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#### Higher autonomic activation predicts better performance in Iowa Gambling Task

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#### Abstract

<u>Objective</u>: To evaluate the relationship between the autonomic nervous system basal state and performance in decision making tasks.

<u>Background</u>: The link between performance in decision making tasks and acute changes in autonomic parameters during their execution has been extensively investigated. However, there is lacking evidence regarding the relationship between decision making and basal autonomic state.

<u>Methods</u>: Resting autonomic nervous system activity in 18 healthy subjects was assessed by means of heart rate variability (HRV) analysis before conducting three different decision making tasks: an ambiguous one, the Iowa Gambling Task (IGT); a test that assesses risk taking behavior, the Game of Dice Task (GDT); and a test that assesses reversal learning behavior, the Reversal Learning Task (RLT). The tasks were administered in a random fashion.

<u>Results</u>: There was a direct correlation between the IGT net score and the resting low frequency HRV (r= 0.73; p<0.001), which is strongly influenced by sympathetic activity. No correlations were found between HRV and the GDT net score or the RLT last error trial. <u>Conclusions</u>: The results are compatible with the idea that a higher basal activation of autonomic nervous system is beneficial for subsequent decision making process.

#### Introduction

Decision making is a cognitive process crucial for daily life. Whether it is an important decision or an irrelevant one, we are unavoidably required to make choices every day. Some of these choices are made on the basis of clear and complete information and are rationally taken. However, in other situations, unconscious processes play an important role in identifying the best option to follow <sup>1</sup>. The processes taking place in these situations are poorly known.

Aiming to bring some light to this issue, Bechara et al. developed the Iowa Gambling Task (IGT), which was designed to recreate uncertain decisions made in real life. Based on prefrontal damaged patients' deficient IGT results, they developed the Somatic Marker Hypothesis, that holds that normal subjects guide their decisions towards advantageous choices, even before consciously knowing they are convenient <sup>1</sup>. For example, it was observed that normal subjects develop a sympathetic activation on the verge of taking disadvantageous choices. Such sympathetic activation would be a marker for avoiding these decisions. Skin conductance responses (sympathetic activation) were not generated in patients with ventral medial prefrontal cortex damage who perform poorly on IGT <sup>1</sup>. In line with this, a low IGT performing group of normal subjects lacked anticipatory skin conductance responses. In addition, the high performing group showed anticipatory deceleration of heart rate prior to choices associated to frequent loses. This cardiac response was also absent in the low scorers <sup>2</sup>.

In spite of these provocative observations, a causal relationship between autonomic activation and IGT performance is far from being established. For example, patients suffering from pure autonomic failure, a pathology that makes them unable to generate

autonomic arousal due to peripheral denervation of the Autonomic Nervous System (ANS), did perform at least as well as healthy controls at IGT <sup>3</sup>. This would indicate that peripheral autonomic modifications are not necessary for guiding decision-making processes. Thus, it has been argued that a deficient IGT performance can be related to alteration of specific decision making mechanisms other than the one explained by the somatic marker hypothesis <sup>4</sup>. The subject's preference for safer or riskier choices is the most studied of these possible alternative mechanisms <sup>4;5</sup>. Reversal learning, i.e., the ability to suppress successfully learnt behavior when it is no longer correct, has also been implicated <sup>4</sup>.

Due to the subtle trial to trial regulation inherent in somatic marker hypothesis, it does not seem possible to test causality by modifying ANS response at this time scale. Thus, the existence of a more general relationship between decision making scores and ANS needs to be assessed.

To our knowledge, there is no published study linking decision making performances with basal ANS activation. To test whether the baseline status of ANS activity relates to complex decision making processes as assessed by IGT, Heart Rate Variability (HRV) analysis was used prior to exposure to the task while controlling for other mechanisms, such as risk taking behavior and reversal learning, that could be involved in the decision making process.

#### **Materials and Methods**

This is an observational study in healthy volunteers on the association between cardiac autonomic activity at rest and performance in the IGT as a decision making process. The study was approved by the local ethics committee.

Subjects

Healthy volunteers (n=18), mean age 47.7 (SD: 15.4 range 22-70, 72.2% female) gave full informed consent and were paid for participating, irrespective of their performance in the tasks.

**Decision Making Tasks** 

Iowa Gambling Task

The IGT was used to assess decision-making. The IGT has a number of design issues that could make difficult its interpretation, like its relation with other specific decision making mechanisms like risk taking behavior or reversal learning <sup>4</sup>. However, it has frequently been used in the assessment of decision-making under ambiguity <sup>1;2;5</sup>.

In this task, participants are given simulated money and presented with four decks of cards. Each deck is either advantageous or disadvantageous in terms of total monetary outcome. Selection of disadvantageous decks leads to high rewards but even higher losses, while advantageous decks bring relatively low rewards but even lower losses. At the beginning of the test, the subjects totally ignore what the best choices are. During its

execution, they must learn the right strategy to win as much simulated money as possible, and/or avoid losing it.

We used a computerized version of the IGT previously described <sup>2</sup>. This version was modified by introducing a six second delay between each decision. This feature was intended to allow future studies that test heart response during the execution of IGT. The IGT net score was calculated as the total number of advantageous choices minus the total number of disadvantageous choices. Following other studies<sup>2;5</sup>, the net score was further divided into five blocks, each of 20 consecutive card choices.

#### Game of Dice Task

The Game of Dice Task <sup>5</sup> (GDT) assesses risk-taking behavior under known probabilities by having explicit rules for gains and losses. Participants are told to maximize 1.000 units of fake money within 18 rounds of dice throws. The task is based on guessing what number or combination of numbers will result from rolling a dice. There are four different alternatives to take a guess: single numbers or combinations of two, three, or four numbers. Each alternative is associated with specific fictive gains or losses according to the probability of winning (for single numbers the bet is 1.000, for combination of four numbers the bet is 500, for combination of three numbers the bet is 200 and for combination of four numbers the bet is 100). Payment in case of winning is always the same amount of money that is betted. Thus, the best option is to choose the combination of four numbers. The GDT net score is calculated by subtracting the number of times the subject selected the disadvantageous options (selecting a single number or a combination of two) from the

number of times the subject selected the advantageous options (selecting a combination of three or four numbers) <sup>5</sup>.

#### **Reversal Learning Task**

In this task, subjects learn to touch one of two simple patterns that are shown one at a time in a touch screen. They gain a point by touching one of the patterns or by not touching the other. They lose a point by touching the one they should not touch or by not touching the one they should. Once they have learnt to do this, the outcomes are switched. The informed result, RLT last error trial, is the last trial in which an error was made <sup>6</sup>. Thus, higher result numbers are associated with worst performance at reversing the learnt behavior.

#### Autonomic Nervous System activity

ANS activity was assessed by HRV analysis. This analysis is based on the fact that the relatively constant heart rate generated by the sinus node, is modulated by several factors that result in a complex heart rate signal. HRV high-frequency component (0.15 - 0.4.Hz) is related to respiratory sinus arrhythmia and therefore mediated solely by parasympathetic activity. The low-frequency component (0.04 - 0.15 Hz) is related to baroreflex control and depends mainly on sympathetic but also on parasympathetic is also found

and has been attributed to thermoregulatory fluctuations in vasomotor tone as well as to humoral factors such as the renin-angiotensin system <sup>7;8</sup>. In addition, HRV shows fractal scaling and nonlinear properties derived from the complex interaction of the autonomic tone and its central organization as well as from exteroceptive and interoceptive influences <sup>9;10</sup>. The nonlinear dynamics of HRV has been characterized in various forms, including short term fractal exponent alpha ( $\alpha$ s) and Sample Entropy (SampEn) <sup>11;12</sup>.

Signal recording: ECG signal was recorded using a digital Holter device (Holter HCAA 348 / Holtech / Servicios Computados S.A. / Buenos Aires / Argentina) and stored in a solid-state memory. Ventricular depolarization (R waves) was detected through the device software. The time elapsed between R waves (RR intervals) was then computed. We visually identified and manually tagged premature and lost beats in the original file of RR intervals. These abnormal beats were replaced by RR intervals resulting from linear interpolation <sup>8</sup>. Only those segments with >85% qualified beats were included in the analysis <sup>13;14</sup>.

Time domain HRV analysis: Quantitative time series analysis was performed on heart rate by evaluating measures of variation over time. Among these, mean RR interval (RRm) quantifies the mean heart rate, standard deviation of all normal RR intervals (SDNN) represents a coarse quantification of overall variability, and square root of the mean squared differences of successive normal RR intervals (RMSSD) measures high frequency heart rate variations <sup>8;10</sup>.

Frequency domain (spectral) measurements of HRV were obtained by Fast Fourier Transform. It included total area (TA, total spectral power, 0-0.4 Hz,  $ms^2$ ), Very Low Frequency (VLF, < 0.04 Hz,  $ms^2$ ), Low Frequency (LF, 0.04-0.15 Hz,  $ms^2$ ), High Frequency (HF, 0.15 - 0.4 Hz,  $ms^2$ ), their percentage values, and the LF/HF ratio <sup>8</sup>. Non - linear HRV analysis: The  $\alpha$ s<sup>11</sup> and the SampEn<sup>12</sup> were used as nonlinear HRV indexes. The scaling exponent  $\alpha$ s, based on the "detrended fluctuation analysis", quantifies the short-term (< 11 beats) fractal correlation properties of the inter-beat time data. Values of  $\alpha$ s close to 0.5 are associated with uncorrelated RR intervals, whereas values close to 1.5 are associated with strong correlation between RR intervals. Values near 1 are characteristic of fractal like processes, associated with the dynamic behavior of time series generated by complex systems, such as the autonomic regulation of the sinus rhythm in healthy subjects<sup>11</sup>. SampEn measures the degree of irregularity of the RR interval time series. Regular sequences will result in lower SampEn values whereas random behavior is associated with larger SampEn values. These methods have been previously described <sup>10-12</sup>. Uncorrelated and irregular behavior is usually associated to parasympathetic prevalence<sup>15</sup>.

#### **Experimental Procedure**

First, individuals were required to sit quietly for 10 min while recording their ECG signal. After this, they were evaluated for decision making. IGT, GDT and RLT were conducted in a randomized order.

#### **Statistical Analyses**

Values were expressed as mean ± SD. Normality of distributions was evaluated by using a Kolmogorov-Smirnov Test.

Association between IGT net score and sex was evaluated by mean of a T test for independent variables. Bivariate correlations of IGT net score with and age, GDT net score and RLT last error trial were explored by means of a Pearson correlation test. Also, correlations between the decision making tasks and the different HRV components were also explored by means of the aforementioned test.

Finally, in order to establish whether significant correlations between IGT net scores and HRV indexes could be explained by age, sex or specific decision making mechanisms underlying IGT, partial correlations were conducted controlling for age, sex, GDT net score (as an index of risk behavior) and RLT last error trial (as an index of reversal learning).

#### Results

Significance of Kolmogorov-Smirnov tests was above 0.10 for all variables except for RLT last error trial, which was between 0.05 and 0.10. This variable was log transformed for statistical analyses to allow a better fit to a normal distribution, being the significance of Kolmogorov-Smirnov test for the transformed variable equal to 0.501.

Mean IGT net score was  $11.3 \pm 29.2$ , mean GDT net score was  $7.9 \pm 8.1$  and mean RLT last error trial was  $11.2 \pm 11.6$ . The 72.2% of the subjects completed the IGT with positive (>0) net scores (that is, more advantageous than disadvantageous choices).

Basal HRV values were (mean  $\pm$  SD): RRm 845.09  $\pm$  104.26 ms, SDNN 41.12  $\pm$  13.97 ms, RMSSD 30.77  $\pm$  11.66 ms, In TA 7.25  $\pm$  0.67 ms<sup>2</sup>, In VLF 6.28  $\pm$  0.75 ms<sup>2</sup>, In LF 6.07  $\pm$  0.91 ms<sup>2</sup>, In HF 5.65  $\pm$  0.98 ms<sup>2</sup>, VLF% 41.56  $\pm$  16.09, LF% 34.78  $\pm$  15.72, HF % 23.66  $\pm$  13.98, LF/HF 2.25  $\pm$  2.26,  $\alpha$ s 1.13  $\pm$  0.25, SampEn 1.66  $\pm$  0.24.

The correlations between decision making tasks scores and HRV indexes are summarized in Table 1. Significant correlations were found for IGT score with global HRV (SDNN, TA) and low frequency HRV (LF and LF%) (table 1 and figure 1). No significant correlations were found between the other tasks and HRV measurements (table 1). HRV indexes that were significantly correlated with IGT net score were further correlated with the scores of the different IGT blocks, as shown in Table 2. Correlations become significant with the last three blocks (Table 2).

IGT net score showed no significant association with sex (T = -1.696, p = 0.109), while was significantly correlated with age (r = -0.60, p = 0.009). GDT net score (r= 0.28, p= 0.260) showed no correlation to IGT net score, neither with the net scores at any block of the task. Transformed RLT last error trial yielded a significant correlation with IGT net score (r= -0.62, p= 0.006), and the net scores at blocks 3 (r= -0.63, p= 0.005) and 5 (r= -0.65, p= 0.003). As a higher RLT last error trial indicates worst performance, the correlation between performance in IGT and RLT is in fact positive.

When controlling IGT net score for sex, age, GDT net score and RLT last error trial, significance was still observed for LF (r= 0.73, p= 0.003) and TA (r= 0.56, p= 0.037) but not for LF% (r= 0.50, p= 0.066) and SDNN (r= 0.52, p= 0.056). Similar results were observed

for the correlation between IGT net scores of the last blocks and HRV indexes, where significance after controlling for other variables was maintained for LF (Block 3: r = 0.667, p = 0.009; Block 4: r = 0.716, p = 0.004; Block 5: r = 0.744, p = 0.002) and TA (Block 4: r = 0.642, p = 0.013; Block 5: r = 0.671, p = 0.009).

#### Discussion

The main finding of this study is that performance in the IGT was related to baseline resting LF heart rate variability, an association that is maintained even after controlling for age, sex, risk taking behavior, and reversal learning processes.

There is growing evidence showing that resting autonomic patterns can influence cognitive performance, although none of these studies specifically assessed decision making. For example, grouping healthy subjects according to their resting HRV, the high HRV group showed better results and faster reaction times in a continuous performance test that assesses both executive and non-executive functions <sup>16</sup>. Our results seem to contradict these findings, since they report that subjects with higher high frequency-HRV (a measure of the parasympathetic activity) perform better at executive function tasks <sup>16;17</sup>. Unfortunately, no mention was made in those studies to the low frequency HRV component.

On the other hand, our results are in line with a study that stated that lower resting baroreflex sensitivity, usually associated with a reciprocal reduction of parasympathetic activity and increase of sympathetic activity <sup>18</sup>, predicted higher values in all parameters of attentional capacity <sup>19</sup>. The results of the study suggest that the intuitive idea of an

association between improved attentional capacity and higher resting levels of parasympathetic cardiac tone (probably as a reflection of lower anxiety) does not universally hold. According to the authors, the sympathetic prevalence is interpreted as necessary to establish a pattern of cardiovascular adjustment suitable for coping with increased mental demand <sup>19</sup>.

Another potential explanation for our results is that at least some of the brain regions involved in complex decision making are the same regions responsible for autonomic arousal. In line with this, Critchley <sup>20</sup> observed that activity in several areas, mainly ACC, was strongly associated with increased LF power during cognitive effort. Furthermore, patients with ACC damage failed to generate contextually appropriate autonomic activation, especially sympathetic. Although related to different aspects of the task, activation in ACC has been repeatedly demonstrated during execution of IGT and some of its variants <sup>21-25</sup>.

Additionally, it must be taken into account the possibility that the correlation between IGT net scores and low frequency HRV could be attributed to other specific decision making mechanisms underlying IGT <sup>4</sup>. Previous publications demonstrated that the GDT could be used as an index of risk taking behavior during the last blocks of IGT<sup>5</sup>. However, our results did not replicate the correlations between those tasks, probably due to the small number of participants. Reversal learning is also known to be a process taking place during IGT execution<sup>4</sup>. Although there is no established test related to the IGT to assess reversal learning, the reported correlation between these tasks makes it reasonable to use the RLT as a control of the reversal learning process during the IGT. The obtained correlation pattern between RLT last error trial and the scores of IGT blocks is different from the published pattern for GDT net score correlation with IGT net score, supporting that both tasks assess different mechanisms involved in decision making <sup>5</sup>. Also, age and sex

differences should be considered, since it is known that decision making ability, as well as the amplitude of all the frequency components of HRV decline with age <sup>26;27</sup> and vary with sex<sup>28-30</sup>.

In the present study, the possibility that correlations between IGT net scores and HRV indexes could be explained by the mechanisms discussed above was ruled out by conducting a partial correlation controlling for age, sex, GDT net score and RLT last error trial. Since the results remained significant for LF HRV, sympathetic activation may play an important role in decision making. In addition, the correlation is only significant in the last three blocks of the IGT, supporting the hypothesis that basal ANS activity is critical in the evolution of decision making processes. <sup>1</sup>

The small sample size should be noted as a limitation of this study. Correlations reported herein are larger than those previously reported between physiological measurements and decision making tasks<sup>31</sup>. A possible explanation is that Pearson's correlation coefficients may be biased towards higher values due to the small sample size of the study. Further research with more participants is necessary to confirm these results.

To sum up, autonomic activity could be an important factor for the decision making processes taking place during the IGT, although it is not established whether previous autonomic arousal is crucial for improving decision making or if it is just an index of neural cortical processes. Future investigations should focus on establishing whether there is a causal relationship between higher LF-HRV and decision making tasks, possibly by interfering ANS basal state, either pharmacologically or by means of physical training.

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## Figure 1

**Figure legend:** Correlation between low frequency heart rate variability and the lowa Gambling Test net score (Pearson's r = 0.73, p < 0.001).

			RLT	
	IGT het score	GDT het score	last error trial	
RRm (ms)	-0.03	-0.06	0.17	
SDNN (ms)	0.56*	0.18	-0.17	
RMSSD (ms)	0.39	0.21	-0.06	
In TA (ms <sup>2</sup> )	0.52*	0.01	-0.05	
In VLF (ms <sup>2</sup> )	0.31	-0.09	0.01	
In LF (ms <sup>2</sup> )	0.73***	-0.05	-0.29	
In HF (ms <sup>2</sup> )	0.30	0.13	0.03	
VLF (%)	-0.29	-0.18	0.16	
LF (%)	0.49*	-0.05	-0.29	
HF (%)	-0.21	0.26	0.14	
LF/HF	0.12	-0.09	-0.08	
αs	0.28	-0.07	-0.23	
SampEn	-0.29	-0.12	0.07	

Table 1. Correlations between resting heart rate variability and decision making tasks

Shown are Pearson's r correlation coefficients. \* p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001. IGT: Iowa Gambling Task; GDT: Game of Dice Task; RLT: Reversal Learning Task; RRm, mean RR interval; SDNN, standard deviation of all normal RR intervals; RMSSD, square root of the mean squared differences of successive normal RR; TA, total area (total spectral power); VLF, very low frequency power; LF, low frequency power; HF, high frequency power;  $\alpha$ s, short term scaling exponent alpha; SampEn, Sample Entropy.

	SDNN (ms)	In TA (ms <sup>2</sup> )	In LF (ms²)	LF (%)
IGT net score Block 1	0.06	0.08	0.01	-0.26
IGT net score Block 2	0.15	0.02	0.19	0.27
IGT net score Block 3	0.40	0.39	0.71**	0.59**
IGT net score Block 4	0.63**	0.65**	0.73**	0.40
IGT net score Block 5	0.57*	0.51*	0.68**	0.44

### Table 2. Correlations of heart rate variability indexes with successive IGT net scores

Shown are Pearson's r correlation coefficients. Correlations were calculated between successive IGT net scores and those heart rate variability indexes that previously shown significant correlations with total IGT net score. \* p < 0.05, \*\* p < 0.01. IGT: Iowa Gambling Task; SDNN, standard deviation of all normal RR intervals; TA, total area (total spectral power); LF, Iow frequency power.