Cardio-respiratory characterization during GOODVIBES usage

Aurelien Bricout, Damien Colas, Ph.D.
Holi, Lyon, France, mars 2017

I. BACKGROUND

INSOMNIA PREVALENCE AND DEFINITIONS

Insomnia is a highly prevalent condition affecting from 15 to 45% of the general population according to various studies (Ohayon 2002, Chan-Chee et al. 2011). Insomnia is associated with a host of detrimental consequences ranging from attention deficits to immune system impairments (Pollack et al. 2009, Buysse 2013). Not surprisingly, the economic burden of insomnia is massive ranging from 10 to 100 billion $ according to studies (Walsh 2004, Wickwire et al. 2016). Insomnia can be inked to difficulties initiating sleep (Ohayon et al. 2012). In such case insomnia is often associated to environmental and/or behavioral mechanisms such as anxiety and mental over-activity (Han et al. 2012, Fernandez-Mendoza and Vgontzas 2013, Palagini et al. 2017).

CBT VERSUS PHARMACOLOGICAL

Correlatively, the first line strategies for managing insomnia are, broadly speaking, sleep hygiene, mind-body approaches and cognitive-behavioral therapies (CBT) (Siebern and Manber 2010, Manber et al. 2011, Watanabe et al. 2015, Bostock et al. 2016, Thiart et al. 2016). These strategies aim at securing a permissive environment for sleep, reducing stress/anxiety/ruminations and learning new associations regarding sleep beliefs.

On the contrary, pharmacological approaches have been associated with a range of side effects and long term consequences that preclude their usage in first line intention and should be kept for the most severe situations (Wafford and Ebert 2008, Ioachimescu and El-Solh 2012). Using hypnotics drugs, in particular benzodiazepines, has been shown to induce memory impairments and may be an aggravating parameter for neurodegenerative diseases (Vermeeren and Coenen 2011, Gallacher et al. 2012, Billioti de Gage et al. 2014).

Overall, non pharmacologic approaches for insomnia are better than pharmacological ones because they are effective at restoring sleep without inducing sides effects (headache, daily torpor, memory disturbances). CBT is 40% more efficient than pharmacotherapy for improving sleep latency (Jacobs et al. 2004).

BREATHING & RELAXATION TECHNICS

A prerequisite for CBT is for the patient to obtain a relaxed state that is a prerequisite for the onset of sleep. Therefore, CBT can extend to relaxation techniques based on breathing and mentation exercises.

Indeed, breathing is a powerful tool to gain control over the mind. It has been shown that paced breathing is effective at mitigating anxiety (Plews-Ogan et al. 2005, Young 2011, Cernes and Zimlichman 2015, Chien et al. 2015, Neuendorf et al. 2015). The neurobiological basis for such a relationship are documented by a number of well established academic results (Porges et al. 1994, Yasuma and Hayano 2004, Scott and Weems 2014, Jennings et al. 2016).

In brief, breathing is the only autonomic function that can be voluntary controlled. Indeed, cortical networks (frontal cortex) can directly influence the autonomic stages (pons-medula-autonomic nerves) for imposing breathing rhythms. In turn, the actual breathing rhythms are sensed by the autonomic neural system and influence the cortical functioning among which anxiety mechanisms (Brugnera et al. 2017).

More specifically, breathing is influenced by two opposing autonomic systems: the sympathetic system is broadly associated with active and/or stress responses, the parasympathetic system (or vagal system) is broadly associated with relaxation (Servant et al. 2009, Gold 2015). During sleep onset, the parasympathetic control of sleep becomes predominant (Trinder et al. 2001). Hence, we can see that relaxation and parasympathetic activation are a premium situation for the onset of sleep.

ACQUIRING BREATHING TECHNICS

Even if paced breathing is a powerful tool for reducing anxiety and unleash sleep mechanisms, it is not broadly used in the general population. Indeed, most people don't even know the positive effects on breathing and lots of them have to learn how to breath again. Breathing exercises can seem difficult and require a personal engagement and discipline. Both aspects can be achieved through personal coaching or yoga for instance.

To overcome those difficulties Holi has conceived GOODVIBES, a personal breathing trainer to help those who want to learn breathing exercises and help them fall asleep faster.

GOODVIBES is a small device that produces a light pattern, users have to follow with their breathing. It is based on the 4-7-8 relaxation method, inspired by yoga. It is a simple exercise that last 3 minutes everyone can perform on its bed before going to bed:

- When GOODVIVES' light is red – inhale (4 seconds)
- When it's yellow – hold one's breathe (7 seconds)
- When it's orange – exhale (8 seconds)

Indeed, it has be shown that breath holding is associated with vagal activation. We believe that GOODVIBES can help people achieve a specific breathing pattern that will help them relax and fall asleep faster.
A way to assess the autonomic control of the cardio-respiratory system is to assess heart rate variability (HRV) using electro-cardiography (ECG).

II. GOAL AND EXPERIMENTAL PLAN

In the current report our goal was to characterize the cardio-respiratory mechanisms occurring during GOODVIBES usage in a sample of random users in the closest to the real life situation possible environment. In particular, we investigated the parasympathetic control of the cardio-vascular system. For this purpose, we wanted to measure the breathing rate (BR), the heart rate (HR) and the HR variability (HRV) of users over the course of GOODVIBES usage.

METHODS

- **Participants:** 9 GOODVIBES users participated in the study. Age range was 23 to 43, with normal physiology and no pathology, 4 males and 4 females. None of the participants reported negative feelings of anxiety at the beginning of the recording session.
- **Recordings** were obtained by a g-tech multipurpose amplifier with a 0.1-100 Hz band-pass and stored on a PC.
- **Electrocardiogram**: Participants were equipped with a two leads ECG. ECG signals were acquired at 256Hz and stored for subsequent analysis at 16 bits.
- **Plethysmography**: participants were equipped with thoracic belt for inductance plethysmography. Breathing signals were acquired at 12.5Hz sampling rate and stored for subsequent analysis at 16 bits.
- **Data analysis**: Signals were visualized in math lab and ECGs were further processed using Kubios (http://www.kubios.com/hrv-standard/). Kubios is a free software that allows the quantification of HR and HRV by calculating the actual R-R intervals from the ECG signal. R-R intervals do not happen as regularly timed intervals, on the contrary R-R intervals are distributed with various length of durations

over time. The frequency domain analysis of R-R intervals is characterized by three majors frequency bands: very low frequency (VLF): [0-0.04]Hz, low frequency (LF): [0.04-0.15]Hz and high frequency (HF): [0.15-0.4]Hz. The HF band is predominantly controlled by the parasympathetic system []. Therefore, the so called "HF/LF" ratio is a surrogate marker for vagal activation when breathing rate is controlled [] and over a minimum stationary segment of 7 minute []. BR were visually scored on the plethysmograph display on a minute basis. Individual breathing signals were subsequently averaged for calculating a mean breathing pattern over time within the experimental group.

- **Experiment protocol**: Experiments were performed in a home style setting in the morning. Participants were installed on a sofa and equipped with recordings probes in a quiet dim room. The GOODVIBES was placed nearby. The recording sessions lasted 23 minutes.

PROTOCOL

Participants were asked to follow the following instructions:

- Baseline: 10 minutes, immobile, eyes open, GOODVIBES off, with a spontaneous (normal breathing), lights on.
- GoodVibes: 3 minutes, immobile, eyes open, GOODVIBES on, instructed breathing, lights off.
- Response: 10 minutes, immobile, eyes closed, GOODVIBES off, spontaneous breathing in relation to previous pace, lights off

Statistics: HR and BR were computed every minute over the course of the experiment. HRV LF/HF were computed over the 10 minutes of baseline and response segments, averages over 10 minutes periods were obtained. HF, BR and LF/HF are expressed as mean±S.E.M (n=9). Statistics used were, two-tailed t test for paired data between the 10 minute response and 10 minute baseline segments with * $p<0.05$.

III. RESULTS

QUALITATIVE

Experimenters ensured that raw data quality met criteria for subsequent analysis. The entire raw data set of the 9 participants were included for data analysis. Full quietness was not reached in the experimental "home setting", as the experiment took place in the morning. Nevertheless, the GOODVIBES stimulation worked as expected showing the timed sequences of red-orange-yellow lights that were clearly visible to the participants. All the participants were alert at the beginning of session while all of them were drowsy at the end of the session. All the participants could follow the GOODVIBES breathing pace (Figure-2).

QUANTITATIVE

Breathing: the mean breathing rate was stable during the baseline and the response session around 15-17 breaths/minutes. As expected during the GOODVIBES stimulation the BR was 3 breaths/minutes (Figure-1.a). Interestingly, when breathing patterns were considered in the whole participants group as an averaged (Figure-2), the following patterns were visible: in baseline, the group shows a typical non synchronized breathing pattern, during GOODVIBES, as expected, a strong synchronized pattern appears. Event more interesting, the pattern did last after GODDVIBES exercise, showing the long term effect of GOODVIBES after its use.

Heart: the mean HR was also stable though showing a trend for a reduction over time (64±3 BPM before GOODVIBES, 59±2 BPM after GOODVIBES). Interestingly, the mean HF/LF ratio was 2.66±0.45 before GOODVIBES and 1.60 ± 0.38 after GOODVIBES, this difference was statistically significant (t-test, $p<0.05$).

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Figure-1: cardio-respiratory parameters

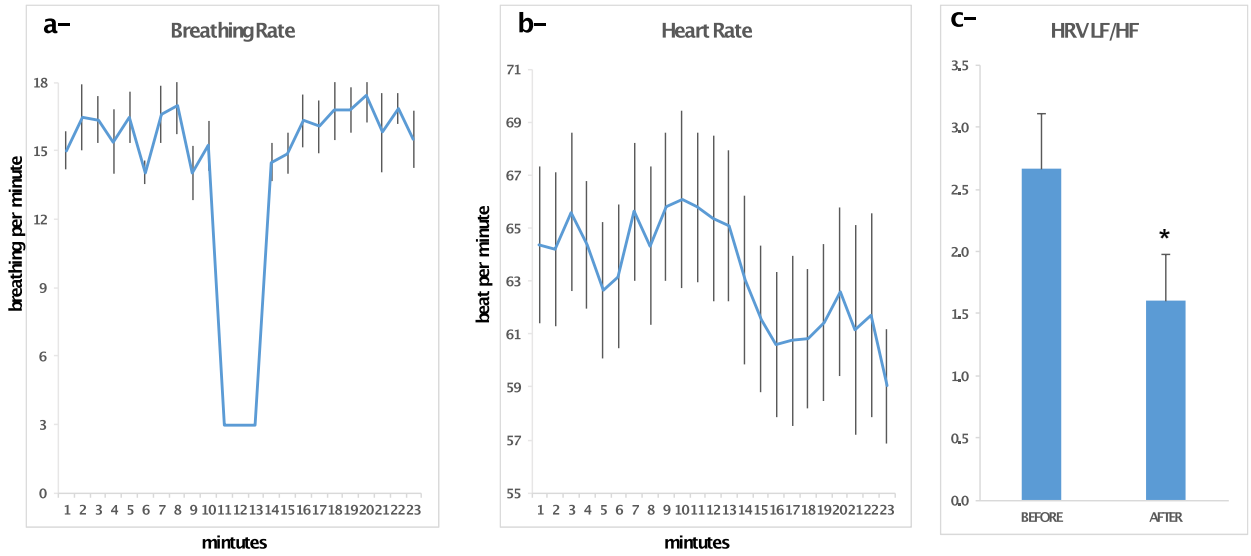

Figure-1: cardio-respiratory function during GOODVIBES usage. (a) Data are mean BR ± S.E.M. per minute over the 23 minutes of recordings, (b) data are mean HR ± S.E.M per minute ober the 23 minutes of recordings, (c) data are mean LF/HF over 10 minutes segments of baseline (before GOODVIBES) and response (after GOODVIBES).

Figure-2: Group breathing synchronization

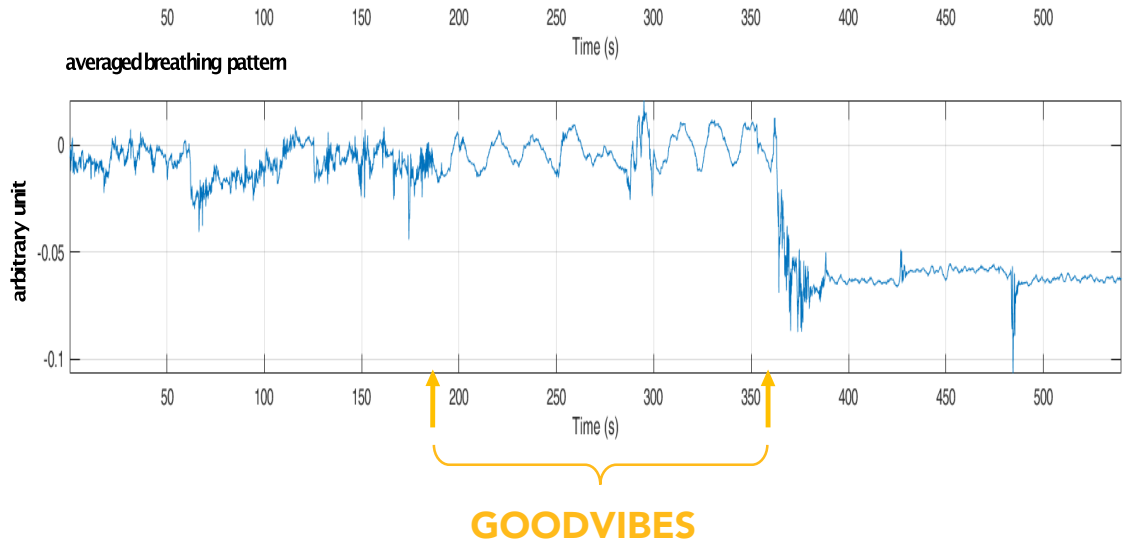

Figure-2: Group breathing synchronization over time before, during and after GOODVIBES usage. Data show the average of raw individual plethysmography patterns (n=8) over 10 minutes including the 3 minutes of GOODVIBES usage. The yellow arrows depict the starting and ending of GOODVIBES stimulation. Prior to GOODVIBES starts, breathing is desynchronized within the group; after GOODVIBES usage, the group of users shows a highly synchronized breathing pattern.

DISCUSSION AND INTERPRETATION

GOODVIBES was easy to use and readily allowed users to implement the recommended highly synchronized breathing pattern. The pattern of respiration indicated by GOODVIBES was easily achieved by all participants. Moreover, the learned pattern during GOODVIBES stimulation was associated with a subsequent increase in breathing synchrony. This shows that while GOODVIBES stimulation only lasts 3 minutes, this imposed pattern elicited a long lasting learning of a synchronized breathing pace. Moreover, using GOODVIBES was able to synchronize the breathing of a whole group of persons which can be useful in some yoga or mindfulness applications.

In the course of the experiment, all the users felt strongly drowsy.

The experiment was carried out in a home style environment which is close to the normal usage conditions of the product but that doesn't allow a strict control of all the environment conditions. Nevertheless, regarding the cardio-vascular parameters the BR and HR obtained after GOODVIBES usage were compatible with those seen in sleep (of note HR during sleep in an equivalent group was found at 58 BPM (Trinder, Kleiman et al. 2001)).

With respect of the cardiac autonomic control, drowsiness was associated with a significantly reduced HF/LF ratio which is indicative of a parasympathetic activation for 89% of GOODVIBES testers. The level obtained after GOODVIBES was intermediate between the levels seen during wake (2,47±1.51) and sleep (0.82±0.81) in a similar group (Chelly et al. 2014). This state of reduced sympathetic activity and increased relaxation is compatible with the onset of sleep (Trinder, Kleiman et al. 2001). GOODVIBES was not associated with a bold reduction in HR, this is likely due to the time of day of the experiment (HR is lower in the morning), the participants were not particularly stressed or exhausted, the participant were randomly picked up yielding to an important inter-individual variability.

Conclusion

Using GOODVIBES is associated with increased parasympathetic activity that facilitates sleep onset. GOODVIBES elicits a robust learning of a specific breathing pattern. GOODVIBES exercise is easy to follow and its effects are significant from the 1st use to induce relation on a non-pathologic group of people.

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