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Carbohydrate vs. Placebo: a fMRI BOLD response during different intensities of motor imagery

Carboidrato vs placebo: resposta de BOLD fMRI durante diferentes intensidades de imaginação motora

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RESUMO

Objetivo. O objetivo deste estudo foi verificar os efeitos da ingestão de CHO na ativação cerebral durante diferentes intensidades de Imginação Motora (IM). **Método**. Nove indivíduos (oito homens, 28±4,6 anos) participaram deste estudo e foram submetidos a paradigma de Ressonância Magnética funcional baseado em blocos de IM (corrida, com percepção subjetiva de esforço definida como "leve" e "intensa") intercalado por momentos de repouso. Duas aquisições foram realizadas, sendo que a solução (CHO ou placebo) era ingerida entre elas. O pré-processamento da imagem e a análise estatística foram realizados com o software SPM8 (p<0,001 não corrigido) para comparar alterações no padrão da atividade cerebral quanto às intensidades e à ingestão das substâncias. **Resultados**. Na intensidade leve, ambas as substâncias ativaram de forma semelhante áreas do córtex do cíngulo posterior e anterior, córtex temporal e fusiforme. Em alta intensidade, ambas as substâncias ativaram o córtex frontal, o caudado e o giro para-hipocampal, tálamo, ínsula e córtex do cíngulo posterior. **Conclusões**. Na intensidade leve, o CHO promoveu semelhante ativação cerebral quando comparado ao placebo, no entanto, com a intensidade "intensa", foram identificadas outras áreas envolvidas na emoção e regulação homeostática.

Unitermos. Metabolismo de Carboidrato, Exercício, Imaginação, Ressonância Magnética, Cérebro

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ABSTRACT

Objective. The aim of this study was to verify the effects of CH ingestion in the brain activation during different intensities of Motor Imagery (MI). **Method**. Nine subjects (eight men, 28±4.6 years) participated in this study and were submitted to a functional magnetic resonance paradigm based in MI block (running, with perceived exertion set as "light" and "intense") interleaved with rest. Two acquisitions were made, and the solution (CH and placebo) was ingested between them. The image preprocessing and the statistical analysis were performed with SPM8 software (p<0.001 uncorrected) to compared changes in the pattern of brain activity as the intensity and the ingestion of substances. **Results**. At the light intensity, both substances similarly activated areas in the posterior and anterior cingulated cortex, temporal and fusiform. For high intensity, both substances activated the frontal, caudate and parahippocampal gyrus, thalamus, insula and posterior cingulated cortex. **Conclusions**. At the light intensity, the CH promoted similarly brain activation when compared to placebo, however, at the intense intensity, other areas involved in emotion and homeostatic regulation were identified.

Keywords. Carbohydrate Metabolism, Exercise, Imagery, Magnetic Resonance Imaging, Brain

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INTRODUCTION

Proper nutrition with a varied diet in carbohydrate (CH), protein, fat and micronutrients are important to maintain physical and psychological health and to improve exercise performance. In relation with neurosciences, studies have shown that CH is the main substrate for physical activities[1]. The possible mechanisms responsible for the increase of physical performance with CH supplementation are: maintenance of glycemia, glycogen-sparing effect, glycogen synthesis in exercise of low intensity and attenuation of central fatigue[2]. The CH is suggested to reduce the central fatigue in the brain and its miss can lead to this phenomenon[3], characterized by feelings of lack of energy, fatigue and malaise[4]. The brain is metabolically active and the exercise can also increases the central requirements of energy. During intense physical activity, central requirements of energy may be more difficult to sustain because of the substantial increase in peripheral energy demand[5].

Is known that the glucose consumption is concentrated in regions with increased neural activity and increased blood flow brings more oxygen and glucose transport to the site in order to supply the energy needs of nerve cells[6]. Nevertheless, little is known about the differences in the brain areas during exercise with glucose consumption.

Studies have shown that there are taste receptors in the mouth that can influence neural pathways, ultimately leading to improved exercise performance and that there are receptors in the mouth sensitive to non-sweet carbohydrate[7,8]. A neuroimaging study have shown that oral glucose intake produces activation brain regions believed to mediate the behavioral and autonomic responses to rewarding stimuli, including taste[9]. Other study suggest that maybe the activation of the taste-related brain regions can influence emotion and behavior and this might impact mood and exercise performance. Despite this assumption, no studies had evaluated the effects of CH during exercise with simultaneously assessment of brain function[10].

Using functional Magnetic Resonance Imaging (fMRI), a noninvasive technique of neural activity[11], it is possible to find out which specific brain areas are activated through hemodynamic changes caused by the increase in neural activity in that area in particular. For proper assessment of brain function individuals must lie down and maintain the head still to capture the reliable images. Since exercising on this required position seems difficult, some studies used the practice of Motor Imagery (MI) to associate to proper exercise[12-14]. Studies argue that there is ample evidence that the motor performance and MI share similar neural mechanisms[15,16]. Since, MI being defined as a mental representation of the action without any concomitant movement of the body[17], studies have showed the feasibility of producing the brain areas activated during a task imagination of a coordinated and complex[18].

The aim of the present study was to verify the effect of CH consumption on brain activation during MI protocol performed in different effort intensities. Using fMRI, we may better understand the role of CH in the brain during the performance of exercise.

METHOD

Sample

Eight men and one woman who were practitioners of recreational physical exercise, including race (28±4.6 years, physical activity minimum of 120 minutes per week) participated in this study. After being properly informed about the purposes, procedures and risks of this study, all participants signed an informed consent form. The study was approved by the Ethical Research Committee from UNICAMP (number 766/2010) and completed according to the Declaration of Helsinki.

During the study period, the participants were instructed to abstain from alcohol and caffeinated substances, as well as to avoid any strenuous physical/mental activity for 24 hours before the tests. During the sample recruitment, participants were asked about any claustrophobic event, as well as the presence of screw, prosthesis or any other metal in the body. Any history of psychological discomfort associated to the presence in small environment or the presence of any metallic material attached to the body were an exclusion criterion in this study.

Procedure

During the first visit, participants initially completed a health questionnaire and had their body mass and height assessed. Then, participants underwent through familiarization procedures where they performed exactly the same MI experimental protocol twice, without ingesting any substance. On the two following visits, participants completed the MI protocol associated to one of the experimental conditions, either Placebo or CH. For the CH condition, participants ingested a solution containing 50g of maltodextrin (lemon flavor) mixed with 200 ml of water and, for Placebo, the same amount of water was prepared with powdered diet juice with similar lemon flavor. Conditions order was randomized and counterbalanced among subjects and had a minimum of one week interval.

Motor Imagery (MI) Protocol

The participants were submitted to a fMRI paradigm based in MI block interleaved with rest. The MI paradigm had two acquisitions being performed and the solution (CH and placebo) was ingested between them. The subjects arrived at the laboratory in fasted state of six hours. During MI, participants were instructed to imagine themselves running (their view in the first person) during four blocks of 30s periods within 30s rest intervals. On the first two blocks, participants had to project their exercise with perceived exertion as "light" while the last two blocks should be associated with "intense" perception. The first four blocks they did the MI without drink, and were considered the control scanning, this was the first acquisition. After this, they stopped the MI and drank the solution.

After the drink, the second acquisition was performed with another four blocks of MI to verify the brain activation related to the ingested substances. For the periods of rest, participants were instructed to project themselves sitting still and to avoid any physically or mentally effort. The MI was done inside the Magnetic Resonance (MR) scanner with low light. All instructions during the MI were given by a screen located inside the MR scanner. After completing MI protocol the scanner was stopped and participants remained lying still inside the equipment.

A tube connected to a recipient was provided by the researcher for the ingestion of one of the experimental solutions at the end of the first four blocks of MI completed. The fMRI acquisition was performed on a 3T Achieva MR scanner (Philips Medical Systems, Best, The Netherlands). The functional data were acquired in 2 EPI (echo-planar image) sequences (3x3x3mm^3 voxel size, 39 slices, no gap, FOV 240x240x117mm^3, TE 30ms, TR 2000ms, flip angle 90º) of 10 minutes each. A T1-weighted anatomical image (180 slices, no gap with 1x1x1 mm3 voxel size, FOV 240x240 mm^2, TE 6.9 ms, TR 3.1 ms, flip angle 8º) was acquired for coregistration with the functional images. The fMRI preprocessing and the subsequential statistical analysis were performed in the Statistical Parametric Mapping (SPM8, http://www.fil.ion.ucl.ac.uk/spm/) running on a PC with Matlab 7.7 (The MathWorks, Natick, USA). The fMRI images were realigned to regress the statistical analysis to the patient movement, normalized to the international MNI (Montreal Neurological Institute) template, and smoothed with a Gaussian kernel of 6 mm at full width at half maximum (FWHM) to reduce high signal variation between neighbor voxels.

Statistical Analysis

The fMRI analyses were performed by two statistical levels. In the first level (single subject) the fMRI task was used as a block paradigm to construct the GLM (General Linear Model) design matrix. With this methodology we aimed the BOLD responses related to each imaginary intensity and condition separately, for all subjects individually. For each intensity (condition), a contrast map was created. In the second level analysis (group analysis) a two sample T-test ($p<0.001$, uncorrected) were performed grouping the contrast maps from all subjects in order to find the differences between Placebo and CH for each imaginary exercise intensities. In addition to these analyzes were conducted an One Sample T-test ($p<0.001$, uncorrected) to check for statistically significant regions overlapping in both groups (CH and Placebo) at each intensity separately.

RESULTS

In this study we evaluated nine subjects (one woman), which the main characteristics were 28±4.6 years, weight 73±12.5Kg, height 1.74±0.08m, 1.74±0.08 of physical activity weekly frequency and 120-270 minutes of physical activity at the week. The consumption of CH associated to MI of running at light intensity, comparing to control, promoted activation in the left anterior cingulate and right medial frontal gyrus (Table 1). In addition, the two substances administered (CH and PLACEBO) activated areas of left posterior cingulate, superior temporal gyrus and right fusiform gyrus and cingulate gyrus (Table 1, Figure 1). The consumption of CH associated to running at light intensity, comparing to Placebo, promoted activation in the left middle frontal gyrus and left middle temporal gyrus (Table 1, Figure 2).

When the intensity change to intense the CH activated the areas of right parahippocampal, middle temporal, superior frontal, inferior temporal gyrus and left middle frontal gyrus, comparing to control (Table 1) and, with consumption of both (CH and Placebo), the areas of right superior frontal gyrus, caudate, parahippocampal gyrus, thalamus and left insula, superior frontal gyrus, posterior cingulate (Table 1, Figure 3). Comparing to Placebo, the CH activated the areas of left cingulate gyrus, ipsilateral inferior frontal gyrus, superior frontal gyrus, middle, superior, transverse temporal gyrus, postcentral gyrus and right anterior cingulate (Table 1, Figure 4).

DISCUSSION

The main findings of this study were that the ingestion of CH during high intensity of MI caused activation in insula and cingulate cortex and, at light intensity, showed only activation in the prefrontal, cortex middle frontal gyrus and temporal gyrus. Thus, MI exercise at high intensity required motor and emotive regulation more than light intensity. Besides, The CH showed acute change in BOLD signal in some areas, like mentioned, in comparison to control and placebo, however this areas are not so important during the exercise. However, the

*Table 1. T*ailarach coordinates of activations when the nine subjects did the different intensities in motor imagery protocol with carbohydrate and placebo.

	Left				Right			
	x	y	z	Z	x	y	z	Z
CH higher than control, light								
Anterior Cingulate BA 32	-9	35	-2	3.42				
Middle Frontal Gyrus BA 10					18	44	-2	3.24
CH equal Placebo, light								
Limbic Lobe								
Posterior Cingulate BA 30	-21	-49	10	4.14				
Cingulate Gyrus BA 32					18	11	40	3.26
Temporal Lobe								
Superior Temporal Gyrus BA 38	-45	14	-14	3.43				
Fusiform Gyrus BA 20					42	-25	-17	3.39
CH higher than Placebo, light								
Middle Frontal Gyrus BA 6	-33	2	40	3.62				
Middle Temporal Gyrus BA 21	-54	-4	-14	3.24				
CH higher than control, intense								
Limbic Lobe								
Parahippocampal Gyrus BA 36					39	-25	-17	4.75
Frontal Lobe								
Middle Frontal Gyrus BA 11	-18	23	-8	4.08				
Superior Frontal Gyrus BA 8					18	38	43	4.05
Superior Frontal Gyrus BA 8					12	32	46	4.04
Superior Frontal Gyrus BA 10	-30	59	-2	3.84				
Temporal Lobe								
Middle Temporal Gyrus BA 21					57	-22	-11	4.05
Inferior Temporal Gyrus BA 20					54	-7	-20	3.99
Middle Temporal Gyrus BA 21					51	-46	4	3.79

(x,y,z): Tailarach coordinates. Z: Z-score; p= 0.001 uncorrected corresponds to Z-score of 3.69. BA: Brodmann area.

Table 1 - cont. Tailarach coordinates of activations when the nine subjects did the different intensities in motor imagery protocol with carbohydrate and placebo.

	Left				Right			
	x	y	z	Z	x	y	z	Z
CH equal Placebo, intense								
Frontal Lobe								
Superior Frontal Gyrus BA 6	6	5	67	4.36				
Superior Frontal Gyrus BA 6	-12	-1	67	3.61				
Sub-lobar								
Caudate	21	-37	10	3.73				
Insula	-27	-7	25	3.72				
Thalamus					6	-25	16	3.56
Limbic Lobe								
Posterior Cingulate Ba 29	-18	-46	13	3.57				
Parahippocampal Gyrus Ba 36					39	-22	-17	3.31
CH higher than Placebo, intense								
Limbic Lobe								
Cingulate Gyrus BA 21	-6	-25	37	3.49				
Cingulate Gyrus BA 24	-3	-19	40	3.20				
Anterior Cingulate BA 24					9	26	19	3.14
Anterior Cingulate BA 32					24	41	7	3.14
Cingulate Gyrus BA 24	-3	-1	34	3.09				
Frontal Lobe								
Inferior Frontal Gyrus BA 45					48	35	4	4.20
Inferior Frontal Gyrus BA 45	-54	26	7	3.13				
Inferior Frontal Gyrus BA 47					48	29	-2	3.12
Temporal Lobe								
Middle Temporal Gyrus BA 21	-51	-22	-8	3.21				
Middle Temporal Gyrus BA 37	-57	-61	-2	3.18				
Middle Temporal Gyrus BA 39	-54	-70	13	3.17				
Superior Temporal Gyrus BA 38	-45	14	-11	3.13				
Transverse Temporal Gyrus BA 41	-45	-22	13	3.11				
Parietal Lobe								
Postcentral Gyrus BA 2	-63	-22	28	3.19				

(x,y,z): Tailarach coordinates. Z: Z-score; p= 0.001 uncorrected corresponds to Z-score of 3.69. BA: Brodmann area.

placebo also activated the insula during the high intensity.

In the intensity light the both substances activated areas related with emotions (limbic lobe) and movements (frontal cortex). The consumption of CH in this intensity activated the middle frontal gyrus and temporal gyrus, not activated by the placebo. The middle frontal gyrus is linked to awareness of feelings, emotional state and is associated with executive functions and decision--related processes[19,20]. Also, the superior and middle frontal gyrus are part of frontal lobe, which is related to initiation of voluntary movements, and includes areas premotor and supplementary motor[21]. It seems that the MI is capable to activate areas related to movements even in light intensity.

The areas that presents BOLD positive with the consumption of the CH and placebo like posterior cingulate and cingulate gyrus are located in the limbic lobe, which is the basic circuit of emotions that functionally related to motivation, emotions and memory[22]. The posterior cingulate is related to nociceptive stimuli, such as pain[23] and angry[19], while the caudate nucleus, other areas active is associated with positive emotions such as happiness and love[24]. This suggests that the practice of any exercise can provide individual psychology change. And the superior temporal gyrus and fusiform gyrus are activated with visual and auditory stimuli[25].

When changed to high intensity, the CH compared to control or placebo, activated more areas than light intensity, as the cingulate gyrus, inferior and superior frontal gyrus, middle and superior temporal gyrus, postcentral gyrus and anterior cingulate. However, again both substances showed activation of motor and emotion/sensory areas and sensory similarly.

The CH activated the anterior cingulate, that besides being related to motor control also involves emotion and cognitive effort[26] and both substances activated the insula, which together with anterior cingulate has an important role in the mechanisms of awareness of the physiological factors involved in dynamic exercise (chronic pain and thermal temperature differences, muscle tension), and their responses to these stimuli by changing the motivation and emotions of the individual against the exercise[27,28]. The insula is related to decision-

Figure 1. Positive Blood Oxygen Level Dependent maps (p<0.001 uncorrected cluster size=3) related to of both (carbohydrate and placebo) ingestion during light motor imagery intensity.

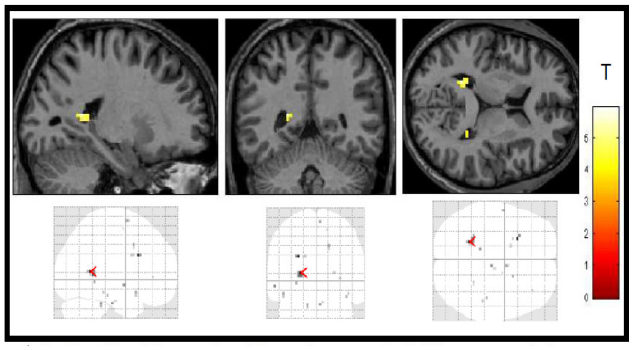


Figure 2. Positive Blood Oxygen Level Dependent maps (p<0.001 uncorrected cluster size=0) related to the carbohydrate ingestion, comparing to Placebo, during light motor imagery intensity.

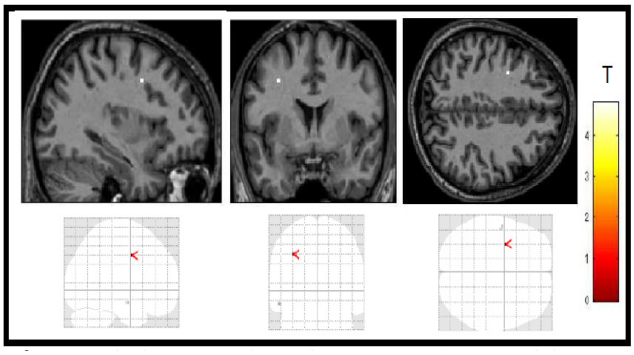


Figure 3. Positive Blood Oxygen Level Dependent maps (p<0.001 uncorrected cluster size=3) related to of both (carbohydrate and placebo) ingestion during intense motor imagery intensity.

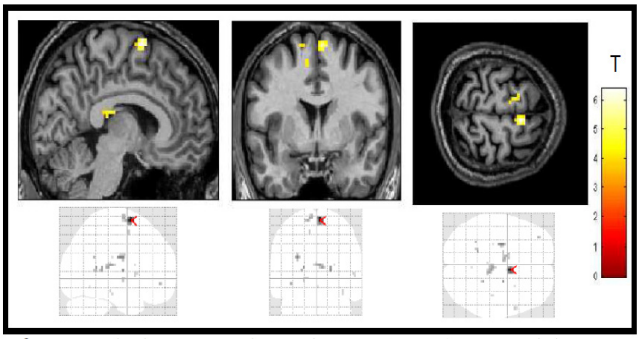
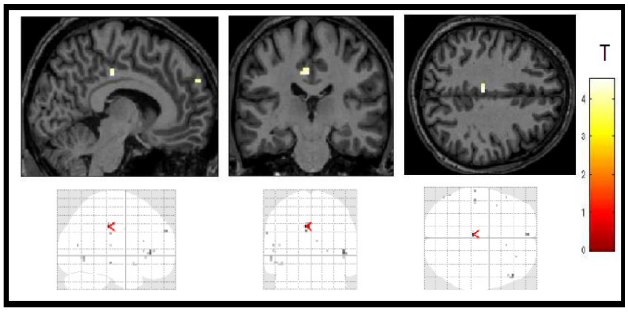


Figure 4. Positive Blood Oxygen Level Dependent. maps (p<0.001 uncorrected cluster size=0) related to the carbohydrate ingestion, comparing to Placebo, during intense motor imagery intensity.



-making[27], which could be crucial in the decision to stop or not exercise.

At high exercise intensities the insular cortex has a higher magnitude of activation and[29], mouthwash with glucose or with sweetener for athletes and found activation of the insula in glucose and also the area of the anterior cingulate cortex before[30]. Since the sweetener also activated the insula. These results are very similar to those found in the present study.

This study had some limitations, one of which was the small number of participants and the absence of control over the diet the volunteers, as it can influence the response of the organism, especially the brain, with the substances offered.

Nevertheless, there are no studies that related the CH with intensity exercise in neuroimaging, so these findings show the importance of deepening the study of the brain during physical activity and consumption of substances. This study is therefore an initial attempt to explore the neurological bases of carbohydrate function in the exercise performance, which we hope future studies will extend.

CONCLUSION

The results showed that ingestion of CH did not differ compared to placebo, because both substances had activation of areas related to emotional awareness and voluntary movements. However, with the change of intensity to higher, other areas were more active as the insula and anterior cingulate.

This study showed that more research needs to be conducted on the effect of nutrients in the brain during exercise. So, we can better understand its mechanisms and propose more effective strategies to relate physical activity with nutrition, psychology and neuroscience fields.

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