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Heart rate variability analysis as an index of emotion regulation processes: Interest of the Analgesia Nociception Index (ANI).

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Abstract — **Autonomic Nervous System (ANS) variations are strongly influence by emotion regulation processes. Indeed, emotional stimuli are at the origin of an activation of the ANS and the way an individual pass from a state of alert in the case of emotional situation to a state of calm is closely coupled with the ANS flexibility.**
We have previously described and developed an Analgesia Nociception Index (ANI) for real time pain measurement during surgical procedure under general anesthesia. This index, based on heart rate variability analysis, constitutes a measure of parasympathetic tone and can be used in several other environments. In this paper, we hypothesized that such an index could be used as a tool to investigate the processes of emotional regulation of a human subject. To test this hypothesis, we analyzed ANI's response to a negative emotional stimulus. This analysis showed that the index decreases during the emotion induction phase and returns to its baseline after 2 minutes. This result confirms that ANI could be a good indicator of parasympathetic changes in emotional situation.

Keywords—**Emotion Regulation, Autonomic Nervous System, Heart Rate Variability analysis.**

I. Introduction

FROM a physiological point of view, emotional stimuli are at the origin of an activation of the Autonomic Nervous System (ANS) to increase the physiological and psychological vigilance in order to face the incoming situation. ANS is composed of two distinct parts; the sympathetic nervous system and the parasympathetic nervous system.

The way an individual pass from a state of alert in the case of emotional situation to a state of calm, that is to say his capacity to regulate his emotions, is closely coupled with the ANS flexibility [1]. According to Porges [2, 3, 4], this ANS flexibility mainly depends on the vagus nerve which constitutes mainly the parasympathetic part of the ANS.

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Heart Rate Variability (HRV) is a commonly used non-invasive measure of ANS cardiac control. Indeed, variations in heart rate (HR) above 0.15 Hz and centered at the respiratory frequency are mediated exclusively by changes in parasympathetic outflow, whereas lower frequency changes are mediated by both changes in parasympathetic and sympathetic outflows [5, 6]. In adult, several studies have shown that pain, fear or anxiety result in a decrease of the HRV high frequency (HF) content (between 0.15 and 0.5 Hz), indicating decrease of the parasympathetic activity during unpleasant stimuli or emotion [7, 8, 9]. During surgery in adult patients, HRV is correlated with the balance between the level of analgesia and the extent of the nociceptive stimulus [7]. On the other hand, other studies have shown that stress and/or anxiety levels are correlated with HRV high frequency content [7, 11, 12].

We have developed an Analgesia Nociception Index (ANI) for pain evaluation during surgery under general anesthesia [13, 14]. This index can be considered as a vagal tone index, based on the ventilatory influence on heart rate, which allows to obtain both a qualitative and a quantitative measurement of HRV.

In this paper, we hypothesized that such an index could be used as a tool to investigate the processes of emotional regulation of a human subject. To test this hypothesis, we analyzed ANI's response to a negative emotional stimulus.

II. Methods and Materials

A – HRV Analysis

ANI is computed from the ECG signal as described below.

The ECG signal is acquired using classical electrodes and digitized at a sampling rate of 250 Hz. The RR series is then built as the time evolution of the time intervals between two successive R waves of the ECG (RR value). R peaks are detected using a previously described R wave detection algorithm [15]. However, RR series is usually disturbed by different kinds of perturbations (ectopic beats, electrode motion…) involving an erroneous analysis of HRV. Therefore, RR intervals series is filtered in real time using an original non linear filtering algorithm [16]. This filtering algorithm, which is based on a morphological analysis of the RR series, is able to detect each disturbed area and to replace the erroneous samples with the most probable ones.

Filtered RR series are then re-sampled at 8 Hz using a linear interpolation algorithm. RRi samples are isolated into

a 64 seconds moving window for analysis and the series is mean centered and normalized for inter patients comparability.

In a first step, the mean value (M) is computed as:

$$M = \frac{1}{N}\sum_{i=1}^{N}(RR_i), \quad (1)$$

Where RR_i represents the RR samples values and N the number of samples in the window. Then M is subtracted from each sample of the window as: $RR_i = (RR_i - M)$. The norm values (S) is then computed as:

$$S = \sqrt{\sum_{i=1}^{N}(RR_i)^2}. \quad (2)$$

and each RR_i is divided by S: $RR'_i = RR_i / S$.

Since the method is based on the analysis of HF changes, the RR'_i series is then band pass filtered between [0.15-0.5 Hz], which leads to RR'_{HF} [17]. In order to perform the band pass filtering, we chose to use a numerical filter based on the 4 coefficients Daubechies wavelet.

HF changes are mainly modulated by respiration. Indeed, breathing influences the way the ANS regulates heart rate. Inhalation temporarily inhibits the influence of the parasympathetic nervous system and increases heart rate, while exhalation stimulates the parasympathetic nervous system and decreases heart rate. These rhythmic oscillations, which are caused by breathing, are called respiratory sinus arrhythmia (RSA).

We observed that, in case of well-being, RSA modulation on HR is important and causes large magnitude on the RR'_{HF} series (figure 1, upper panel), while in case of pain, stress or anxiety, the influence of each respiratory cycle is more chaotic and the series magnitude decreases (figure 1, lower panel).

In order to transform this qualitative observation into quantitative information, we designed a graphical index by computing the area under the RR'_{HF} series curve as shown in figure 1. Local minima and maxima are detected and the upper and lower envelopes are plotted by connecting the local maxima together and the local minima as well. This envelope estimation allows to obtain an index which not depends on respiratory frequency changes [13].

In order to improve the time sensitivity of the method, we then divide the 64sec moving window into four sub-windows of 16 sec. The areas between the lower and upper envelopes are then measured in the four sub-windows. We defined AUCmin as the smallest of these sub-areas.

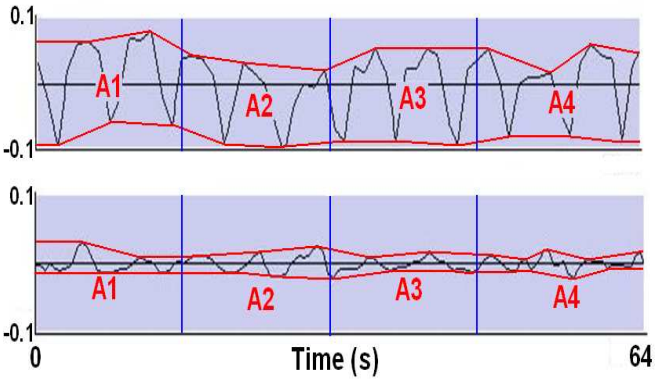


Fig. 1: normalised, mean centered and band pass filtered RR series in two different states of analgesia / nocicetion during general anaesthesia with controlled ventilation: adequate analgesia (upper window) and in the case of surgical stimulus, few minutes before haemodynamic reactivity (lower window).

ANI is then computed in order to express a fraction of the total window surface, leading to a measure between 0 and 100:

$$ANI = 100 * [a*AUCmin+b] / 12.8 \quad (3)$$

Where *a* = 5.1 and *b*= 1.2 have been empirically determined in a general anesthesia data set of more than 100 patients in order to keep the coherence between the visual effect of respiratory influence on RR series and the quantitative measurement of ANI.

This parameter is available through the Physiodoloris® monitor (Fig. 2) commercialised by MetroDoloris® (Lille, France) [18].

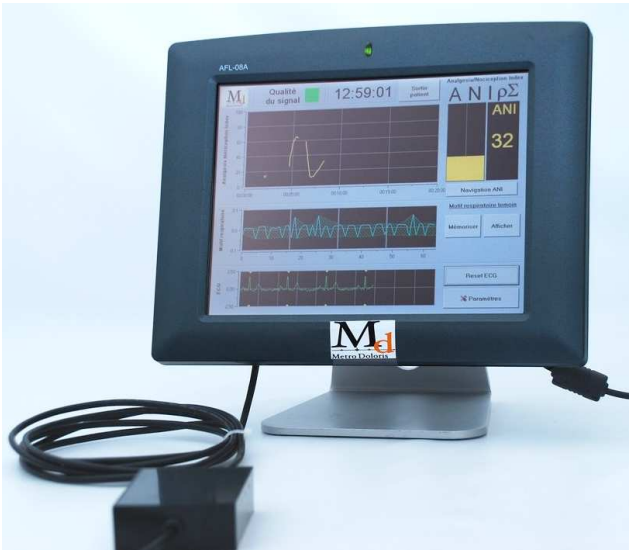


Fig. 2: Physiodoloris monitor. Lower scope: ECG signal. Middle scope: normalised, mean centered and band pass filtered RR series. Upper scope: ANI trend curve.

B – Experimental validation

After institutional approval, ANI response to negative emotional stimuli has been evaluated in a prospective, observational study on adult participants. Participants were student recruited at the Lille 3 university and gave written informed consent. Participants presenting mental or somatic pathologies were excluded from the study. In order not to affect the participant's emotional state, the participant was blind to the Physiodoloris® Monitor. All inclusions were realized between 1 and 3 pm in order to avoid any circadian rhythm variability interaction.

A negative emotional stimulus was induced through the projection of an 80 seconds video. The chosen video was a sample of the film "American History X" which has been characterized by experts as a negative emotion-eliciting film sample with a high level of activation [19].

ANI was measured T1) before the film presentation, T2) just after the film presentation, T3) 2 minutes after the end of the film and T4) 4 minutes after the end of the film.

We tested the difference between the four ANI measures using the Wilcoxon non-parametric statistical test. The statistical tests were considered significant at a p value of 0.05.

At the end of the test, the participants were asked to assess their subjective emotional experience about the film on an 8-point Likert scale ranging from 0 (complete disagreement) to 7 (complete agreement).

III. Results

We investigated 25 participants aging from 18 to 27 years. Emotional experience evaluation results (Table 1) confirms the fact that the visioning of the movie sample can be considered as a high level negative emotional stimulus.

Table 1: Film emotional evaluation

Pleasant	0.91 (1.65)
Unpleasant	5.81 (1.55)
Positive	0.61 (0.83)
Negative	6.35 (0.84)
Funny	0.30 (0.76)
Sad	4.96 (1.92)
Irritant	6.17 (1.43)
Happy	0.30 (0.765)

Data are presented as mean (standard deviation).

As shown in Fig. 3 and Table 2, ANI was significantly lower in T2 vs T1 ($p=0.023$), vs T3 ($p<0.001$) and vs T4 ($p=0.003$). There were no significant differences between T1, T3 and T4.

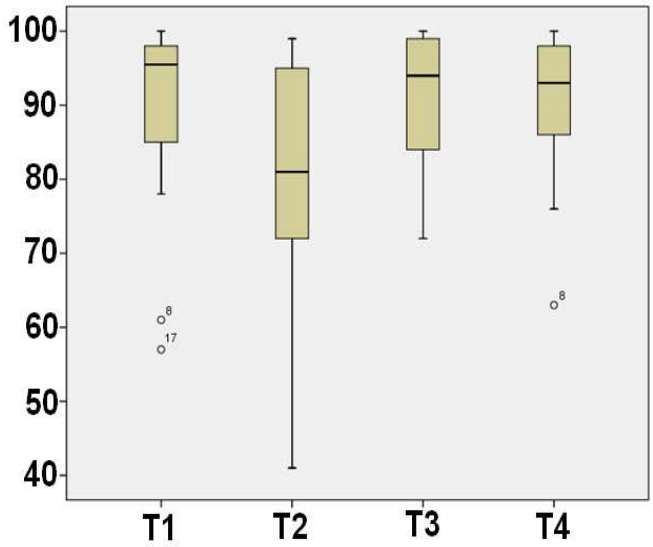


Fig. 3: Box plot for ANI values at T1) before the film presentation, T2) just after the film presentation, T3) 2 minutes after the end of the film and T4) 4 minutes after the end of the film.

Table 2: ANI values at T1, T2, T3 and T4

T1	95.5 (85-98)
T2	81 (71.5-95.5)
T3	94 (84-99)
T4	93 (85-98)

Data are presented as median (25 centile – 75 centile).

IV. Conclusion

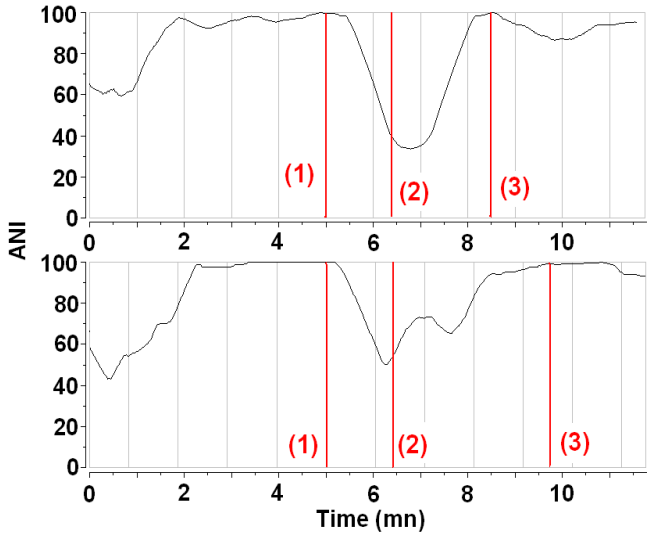
This paper presents the application of a HRV index to the particular domain of the evaluation of ANS changes related to a negative emotional stimulus.

The clinical study presented in this paper indicates that a negative emotional stimulus is associated with a decreased ANI, thus confirming ANI monitoring as a tool capable of measuring a change in the emotional status of a healthy volunteer.

Indeed, the low ANI level during the stimulus induction could be interpreted as a parasympathetic drop during a negative emotion or experience confirming the results of [7] and [8]. Furthermore, we can see that, most of time, ANI returns to its baseline measurement during the two minutes following the stimulus (T3-T2). This main result could be interpreted as the mean time the healthy volunteers need to retrieve a state of calm or regulate their emotional activation.

However, this duration value can vary from a subject to another even in our sample of healthy volunteers. Indeed, individual ANI trend curves presented in fig. 4 shows the example of a participant who needed 2 minutes to retrieve

his baseline ANI value (Upper panel) and another one who needed 3 minutes (Lower panel).



Legend: (1) Start of the stimulus, (2) end of the stimulus, (3) return to baseline

FIG. 4: Two examples of individual ANI trends.

Even if further experimental and clinical studies are needed to assess whether ANI can be used as an indicator to assess parasympathetic changes related to the emotional state of a human subject, this preliminary study suggests that ANI could be able to measure the time a patient needs to regulate his emotional responses (pass from a state of alert to a state of calm) and could constitute an helpful tool for emotional regulation physiological mechanisms understanding.

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