Frontal and cerebellar contribution to pitch and rhythm processing: a TMS study

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Short Report

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Abstract

Music represents a salient stimulus for the brain with two key features: *pitch* and *rhythm*. Few data are available on cognitive analysis of music listening in musically naïve healthy participants. Beyond auditory cortices, neuroimaging data showed the involvement of prefrontal cortex in pitch and of cerebellum in rhythm. The present study is aimed at investigating the role of prefrontal and cerebellar cortices in both pitch and rhythm processing. The performance of fifteen participants without musical expertise was investigated in a listening comparative task. The task required to decide whether two eight-element melodic sequences were equal or different according to pitch or rhythm characteristics. Before the task, we applied a protocol of continuous theta burst transcranial magnetic stimulation interfering with the activity of the left cerebellar hemisphere (lCb), right inferior frontal gyrus (rIFG), or vertex (Cz-control site), in a within cross-over design. Our results showed that participants were more accurate in pitch than rhythm tasks. Importantly, following rIFG or lCb relative to Cz stimulations, the reaction times were slower and with no difference in both tasks. Notably, no lateralized motor stimulation effect was observed. The present findings point to the role of the fronto-cerebellar network in music processing with a single mechanism for both pitch and rhythm patterns.

Introduction

Music is inherent to the human being across cultures and it represents a salient stimulus for the brain regardless of an explicit musical education (Vuust et al., 2022). For the human brain, music listening is not only a passive acoustic bottom-up input, but it also involves affective and cognitive functions that go beyond the auditory experience (Reybrouck et al., 2021). In neurosciences, music listening has been partially investigated and most studies have been interested in motor practice with musical instruments or they have regarded professional musicians or clinical populations exposed to music (Vuust et al., 2022). Nowadays, few data are available on cognitive processes related to music listening in musically naïve healthy participants.

In the complexity of the musical experience, *pitch* and *rhythm* represent two key features (Zhang et al., 2020). In fact, each note corresponds to a specific frequency value — the pitch — and a melody is the arrays of ups and downs of pitch unfolding over time. Moreover, each note has a specific duration and the melody is also the arrangement of long and short sounds over time — the rhythm. Such processes are relevant not only in the perception of music, but also in the analysis of speech sounds (Yu et al., 2017). Neuroimaging findings showed that pitch and rhythm patterns are subserved by distinct, although partially overlapping, neural networks (Janata, 2015; Koelesh, 2011). Beyond auditory cortices in the temporal lobe, music processing involves the prefrontal cortex and cerebellar areas (Daly et al., 2019). In particular, the inferior frontal gyrus, especially in the right hemisphere, is entailed in pitch discrimination (Royal et al., 2018; Palomar-Garcia et al., 2020; Bianchi et al., 2017; Leipold et al., 2019), while cerebellar areas, more often left-sided, are entailed in rhythm elaboration (Kasdan et al., 2022; Nozaradan et al., 2017).

The present study was aimed at investigating the functional role of the right inferior frontal gyrus (rIFG) and of the left cerebellar hemisphere (lCb) in processing pitch and rhythm of brief musical sequences in non-musicians. Notably, most researchers employed monotonous or isochronous sound sequences to separately investigate pitch and rhythm processing (Thaut et al., 2014). We decided to provide a musical task including both features concurrently, as occurring in typical Western musical patterns, although the participants were required to focus on one component at a time. One strength of this study is employing non-invasive brain stimulation to collect direct information on the role of prefrontal and cerebellar areas in pitch and rhythm discrimination. This approach allowed completing the correlational findings provided by previous neuroimaging studies (Griffith et al., 1999; Chan and Han, 2022). Specifically, we applied an offline protocol of repetitive Transcranial Magnetic Stimulation (TMS) called continuous Theta Burst Stimulation (cTBS) to induce transient interference of rIFG or lCb activity (Picazio et al., 2020), before a pitch and rhythm discrimination task. If these areas were involved in pitch or rhythm processing, participants should perform worse following cTBS applied on rIFG or lCb than following cTBS on the vertex (Cz), used as control site.

Materials and Methods

The present study used methods the same as or similar to those in our prior publications (Picazio et al., 2015; Picazio et al., 2020). Consequently, some text included here is recycled from those sources.

Participants

Fifteen healthy volunteers (9 women; 23.6 ± 2.2 years; schooling > 13 years) were enrolled in this cross-over study. All participants were right-handed as assessed with the Edinburgh Handedness Inventory (Oldfield, 1971) and reported normal-or corrected-to-normal vision and no hearing problems. None of the participants was a musician or even non-professional player as reported in a brief telephone interview at the time of recruitment. The study was in accordance with the declaration of Helsinki and was approved by the Local Ethics Committee of the Santa Lucia Foundation IRCCS of Rome. Written consent was obtained from all participants after a full explanation of study procedures.

Melodic Stimuli

Stimuli were eight-element sequences (Fig. 1) built with Ableton Live version 9. The elements were all pure tones with no gap between each tone, composing simple melodies, lasting each one 3000 ms (6/4 musical bar at 120 bpm). For each note (Do - C2/129 Hz; Re - D2/148 Hz; Mi - E2/161Hz; Fa - F2/170 Hz; Sol - G2/196 Hz; La - A2/219 Hz; Si - B2/251 Hz), a target sequence was built in which the first and the last tone was the same note with the same duration (Fig. 1). In each sequence, the elements could have a duration of 250 ms (quaver note) or 500 ms (quarter note). The lowest pitch used in any melody was Do (C2/129 Hz) and the highest pitch was Si (B2/251 Hz), so that the lowest and the highest pitch belonged to the same octave. Thus, 7 target sequences were built. For each target sequence, 4 melodies were built that could have: 1) same notes (same pitch) and same tone durations (same rhythm) relatively to the target sequence; 2) same notes (same pitch) and different tone durations (different rhythm); 3) different notes (different pitch) and same tone durations (same rhythm); 4) different notes (different pitch) and different tone durations (different rhythm). A total of 28 melodies was finally obtained. All melodies were built with a Clarinet timbre. The sequences were presented binaurally at a sensation level of 60 dB, by means of Pioneer Stereo Headphones SE-M290.

Listening comparative task

The participant was required to listen to a couple of the eight-element melodic sequences and to decide whether they were equal or different. Each trial started with a beep presented for 500 ms, followed by the first 3000 ms-melodic sequence, 1150 ms-break and then the second 3000 ms-melodic sequence. From the end of the second melody the participants were given a maximum time of 5000 ms to respond. The next trial started after 350 ms from the response (Fig. 2). In one block the participant responded according to the pitch feature and in another block according to the rhythm feature of sequences. Each block included 56 randomized trials (two for each of the 28 couples of sequences) with a 50% probability of “equal” or “different” responses. According to the feature required in the block, participants were instructed to press on a standard QWERTY keyboard the “A” key with the left index finger, whenever they considered the two sequences as “equal”, and the “L” key with the right index finger, whenever they considered the sequences as “different”. Participants were told to keep their eyes closed during the task. The order of blocks was counterbalanced across participants and sessions. Each block required about 12 minutes. The present task was a modified version of a previous test (Griffiths et al., 1999).

Each participant underwent a training before the experimental phase, in which a subset of randomized 16 trials for each (pitch/rhythm) block was presented. The training phase was overcome when the participant reached at least 70% of correct responses. If the criterion was not reached, the training was repeated. Since the sample was composed by non-musicians, participants needed to be supported in the training phase with labels and visual feedback. During the training phase, visual cues indicating “listening 1”, “listening 2” and “correct” (in green) or “wrong” (in red) response, appeared on the screen. Once completed the training, participants performed the task with eyes closed (Fig. 2). Task parameters considered were: reaction times (RTs) in ms; percentage of correct responses (accuracy scores).

Overview of the procedure

Each participant underwent three cTBS sessions spaced by 1 week apart. cTBS consists of three-pulse bursts at 50 Hz repeated every 200 ms for 40 s (600 pulses) inducing a long term depression (LTD)-like decrease in the activity of stimulated neurons, lasting a period of up to 40 minutes. In each weekly session, the participant performed the training, then underwent cTBS, and immediately afterwards performed the task. cTBS was delivered in counterbalanced order over the right inferior frontal gyrus (rIFG), the left cerebellar hemisphere (lCb), or the vertex (Cz) as control site in the three sessions (Fig. 3). See supplementary information for details.

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Statistical Analysis

Two two-way ANOVAs with repeated measures [Task (pitch *vs.* rhythm) x Site (lCb, rIFG, Cz) as within factors] were run on RTs and accuracy scores. To exclude possible interactions between the stimulation Site and the responding hand, two three-way ANOVAs with repeated measures [Task (pitch *vs.* rhythm) x Site (lCb, rIFG, Cz) x Hand (left *vs.* right) as within factors] were run on RTs and accuracy scores. Statistical analyses were performed with STATISTICA 8.0 using two-tailed alpha levels of < 0.05 for defining significance. Post-hoc Duncan's tests were performed when required. Effect size was indicated as partial eta square ($\eta^{P}{}_{2}$).

Results

Two-way ANOVA on RTs showed a significant effect ($F_{2,28}$=3.48, p = 0.04, ηP_2 = 0.2) of Site, while no significant effects of Task and Interaction emerged (p > 0.53 for all comparisons). Post-hoc analysis showed higher RTs for rIFG (p = 0.03) and lCb (p = 0.03) relative to Cz stimulation, while no difference emerged between rIFG and lCb stimulations (p = 0.9) (Fig. 4a). Two-way ANOVA on accuracy scores showed a significant effect ($F_{1,14}$=7.44, p = 0.02, ηP_2 = 0.3) of Task and no significant effects of Site and Interaction (p > 0.48 for all comparisons) (Fig. 4b). The results indicated higher accuracy for the pitch than the rhythm task (Fig. 4b). No significant interactions between stimulated Site and responding Hand emerged by three-way ANOVAs on RTs ($F_{2,28}$=1.09, p = 0.35) and accuracy scores ($F_{2,28}$=1.01, p = 0.38). These findings allowed excluding any lateralized motor effect of cTBS.

Discussion

The main results show that non-musician participants were more accurate in pitch than rhythm tasks, and prefrontal or cerebellar stimulations interfered with the time required to respond to both tasks, independently from the responding hand. The finding of the superior accuracy in the pitch in respect to rhythm may reflect an intrinsic feature of the present listening comparative task, with rhythm more difficult than pitch, or it may represent a general more skillful pitch ability, or finally it may indicate a prioritization of pitch over rhythm processing. Interestingly, it has been reported that musicians (string players) are able to perform pitch tasks more accurately than rhythm tasks (Alexander and Henry 2015), showing a similar bias of our musically naïve participants. Unfortunately, literature data do not provide evidence to disambiguate this topic in listeners without musical expertise. The present findings indicating a general tendency to care more about pitch than rhythm when concurring in the same melodic sequence are very intriguing and warrant future focused research.

The lack of interaction between the site of stimulation (rIFG or lCb) and responding hand ensures that the effects we obtained were not influenced by the motor output. Consistently, it has been repeatedly observed the activation of motor circuits involving the right premotor cortex and the left cerebellar hemisphere during pure music listening, though without any movement (Gordon et al., 2018; Petacchi et al., 2005; Picazio et al., 2013; 2015).

Based on the results of neuroimaging studies, there is a temptation to assign the processing of pitch and rhythm to distinct brain areas (Janata, 2015 for a review). Namely, pitch is considered to be mainly processed by a network involving the inferior frontal gyrus, and rhythm by a network involving the cerebellum (Palomar-Garcia et al., 2020; Kasdan et al., 2022). Accordingly, we applied non-invasive brain stimulation to rIFG and lCb to modulate pitch and rhythm performances. The increase of RTs following either prefrontal and cerebellar stimulations in pitch and rhythm tasks indicates that both areas are together involved in processing both musical features.

Consistently with cerebellar involvement in pitch processing, patients with cerebellar ataxia performed poorer than controls in pitch discrimination tasks, with performances proportional to the degree of cerebellar ataxia severity (Parsons et al. 2009). Furthermore, a positron emission tomography (PET) study found increased middle and left lateral cerebellar activation in a pitch recognition task (Holcomb et al. 1998). Finally, cerebellar patients are reported to reach scores lower than healthy controls in a task requiring comparison of melodic pitch sequences (Tölgyesi & Evers, 2014).

Furthermore, suppressing cerebellar activity by means of inhibitory TMS trains affects the ability to discriminate pitch but not timbre of sounds (Lega et al., 2016). Correspondingly, several neuroimaging studies have reported rhythm-related activations in the right IFG (Bengtsson and Ullén, 2006; Bengtsson et al, 2008; Koinoke et al., 2015), suggesting that during rhythm encoding the IFG might organize perceived sound elements into a structured temporal sequence of rhythm and to be involved in the internal representation of temporal sequences.

An earlier PET activation study (Griffiths et al., 1999) on musically naïve healthy participants proposed a common neural network including inferior frontal cortex, cerebellum and temporal cortex to process both pitch and rhythm

patterns within musical sequence pairs similar to our stimuli. More recent studies have emphasized that music listening activated multiple brain networks involving frontal and cerebellar regions, not modulated by music training experience (Chan et al., 2022). Moreover, it was reported that the maturation of fronto-cerebellar networks is different according to the age at which the musical training begins with an impact on interrelated brain volumes important for optimizing sensorimotor performance (Shenker et al., 2022). Namely, neuroimaging studies have confirmed repeatedly the involvement of frontal and cerebellar regions in tasks related to rhythm perception (Cannon and Patel, 2021) and also in tasks evaluating nonrhythmic aspects of music, such as melody (Brown and Martinez, 2007).

It has been already hypothesized that brain areas, typically belonging to the motor circuit, such as frontal neocortex and the cerebellum could mediate the coding of perceptual contents (Hommel, 2013; Foti et al., 2010). Multiple theories (Patel and Iversen, 2014; Rauschecker, 2011; Schubotz, 2007) advance that the motor system plays a role even in passive music listening and that it has a predictive contribution in perception (James et al., 2014). Not by chance, research on sensorimotor adaptation has emphasized the role of the cerebellum and its connections in predicting sensory consequences of movement and adapting to errors in these predictions (Petrosini et al., 2022). This involvement in predictive processes might be active in music listening regardless of active motor control is needed, the complexity of auditory stimuli requiring however a high level elaboration. In conclusion, processing of musical stimuli with a complex melodic structure, requires the contribution of frontal and cerebellar networks likely involving mechanisms of perception-action coupling and sensorimotor prediction. This knowledge provides interesting elements on the brain mechanisms underlying music listening *per se* and it could be useful to study the listening of other complex auditory stimuli, such as speech, that could share common networks.

Declarations

Data Availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

No funding was received for conducting this study.
The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Silvia Picazio, Barbara Magnani and Laura Petrosini. The first draft of the manuscript was written by Silvia Picazio and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Figures

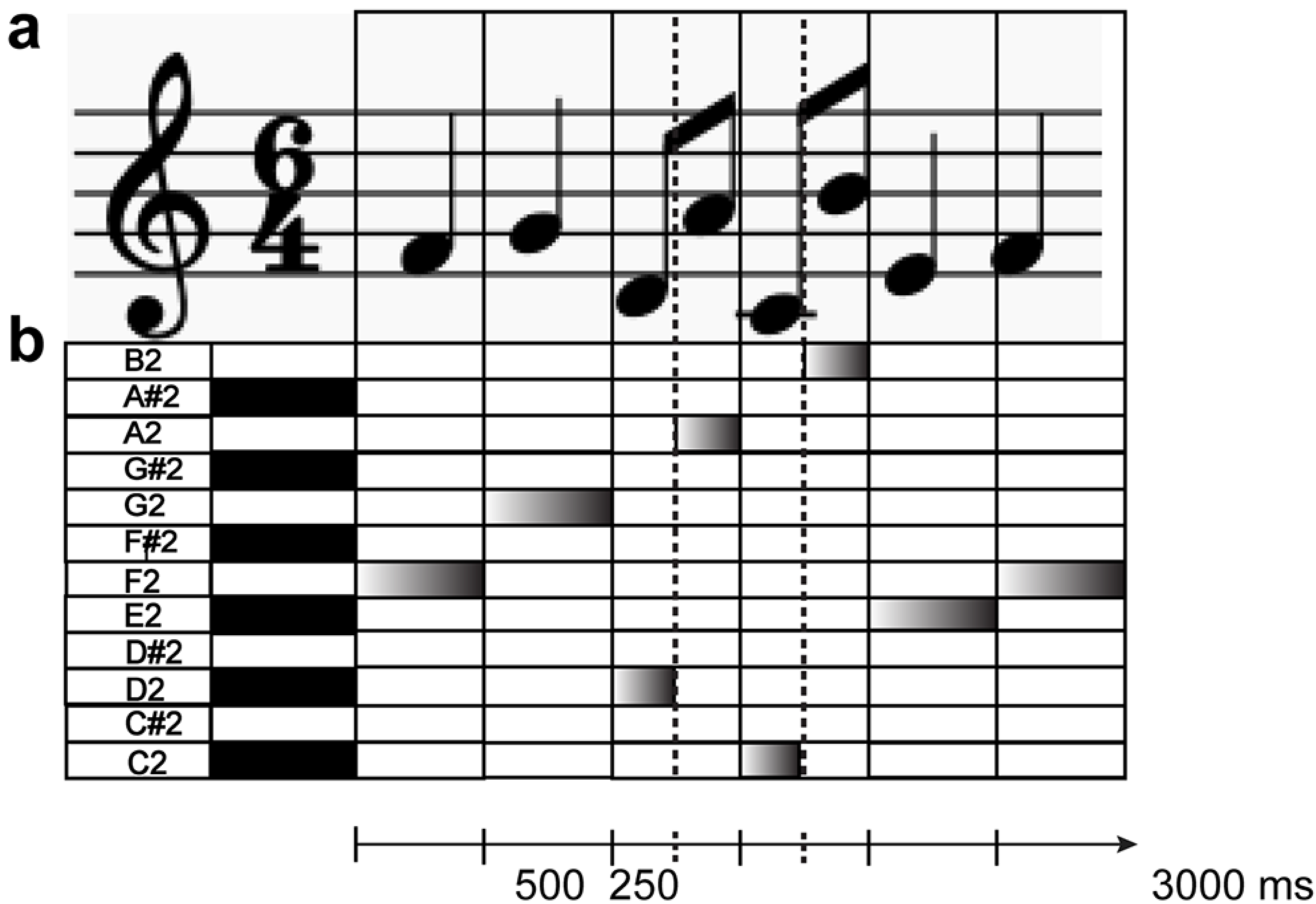

Figure 1

Graphical representation of a stimulus **a** on pentagram and **b** on Ableton live software layout. The length (long and short) of black lines indicates tone duration, the vertical (up and down) placement of black lines indicates tone pitch. The combination of the two features shapes the melody. The bottom timebar indicates the duration of each note that could last 500 or 250 ms for a total of 3000 ms of duration for each melody.

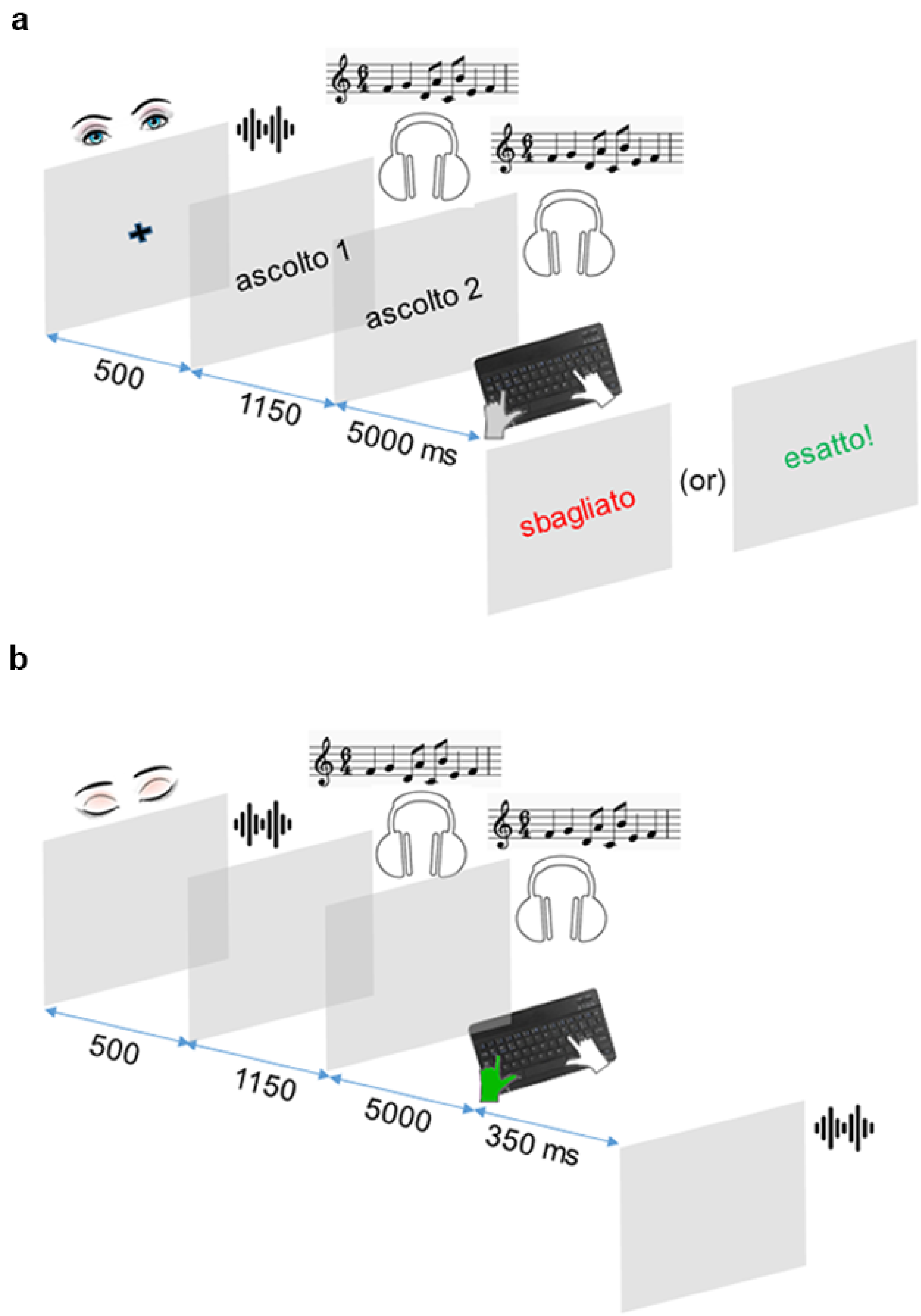

Figure 2

Training and task. **a** The training was executed with eyes open. On a gray screen following a beep and a fixation cross, “listening 1” (ascolto 1) or “listening 2” (ascolto 2) labels as well as response feedback (“right!” - esatto! and “wrong” - sbagliato) appeared. **b** The task was executed with eyes closed without any visual cue. Participants responded by pressing the “A” (different) or “L” (equal) key with the index fingers. The green hand indicates the correct (right) response for the item shown.

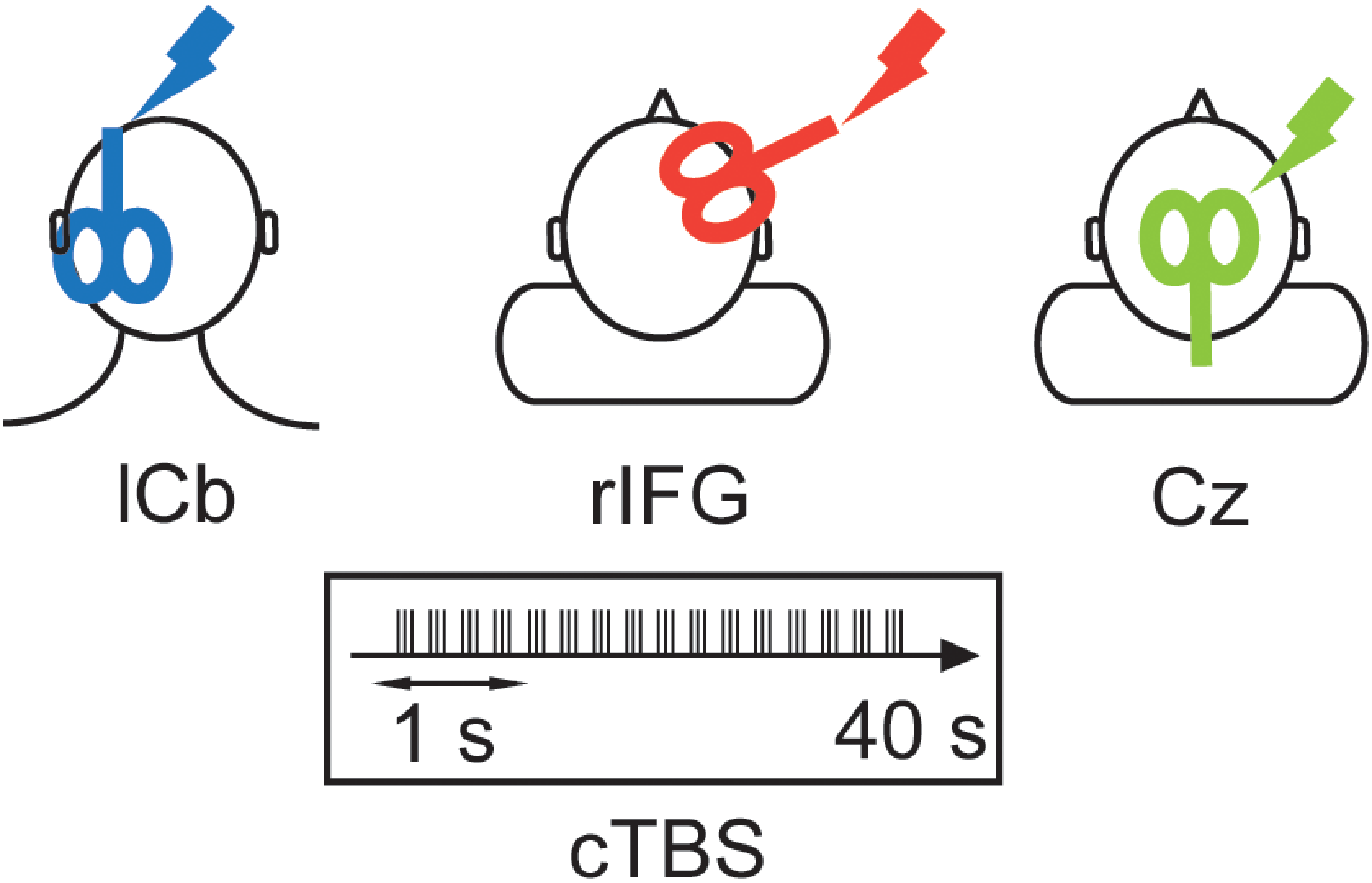

Figure 3

Continuous theta burst stimulation (cTBS) over the left cerebellar hemisphere (lCb-blue), right inferior frontal gyrus (rIFG-red), or the vertex (Cz-green) as control site.

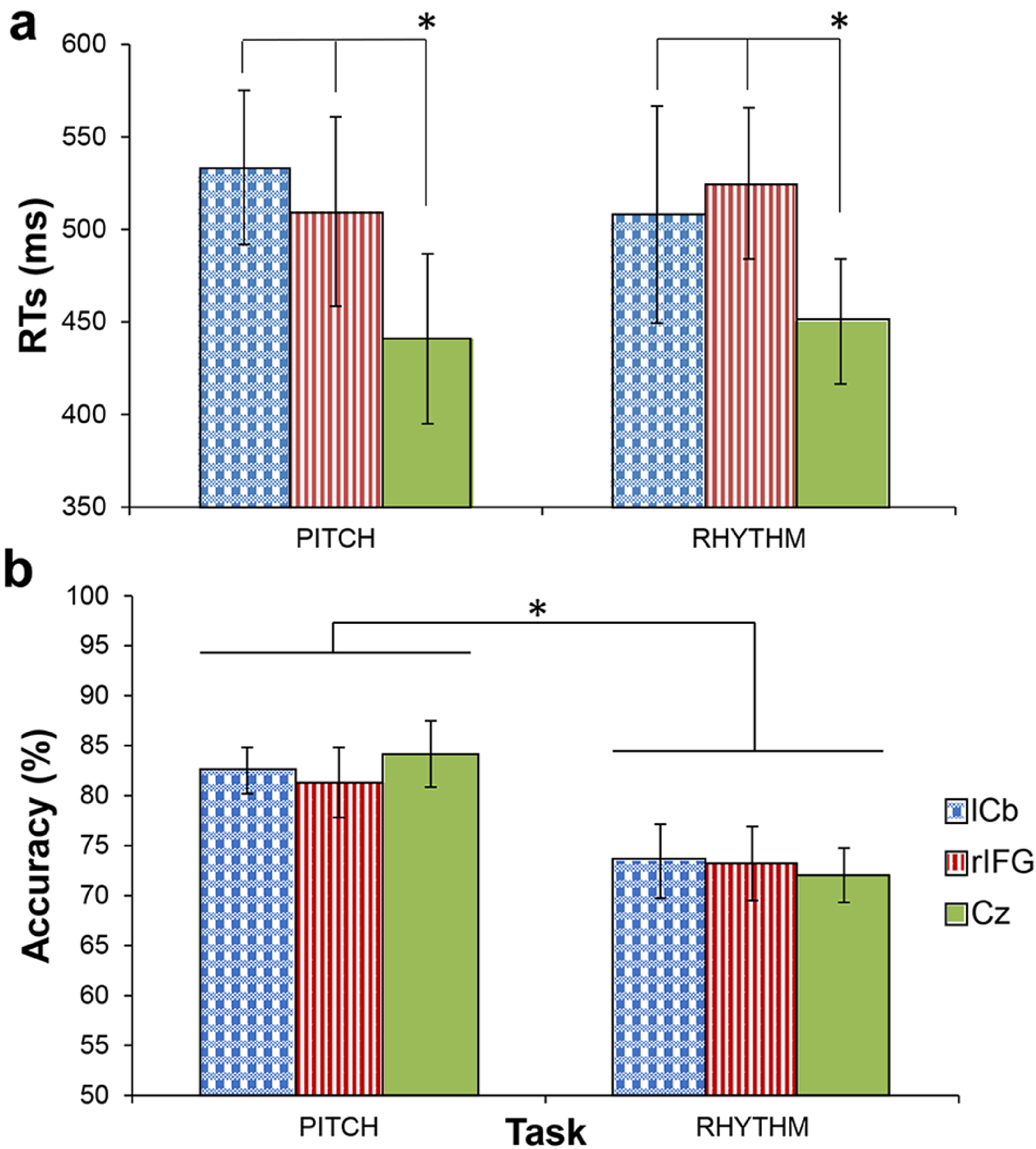

Figure 4

Reaction times (RTs) in milliseconds (ms) and accuracy scores in percentage (%) for pitch and rhythm. Blue crossed columns represent left cerebellar (lCb) stimulation, red vertical striped columns represent right inferior frontal gyrus (rIFG) stimulation, and green filled columns represent vertex (Cz) control site stimulation. Significant effects ($p<.05$) are indicated with *. Bars represent mean standard errors. **a** RTs increased following lCb and rIFG stimulation with respect to Cz stimulation. **b** Participants were less accurate to respond to the rhythm than to the pitch task.

Supplementary Files

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- SupplementaryInformation.pdf