was used to analyze the effect of working memory load (3 loads) and the performance group (2 groups: good and poor performers) on 8 HRV measures (dependent variables) such as AVNN, SDNN, rMSSD, NN50, pNN50, LF, HF and LF/HF ratio. Significant working memory load effects were further investigated post-hoc applying a Bonferroni correction of $p < 0.05$. Spearman rank order correlation coefficients were used to estimate the relationship between error rate and HRV measures that showed significant changes. To test the significance of the correlation coefficients, two-tailed tests were used.

## 3. Results

### 3.1. Effect of working memory load and performance on error rate

The working memory load had significant effect on the error rate ($F$ (2, 66) = 81.046, $p < 0.001$). Post-hoc analysis indicated that the error rate significantly increased with an increase in the memory load ($p$ (I vs. II) = 0.016, $p$ (I vs. III) < 0.001, $p$ (II vs. III) < 0.001). There was significant difference in the error rate between high and low performers ($F$ (1, 66) = 24.085, $p <$ 0.001).

### 3.2. Effect of working memory load and performance on heart rate variability

Among the HRV measures, SDNN, NN50, pNN50 and LF/HF ratio showed significant changes in the working memory loads (Table 1). Further post-hoc analysis revealed that all these variables decreased in higher working memory loads except LF/HF ratio which showed increase in higher memory loads (Table 1). AVNN, LF and LF/HF ratio showed significant difference among the HRV variables between performance groups (Table 2).

| Measures | F (2, 66) | P value | Post-hoc Bonferroni correction (P < 0.05) | | |
|---|---|---|---|---|---|
| | | | Load I Vs II | Load II Vs III | Load I Vs III |
| SDNN | 10.949 | 0.001 | ns | ns | I > III |
| NN50 | 5.12 | 0.009 | I > II | ns | I > III |
| pNN50 | 3.831 | 0.027 | ns | ns | I > III |
| LF/HF | 7.561 | 0.001 | I < II | ns | I < III |

**Table 1:** HRV measures which showed significant difference due to working memory load. ns – Denotes not significant; I, II and III – Denotes memory loads I, II and III, respectively.

| Measures | F (1, 66) | P value | Good Vs Poor performers |
|---|---|---|---|
| AVNN | 12.671 | 0.001 | Good > Poor |
| LF power | 7.971 | 0.006 | Good < Poor |
| LF/HF | 8.547 | 0.005 | Good < Poor |

**Table 2**: HRV measures which showed significant difference between performance groups. Good & Poor – denotes good performers and poor performers, respectively.

3.3. Correlation of error rate with heart rate variability

We performed correlation analysis between error rate and HRV measures that showed significant changes with the working memory load and the performance. Error rate had significant negative correlation with AVNN ($r_s$ = -0.311; $p$ = 0.008), SDNN ($r_s$ = -0.441; $p$ = 0.001), NN50 ($r_s$ = -0.236; $p$ = 0.046) and had significant positive correlation with LF power ($r_s$ = 0.274; $p$ = 0.02), (LF/HF ratio ($r_s$ = 0.337; $p$ = 0.004).

## 4. Discussion

In the current study, we have tried to explore the effect of working memory load and performance capacity on HRV measures. We used a VSWM paradigm that involves simultaneous encoding, maintenance, active manipulation and retrieval which simulates day-to-day routine activities. The results of the present study showed that the error rate increased (performance of the subjects decreased) with an increase in the working memory load. This is in line with previous study that revealed the capacity limitation of human working memory (Todd and Marois, 2004).

From our results, it is evident that HRV decreased with an increase in the working memory load as SDNN, NN50 and pNN50 decreased and LF/HF ratio increased in higher working memory loads. Previous evidences suggest that the primary source that produces changes in SDNN, NN50 and pNN50 is parasympathetically (vagal) mediated respiratory sinus arrhythmia (RSA) and hence suited for its assessment (Shaffer et al., 2014). LF/ HF ratio is believed to quantify sympatho-vagal balance, although recent studies have challenged it (Reyes del Paso et al., 2013). Our results suggest that increase in the working memory load decreases the parasympathetic activity to produce low HRV in higher memory loads. This is in line with previous studies which have also reported low HRV with an increase in the difficulty and memory load of the working memory task ( Backs et al., 1994; Hansen et al., 2003; Middleton et al., 1999). Error rate correlated negatively with AVNN, SDNN, NN50 and pNN50 and positively with LF power and LF/HF ratio. As mentioned earlier, error rate increased with an increase in the memory load as the difficulty level is expectedly high in the higher memory loads. This might signify that when the subjects were challenged with more difficult VSWM task, parasympathetic activity decreased and the error rate increased. This is in line with the previous studies which also reported association between low HRV during the cognitive task performance and an increase in the error rate ( Backs et al., 1994; Hansen et al., 2003; Middleton et al., 1999). From our results, it becomes apparent that HRV may be more than just an index of heart function, and might indicate an individual's cognitive capacity to function effectively in a complex environment. Recently, Thayer et al. (2012) performed meta-analysis of neuroimaging studies on the relationship HRV and regional cerebral blood flow (Thayer et al., 2012). Thayer et al. (2012) also suggested that HRV may index the degree to which medial prefrontal cortex (mPFC) guided "core integration" system is integrated with the brainstem nuclei that directly regulate the heart (Thayer et al., 2012).

More interestingly, the poor performers showed significantly higher LF power, LF/HF ratio and lower AVNN compared to good performers. This finding was in agreement with previous study, which also reported similar observation i.e. good performers showed higher HRV than poor performers (Backs and Seljos, 1994). The HF peak is widely believed to reflect cardiac parasympathetic nerve activity and the LF, although more complex, is assumed to represent sympathetic component (Berntson et al., 1997; Billman, 2013, 2011; Electrophysiology, 1996). The LF/HF ratio is used to quantify the dynamic relationship between sympathetic and parasympathetic nerve activities i.e., the sympatho-vagal balance (Malliani et al., 1991; Pagani et al., 1986) in both health and disease. However, recent data challenge the interpretation of the LF and LF/HF ratio, as indices of sympathetic cardiac control and sympatho-vagal balance respectively and also suggest that the HRV power spectrum, including its LF component, is mainly determined by the parasympathetic system (Reyes del Paso et al., 2013). On this account, it appears that the HRV analysis is more suited for the estimation of parasympathetic influences on the heart rate (Reyes del Paso et al., 2013). A large number of studies have shown that total vagal blockade essentially eliminates HF oscillations and reduces the power in the LF range (Malliani et al., 1991; Pomeranz et al., 1985). Hence, our results indicate that the good performers with low LF power and LF/HF ratio had higher parasympathetic vagal activity when compared to poor performers when challenged with visuospatial working memory task. Elite athletes who are known for having high parasympathetic tone and high HRV (Giblin et al., 2013), might have an advantage of coping up to difficult cognitive demands. Thayer et al. (2012) suggested a common reciprocal inhibitory cortico-subcortical neural circuit between mPFC and subcortical structures like amygdala, brainstem nuclei to serve as the structural link for the psychological processes like cognition with the physiological processes, such as heart rate

(Thayer et al., 2012). This integrated circuit is believed to control the sympatho-vagal balance to effectively respond to the psychological and physical challenges posed by the environment. Thus, HRV may serve as an easily measured output of this neural network that may provide valuable information about the cognitive capacity of an individual to effectively function in a complex environment.

Our results revealed that the poor performers had low HRV when compared to good performers, when challenged with visuospatial working memory task. This highlights the potential importance of autonomic activity as a predictive tool for cognitive performance in VSWM. This could potentially be applied for the early detection of disease states with VSWM impairment, which would allow for the intervention methods to be applied sooner to slow or cease cognitive decline progression (Berkoff et al., 2007). Diet, exercise, biofeedback and stress reduction techniques such as meditation are some of the several behavioral strategies that can be used to increase HRV (Thayer and Lane, 2009).

## 5. Conclusion

To summarize, the current study for the first time has investigated the relationship of HRV with the cognitive performance of the task, which involves VSWM in normal healthy subjects. Our results showed that the parasympathetic activity decreased (Low HRV) in higher memory loads and good performers had relatively higher HRV compared to poor performers while performing the visuospatial working memory task. Our results indicate that the HRV during the VSWM task could predict the qualitative differences in the cognitive performance between the individuals.

The current study result implies an 'integrated' neural network of adaptive regulation, which controls cognitive performance and autonomic functions such as heart rate. HRV may serve as an index of this neural network and might indicate an individual's capacity to effectively function in a complex environment. The outcome of the current study supports Claude Bernard's notion that the vagus nerve serves as a structural and functional link between the brain and the heart.

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