The use of cognitive mobile games to assess the interaction of cognitive function and breath-hold

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A B S T R A C T

The relationship between cognitive function and breath-holding time is in need of further investigation. We aim to determine whether cognitive mobile games (CMG) are sensitive enough to assess the link between cognition and breath-holding time in non-trained subjects. Thirty-one healthy subjects participated in this study. A set of 3 short CMGs: Must Sort (response control), Rush Back (attention, working memory) and True Color (mental flexibility, inhibition) was used. Apneic time was recorded in three different conditions: Total Lung Capacity (TLC): 88 ± 35 s, Functional Residual Capacity (FRC): 49 ± 17 s, and Residual Volume (RV): 32 ± 14 s. In males, breath-holding time at RV was correlated with True Color (r = 0.48) and Rush Back (r = 0.65) and at TLC with True Color (r = 0.45). In women, breath-holding time at TLC and FRC was inversely correlated with Must Sort (r = −0.59 and r = −0.49 respectively). Males and females appeared to differ in their use of cognitive resources during different breath-holding conditions.

1. Introduction

Over recent years, the relationship between cognitive function and athletic performance has become investigated in more detail (Walsh, 2014). It is well-documented that competitive and elite athletes in several sports such as volleyball (Alves et al., 2013), football (Vestberg et al., 2012), taekwondo (Brevers et al., 2018), as well as in endurance sports like cycling (Martin et al., 2016) and ultra-marathons (Cona et al., 2015), present higher levels of attention, cognitive control, inhibition and executive function compared to control populations. Executive function is an important factor for self-regulation and decision-making, as well as for physical agility in sport and endurance performance (Hyland-Monks et al., 2018). Voluntary apnea in sports may also require significant self-regulation and cognitive control.

Other sports like biathlons and freediving also require coordination of breath-holding control. Furthermore, breath-holding is also a technique used prior to the trigger pull in rifle shooters to increase shooting accuracy (Kontinen and Lyytinen, 1992). Conversely, increases in minute ventilation and respiratory rate have been shown to decrease shooting accuracy (Groslambert et al., 1998). The most probable explanation for these findings is related to increased postural sway when ventilation is increased (David et al., 2015), since body sway is a factor that is known to influence shooting performance (Laaksonen et al., 2018). Some authors suggest that breath-holding improves postural control (Caron et al., 2004), but this hypothesis is disputed (Malakhov et al., 2014).

Apnea has been mainly studied from a physiological point of view regarding neurophysiological modulations elicited by hypoxic and hypercapnic conditions (Bain et al., 2018). However, other factors such as emotional stimuli may also play an important role (Menicucci et al., 2014). The process of breathing can be automatic or voluntary (e.g., apnea, forced expiration). Automatic breathing can be subdivided into three phases: expiration, inspiration, and post-inspiratory (Dutschmann et al., 2014), and control of ventilation is carried

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out in the spinal bulb, specifically at the rostral ventral lateral medulla level (Morrell et al., 2001). During quiet breathing there is no activation of the cortex (Nguyen et al., 2018; Raux et al., 2007); the cortex is activated during breathing throughout inspiratory and expiratory load (Raux et al., 2007), expiratory load (Morawiec et al., 2015), in patients with expiratory flow limitation (Nguyen et al., 2018), during the voluntary sniff (Hudson et al., 2016), and during breath-holding (McKay et al., 2008).

The active inhibition of breathing involves the insula, basal ganglia, and parietal and frontal cortices (McKay et al., 2008). Since most of the cortical regions are also involved in several cognitive processes, it is not surprising that apnea may interfere with cognitive functioning (Nierat et al., 2016). Interestingly, not all cognitive functions are affected by apneic interference, though amongst those that are, response inhibition appears to be the most affected function (McKay et al., 2008; Pattinson et al., 2009).

Owed to the evolution of informatics and gaming technology, the popularity of video games is ever increasing, not only for entertainment purposes but also for their use in the rehabilitation field: studies investigating the therapeutic use of video games are increasing in number, as well as the pathologies showing potential to be managed by them (Bonnehère et al., 2016). A useful aspect of game training is that it can be combined with cognitive (Bonnehère et al., 2018b) or physical (Bonnehère et al., 2018a) assessments to provide lower-cost and more regular screening and follow-ups of cognitive function without the need of a healthcare professional, since the results of the games are correlated with clinical scales (Bonnehère et al., 2018b).

Our hypothesis is that prolonged apnea time in non-trained breath-holders is determined by cognitive function and that the scores obtained in cognitive mobile games (CMG) designed for brain training can reflect the relationship between prolonged apnea and cognitive function.

The aim of this study was to therefore determine whether specific CMG designed for cognitive training can be used to explore the links between cognitive function and breath-holding time. To the authors’ knowledge, the majority of existing studies concerning the links between the physical performance and cognitive function discuss those of elite athletes, and do not compare effects between genders. Thus, our second aim was to study those links in untrained male and female subjects.

2. Materials and methods

2.1. Participants

Thirty-one healthy participants aged 21–31 were recruited in this study (Table 1). The Ethical Committee of Erasme Hospital (P2016/ 468/B406201629933) approved this study and all subjects provided written informed consent prior to their participation. Exclusion criteria included any diagnosed neurological conditions, known cognitive impairment and/or abnormally low respiratory values as measured by FEV1 (forced expiratory volume in 1 s) below 70% of the predicted value (Miller et al., 2005).

2.2. Protocol

All subjects underwent anthropometric and lung function measurements. Lung function was assessed by spirometry (hand-held spirometer/USB Pocket-Spiro® MPM100 MEC Medical Electronic Construction R&D Manufacturer: M.E.C. R&D sprl, Brussels, Belgium) including FEV1 and vital capacity (VC) following the guidelines of the American Thoracic Society and European Respiratory Society (Miller et al., 2005). The FEV1 and VC values were determined as the best of three consecutive attempts as recommended by the aforementioned societies.

Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Whole group (n = 31)</th>
<th>Male (n = 16)</th>
<th>Female (n = 15)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>24.8 (2.2)</td>
<td>25.6 (1.9)</td>
<td>24.3 (2.3)</td>
<td>0.11</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.1 (8.7)</td>
<td>73.0 (5.5)</td>
<td>60.4 (6.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>173 (7.5)</td>
<td>178 (5.5)</td>
<td>168 (5.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.3 (2.1)</td>
<td>23.1 (2.0)</td>
<td>21.4 (1.8)</td>
<td>0.017</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>3.8 (0.6)</td>
<td>4.1 (0.44)</td>
<td>3.4 (0.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV1 (predicted%)</td>
<td>98.9 (10.2)</td>
<td>98.8 (11.6)</td>
<td>99.0 (8.8)</td>
<td>0.94</td>
</tr>
<tr>
<td>VC (L)</td>
<td>4.3 (0.7)</td>
<td>4.8 (0.3)</td>
<td>3.8 (0.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Mean (std), p-values are the results of t-tests for gender comparisons; VC, Vital Capacity; FEV1, forced expiratory volume in the 1st second.

Moreover, three breath-hold conditions were tested:

1) Breath-holding at Total Lung Capacity (TLC). Subjects were asked to take in as much air as possible after a calm breath and to hold their breath for as long as possible.

2) Breath-holding at the end of normal expiration (FRC). Subjects were asked to breathe normally. Following normal expiration, subjects held their breath for as long as possible.

3) Breath-holding at Residual Volume (RV). Subjects were asked to hold their breath following complete expiration.

For each condition we recorded the total duration of subjects’ breath-holding time (referred to later on in the text as ‘time’) as well as the time the subjects spent without pain or discomfort (referred to later on as the ‘time without symptoms’; TWS).

The order of the conditions was randomized to avoid any potential bias (Schagatay et al., 1999). To ensure that breath-holding was carried out correctly, the subjects were connected to a spirometer and wore a nose clip. Subjects were not allowed to hyperventilate before the different breath-hold conditions and both blood oxygen saturation and heart rate were monitored.

For each condition, the subjects were instructed to indicate at what point they began to experience any symptoms of pain or discomfort by pressing a stopwatch button, allowing us to compute the TWS.

Unpleasantness and the degree of effort were evaluated in each condition using a modified version of the ‘Breath-holding task-experience questionnaire’ developed by Süttelin et al. on the following scales (Süttelin et al., 2013):

a) The unpleasantness experienced, on a 10-centimeter analog visual scale (0: extremely unpleasant, 10: extremely pleasant).

b) The degree of effort required to perform the task (0: absolutely no effort, 10: an extreme amount of effort).

Depressive symptoms of the participants using the Hospital Anxiety and Depression Scale (HAD).

2.3. Cognitive evaluation

Three short CMG were used to evaluate domain-specific cognitive functions, and were selected based on their similarities to neuropsychological assessment tests. Screenshots and descriptions of the CMG are presented in Table 2. The use of these CMG has been previously validated as a tool to assess acute modifications of cognitive function induced by various inspiratory loads (Van Hove et al., 2019).
Table 2

<table>
<thead>
<tr>
<th>Games</th>
<th>Screenshot</th>
<th>Instruction</th>
<th>Score</th>
<th>Objective</th>
<th>Tests</th>
</tr>
</thead>
</table>
| Must Sort  | ![Must Sort Screenshot](image1) | Sort the items correctly by tapping on the corresponding sides               | Base score multiplied by streak multiplier, streak is incremented by correct answers and is reduced to 1 on incorrect or more than 5 seconds between answers. | • Response control  
• Task shifting                  | Go/No-Go task |
| Rush Back  | ![Rush Back Screenshot](image2) | Memorize the card and respond to whether the current card matches the card that came before it | Base score with a multiplier which goes up and down based on streak. Streak up of 4 correct in a row but not changed during game play  
Bonus for end of game, current streak multiplier * bonus | Sustained attention  
• Visual recognition  
• Working memory | N-Back        |
| True Color | ![True Color Screenshot](image3) | Respond to whether the word on the bottom corresponds to the correct color (top word) | Base score with a multiplier which goes up and down based on streak. Streak up of 4 correct in a row but not changed during game play  
Bonus for end of game, current streak multiplier * bonus | Inhibitory control  
• Mental flexibility | Stroop Task    |

Prior to the start of the task, the game instructions were given to the subjects and they played each CMG once before testing commenced to allow familiarization with the games. The order of the CMG was randomized.

2.4. Statistics

Normality measures of each parameter were checked using graphical methods (boxplots, histograms and QQ-plots) and homogeneity of variances using Levene’s test. Two-way analysis of variance (ANOVA) tests were applied to compare the three breath-hold conditions and gender, as well as interactions between those factors. Pearson’s correlation coefficients (r) were computed between the CMG and the breath-hold parameters. A two-sided level of significance was set at $p < .05$. Statistical analyses were carried out using the software RStudio (version 1.1.442) with R version 3.4.4.

3. Results

Results of the CMG and data collected during the three breath-hold conditions are presented in Table 3. No statistically significant differences were found in CMG scores between males and females: $t(29.6) = −1.5, p = .15$ for Must Sort, $t(29.4) = −1.4, p = .15$ for Rush Back and $t(25.1) = −1.6, p = .12$ for True Color.

Concerning the different breath-hold conditions, the two-way ANOVA yielded main effects on time for gender, $F(1, 90) = 10.1, p = .002$ – such that the average breath-hold time was significantly higher in men (15 s [95% CI: 6–25]) – and for breath-hold condition $F(2, 90) = 47.6, p < .001$. The interaction effect between the gender and the breath-hold conditions was non-significant, $F(2, 90) = 0.46, p = .63$. In the TWS condition, the effect of gender was not significant, $F(1, 90) = 2.4, p = .12$, the breath-hold conditions was significant $F$...
Let's analyze the given text step by step.

First, we identify key sections of the text:

1. **Parameters**
2. **Functional Residual Capacity**
3. **Residual Volume**
4. **Discussion**

Next, we extract relevant parts of the text and organize them into a coherent format

### Table 3

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Whole group (n = 31)</th>
<th>Male (n = 16)</th>
<th>Female (n = 15)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive evaluation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rush Back</td>
<td>20.43 (1854)</td>
<td>21.03 (1918)</td>
<td>19.36 (1850)</td>
<td>0.31</td>
</tr>
<tr>
<td>True Color</td>
<td>8566 (3003)</td>
<td>9317 (2554)</td>
<td>7482 (3358)</td>
<td>0.20</td>
</tr>
<tr>
<td>Total Lung Capacity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time (s)</td>
<td>88 (35)</td>
<td>96 (44)</td>
<td>77 (23)</td>
<td>0.06</td>
</tr>
<tr>
<td>Functional Residual Capacity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time with symptom (%)</td>
<td>38 (21)</td>
<td>44 (19)</td>
<td>32 (21)</td>
<td>0.11</td>
</tr>
<tr>
<td>Unpleasantness</td>
<td>5 (1)</td>
<td>5 (1)</td>
<td>5 (2)</td>
<td>0.89</td>
</tr>
<tr>
<td>Effort</td>
<td>7 (2)</td>
<td>7 (1)</td>
<td>7 (2)</td>
<td>0.95</td>
</tr>
<tr>
<td>Time (s)</td>
<td>49 (17)</td>
<td>54 (20)</td>
<td>45 (14)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

### Table 4

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Time</th>
<th>TWS</th>
<th>Unpleasant-ness</th>
<th>Effort</th>
<th>Time</th>
<th>TWS</th>
<th>Unpleasant-ness</th>
<th>Effort</th>
<th>Time</th>
<th>TWS</th>
<th>Unpleasant-ness</th>
<th>Effort</th>
<th>Time</th>
<th>TWS</th>
<th>Unpleasant-ness</th>
<th>Effort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rush Back</td>
<td>0.35</td>
<td>0.23</td>
<td>0.20</td>
<td>0.17</td>
<td>0.29</td>
<td>0.02</td>
<td>0.12</td>
<td>0.13</td>
<td>0.25</td>
<td>0.13</td>
<td>0.31</td>
<td>0.35</td>
<td>0.22</td>
<td>0.03</td>
<td>0.09</td>
<td>0.23</td>
</tr>
<tr>
<td>True Color</td>
<td>0.33</td>
<td>0.16</td>
<td>0.06</td>
<td>0.10</td>
<td>0.25</td>
<td>0.13</td>
<td>0.31</td>
<td>0.03</td>
<td>0.35</td>
<td>0.22</td>
<td>0.03</td>
<td>0.35</td>
<td>0.14</td>
<td>0.14</td>
<td>0.02</td>
<td>0.02</td>
</tr>
</tbody>
</table>

### Discussion

This study has two main conclusions: 1) there were no sex-related differences in cognitive scores, but 2) there were differences in total breath-holding time in favor of the males, which is not in line with results from previous studies (Cherouev et al., 2013).

The different CMG require the use of differing cognitive functions: sustained attention and working memory in Rush Back (In-back game), inhibitory control and mental flexibility in True Color (Stroop Test-like game), and inhibition in Must Sort (a simplified Go/no go test). Breath-holding is associated with, among other brain regions, the parietal cortex, frontal cortex (McKay et al., 2008) (associated with inhibitory response (Watanabe et al., 2002)) as well as areas responsible for working memory (Funahashi, 2017) and flexibility (Kim et
al., 2011). Our study shows a moderate and significant correlation between scores in True Color and Rush Back and breath-holding time at RV in the whole group. Rush Back also presents a moderate but statistically significant correlation with time at TLC. In a relatively similar protocol, Sütterlin et al. observed a link between executive function and breath-holding time at RFC (Sütterlin et al., 2013), which was not the case in our study. In another study, self-assessed persistence with difficult tasks was not related to breath-hold time after deep breathing (Thompson-Lake et al., 2017).

We then performed gender-based subgroup analyses. For the males, breath-holding time at RV was strongly and significantly correlated with scores in Rush Back. The same observation was found for the TWS at RV. Scores in True Color showed a moderate and significant correlation with the time at TLC and at RV in the male subjects.

The female subjects showed a strong and statistically significant negative correlation between Must Sort and breath-holding time at TLC and a moderate and significant correlation with the time at RFC. In the study by Sütterlin et al., where there was no correlation between the executive function and the breath holding at RFC, the level of unpleasantness experienced by subjects was moderate (Sütterlin et al., 2013), however in our study, the levels reached were higher and, consequently, executive control resources may have been more affected. However, the effect of the level of unpleasantness of the executive resources was only observed in women in our study.

The link between game scores and breath-holding time appears more obvious here compared to previous study (Sütterlin et al., 2013). Interestingly, this link differed in females and males. For the females, Must Sort scores were inversely correlated with breath-holding time. For males, breath-holding was positively correlated with scores in Rush Back and True Color. We observed the same phenomenon when we investigated the correlation between unpleasantness scores and game scores. Males with higher Must Sort scores tolerated more unpleasantness than those with lower Must Sort scores (at RFC); for the females, we observed the opposite effect (at TLC). For the other games there were no statistically significant correlations. Differences in unpleasantness tolerance have already been shown in males and females (Smith et al., 2019). In tests of breathing, females have been shown to possess a more sensitive (but less specific) perception of altered respiratory function (Becklake and Kauffmann, 1999). Males and females do not react in the same way to a sustained inspiratory load. While there is no increase in sensitivity during sustained breathing to a high inspiratory load in males, females present potentiation of the perceptual response, thus demonstrating a habituation effect in males and increased perception in females (Alexander-Miller and Davenport, 2010). Indeed, during prolonged breathing through an inspiratory load, females demonstrated a more significant sentiment of displeasure, fear of suffocation or dizziness compared to males (Miller and Davenport, 2015). The present study is the first, to our knowledge, to demonstrate that males and females do not react in the same way during cognitive and breath-holding tasks. Furthermore, like the previous study, there was no significant difference in breath-holding time at TLC and RFC (Cherouve et al., 2013). In our study there was a significant difference between males and females in breath-holding time at RV. This may be explained by physiological factors as discussed previously. There is indeed a moderate correlation between the time at RV and the FEV1 and VC. But the VC is significantly smaller in females than in males. The previous study demonstrated links between pulmonary function, breath-holding time and lung volume in apneic divers (Ferretti et al., 2012; Schagatay et al., 2012), however not in healthy subjects at RV (Viecelli et al., 2012).

There are a number of limitations to our study. The first is that we did not assess participants’ baseline cognitive performance prior to the study using conventional tests and scales, so we cannot rule out the possibility of existing between-gender cognitive differences. Instead of using pen and paper tests, we used the CMG results as a proxy of cognitive function and did not observe any between-gender differences in CMG scores. Though it could be argued that the use of traditional clinical tests would have been more effective in evaluating subjects’ cognitive functioning, the use of digital games as an assessment of cognitive performance has already been validated in a previous study (Anguera et al., 2013). Furthermore, the games used in the present study have been shown to be good indicators of cognitive function (Bonnehère et al., 2018b; Van Hove et al., 2019).

A second limitation is that we did not assess subjects’ quality or quantity of sleep the night preceding the experiment. This variable may have confounded results as it is known that a lack of sleep negatively affects cognition (Rana et al., 2018) and physical capacity (Watson, 2017) and could have therefore influenced both breath-holding times and the results of the CMG. We did, however, assess depressive symptoms of the participants using the HAD and found no difference between the genders.

Despite its limitations, our study suggests that males and females use cognitive resources differently under cognitively stressful conditions.

5. Conclusion

Breath-holding requires a variety of cognitive resources and involves some of the same cortical areas as those required for executive functions. This study suggests that CMG can assess the links between cognitive function and maximum breath-holding time.

The scores obtained with the CMG reflect an interaction of breath-holding time and cognitive function. Interestingly, males and females appeared to differ in their use of cognitive resources during different breath-holding conditions.

Authors’ contributions

OVH and BB designed the protocol of the study, OVH did the experiments, BB performed the data analysis and statistics, OVH, AVM, VA and DL interpreted the results. OVH, GD and BB draft the first manuscript, AC, VF and BB revised the manuscript. All the authors participated in the revision of the last version of the manuscript and approved it.

Declaration of Competing Interest

None of the authors declare competing financial interests.

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References


