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Primate beta oscillations and rhythmic behaviors

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Abstract The study of non-human primates in complex behaviors such as rhythm perception and entrainment is critical to understand the neurophysiological basis of human cognition. Next to reviewing the role of beta oscillations in human beat perception, here we discuss the role of primate putaminal oscillatory activity in the control of rhythmic movements that are guided by a sensory metronome or internally gated. The analysis of the local field potentials of the behaving macaques showed that gamma-oscillations reflect local computations associated with stimulus processing of the metronome, whereas beta-activity involves the entrainment of large putaminal circuits, probably in conjunction with other elements of cortico-basal ganglia-thalamo-cortical circuit, during internally driven rhythmic tapping. Thus, this review emphasizes the need of parametric neurophysiological observations in non-human primates that display a well-controlled behavior during high-level cognitive processes.

Keywords Interval timing · Basal ganglia · Putamen · Beta oscillations · Neural encoding · Rhesus macaques

Introduction

Time processing in the hundreds of milliseconds scale is critical for many behaviors, ranging from actions performed across the animal kingdom such as the interception

of a moving target (Merchant and Georgopoulos 2006; Merchant et al. 2009), to complex human cognitive functions, such as speech perception and articulation (Diehl et al. 2004), and the execution and appreciation of music (Janata and Grafton 2003; Merchant and de Lafuente 2014a). Human and non-human primates have the ability to quantify single or multiple intervals, defined by different sensory modalities, in a variety of perceptual or motor activities (Merchant et al. 2008a, b; 2013a; Mendez et al. 2011, 2014; Merchant and de Lafuente 2014b). Nevertheless, recent studies have come to the conclusion that there are at least two distinct types of temporal processing. One engaged in timing intervals immersed in a sequence, where time is quantified in relation to a regular perceived beat, called beat-based timing. The other, called duration-based timing, where the duration of individual intervals is encoded discretely, like a stopwatch and no entrainment is possible (Grahn and Brett 2007; Schwartz et al. 2011; Teki et al. 2011; Kung et al. 2013; Merchant et al. 2015b). Notably, the motor cortico-basal ganglia-thalamocortical circuit (mCBGT), which includes the medial premotor areas (MPC; pre-supplementary and supplementary motor area proper) and the putamen, is deeply involved in beat-based timing (Grahn and Brett 2007; Schwartz et al. 2011; Teki et al. 2011; Kung et al. 2013; Merchant et al. 2013a). In contrast, the cerebellum takes part in absolute timing (Grahn and Rowe 2009; Grube et al. 2010; Teki et al. 2011), as well as in the processing of temporal prediction errors (Teki et al. 2012).

Both types of temporal processing can use different neural encoding mechanisms to represent the passage of time (Gupta and Merchant 2017). These include: ramping activity (Merchant et al. 2011; Knudsen et al. 2014; Jazayeri and Shadlen 2015), interval tuning (Mita et al. 2009; Merchant et al. 2013b; Perez et al. 2013), neural population

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avalanches (Crowe et al. 2014; Merchant et al. 2015b), state network dynamics (Mello et al. 2015; Gouvêa et al. 2015; Petter and Merchant 2016), or brain oscillations (Matell and Meck 2004; Large et al. 2015; Bartolo and Merchant 2015). The latter is the main focus of this review, specifically in the beta band. However, we will initially provide a brief overview on the former encoding mechanisms of time information.

Neural encoding of time and serial-order during rhythmic behaviors

During the last years, our laboratory has investigated the neurophysiological underpinnings of beat-based timing in the primate mCBGT during the execution of a synchronization-continuation task (SCT) (Donnet et al. 2014). In this classical paradigm of motor timing (Repp and Su 2013; Wing 2002), macaques tapped first in synchrony with a sensory metronome for three intervals, and then continued tapping at the same pace without sensory guidance for three more intervals, timing their behavior internally (Zarco et al. 2009). Thus, the task has three independent parameters: the interval duration (five durations in a range from 450 to 1000 ms), the serial-order (one to six elements produced in a sequence), and the task condition (synchronization vs continuation phase). The extracellular recordings of single neurons in MPC and the putamen revealed the following essential mechanisms engaged in time production during the SCT:

1. **Ramping activity:** We found different MPC neural populations that encode different temporal features of the isochronous tapping of SCT by modifying their instantaneous discharge rate on a linearly increasing or decreasing fashion. One population exhibits an increase in ramp duration but a decrease in slope as a function of the monkey's produced duration, reaching a particular discharge magnitude at a specific time before the button press (Fig. 1a, middle). These cells are called relative-timing cells because their ramping profile appears to signal how much time is left to trigger the button press. Another group of cells shows a consistent increase followed by a decrease in their instantaneous discharge rate when the neural activity was aligned to the previous button press. In these cells, called absolute-timing neurons, the duration of the up-down profile of activation increases as a function of the produced interval, encoding the elapsed time since the previous tap (Fig. 1a, left). Finally, the time-accumulator cells show an increase in the magnitude of the ramps' peak as a function of elapsed time, working as an hourglass that accumulates in its discharge rate how much time has passed since the last tap. Thus,
2. **Tuning:** Previous psychophysical studies suggested the existence of duration-specific circuits in the brain (Wright et al. 1997; Bartolo and Merchant 2009). Indeed, we found that cells in MPC and the putamen are tuned to the duration and/or serial-order of the produced intervals between taps during the SCT (Merchant et al. 2013b; Bartolo et al. 2014). This implies that single cells show an orderly decrease in discharge rate around a preferred value (Merchant et al. 2012). Notably, most of the cells were able to multiplex the two key parameters, since they exhibited both a preferred duration and a preferred serial-order (Fig. 1b). The preferred magnitudes of these cells cover all the tested durations and serial-order elements of our SCT (Merchant et al. 2013b).
3. **Neural population avalanches:** The MPC represented the temporal and sequential structure of rhythmic movements by activating small ensembles of tuned neurons in rapid succession, so that the pattern of active neurons changed dramatically within each interval of the SCT (Crowe et al. 2014) (Fig. 1c). The small groups of cells were interconnected, providing a strong synaptic drive to the next ensemble in a consecutive chain of neural events (Crowe et al. 2014). Consequently, these tuned neural circuits were dynamically organized to trigger a neural population avalanche within an interval. In addition, the neural avalanches were repeated for each of the serial order element of the task, with a different speed of neural recruitment depending on the duration of the produced interval (Merchant et al. 2015b; Perez et al. 2013).
4. **State network dynamics:** From the previously described encoding mechanisms, it is evident that MPC neurons display a complex repertoire of individual responses, exhibiting a great variety of multiphasic patterns during the SCT. This ample diversity of time-varying responses is characteristic of dynamic systems. Hence, we decided to analyze the underlying activity structure on large neural populations during the SCT. The projection of the high dimensional individual neural activity into a low dimensional topological space generates a robust periodic organization (Fig. 1d). The resulting rotatory neural-state trajectories show systematic changes in their amplitude and variability as a function of the interval and serial order of the SCT. Indeed, the periodic nature of the neural-state oscillations is present when monkeys entrain their movements with a metronome and during internally

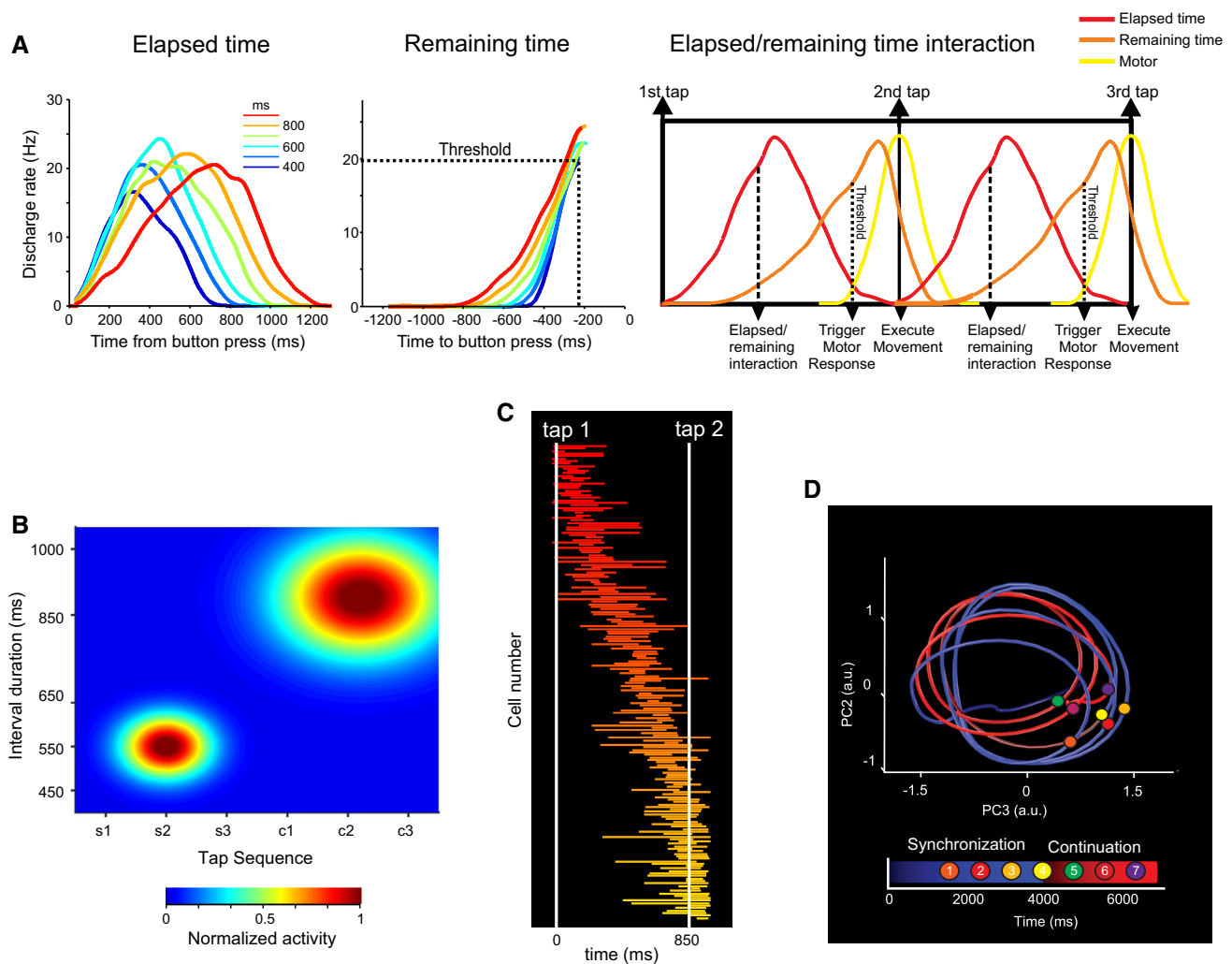


Fig. 1 **a** Ramp population functions for absolute-timing cells that encode elapsed time (*left*), and relative-timing cells that encode remaining time for a tap (*center*). The former are aligned to the previous button press, whereas the latter are aligned to the next button press. The *color code* in the *inset* of **a** corresponds to the duration of the produced intervals during the SCT (modified from Merchant et al. 2011). *Right* model that suggests that the tight interaction between the elapsed and remaining time ramping cells defines the dwell between stereotypic tapping movements. Once the remaining time cells reach a response threshold, they trigger the activity of the motor ramps that control of the fixed chain of movements engaged in a single tapping behavior (modified from Donnet et al. 2014). **b** Neural tuning for both the duration and sequential order of the SCT in two MPC neurons: one with a short preferred interval and a preferred serial order during the second interval of the synchronization phase, and another with a long preferred interval and a preferred serial order during the second interval of the continuation phase. *s1*, *s2*, *s3* are the three intervals of the synchronization, and *c1*, *c2* and *c3* are the three intervals of the continuation. The *color bar* corresponds to the magnitude of the

timed tapping, but not during a serial control task, where the same movements are executed but timing is precluded. Interestingly, the representation of the three SCT parameters (interval duration, serial order, and task condition) is highly distributed among the cell population.

normalized discharge rate of the neurons. (modified from Merchant et al. 2013b). **c** Response profiles for the cells with significant activation periods in a Poisson-train analysis (Merchant et al. 2001). *Each row* is associated with one neuron and the onset and extent of each activation period are illustrated as a *horizontal line*. The two *white vertical lines* correspond to the first and second tap of the continuation phase of the SCT. The cells are aligned and sorted to the peak of maximum response. Indeed, the *color code* used in the activation profiles is used to highlight the continuum in the peak response of the MPC cells (modified from Merchant et al. 2015b). **d** Neural population trajectories during the SCT, which correspond to the projection of the neural activity in the MPC onto the two dimensional principal components (PC2 and PC3) of the cell population. *Each point* in the *trajectory* represents the neural network state at that moment. The trajectory completes an oscillatory cycle on every produced interval during the synchronization (*blue*) and continuation (*red*) phases of the SCT (modified from Gamez et al. 2017). Each tap in the task is projected into the neural trajectories as a *circle*, whose *number* and *color code* is in the *inset*

Consequently, the dynamic state of MPC neural populations acts as a clock that explains complex features of individual-neuron responses, and that can be used to predict sensory and motor rhythmic events (Merchant et al. 2014; Gamez et al. 2017).

It is important to mention that these neural codes are used by the primate mCBGT to encode the duration of produced intervals. However, the brain can also use temporal neural codes to represent other cognitive processes, such as visual, auditory and, tactile sensation and perception (Zarco and Merchant 2009).

Beta oscillations and motor behavior

Brain oscillations are a fundamental element of information processing in the brain because they provide an effective means to control the timing of neuronal firing. As a consequence, they can temporally coordinate the information transfer across brain regions and support spike-timing dependent plasticity (Buzsaki 2006; Buzsaki and Draguhn 2004; Engel et al. 2001). Numerous primate studies have provided evidence that motor cortical beta-band oscillations (12–30 Hz) increase after the presentation of a cue that guides a movement, decrease during movement execution, and increase again during holding periods after the movement (Sanes and Donoghue 1993; Murthy and Fetz 1996; Baker et al. 1997). Furthermore, neostriatal beta activity has been associated with top-down control of behavior (Courtemanche et al. 2003), as in the execution of previously entrained responses (Howe et al. 2011). Recently, however, different lines of evidence support the notion that beta-activity serves as a general coupling mechanism of neuronal activity within (Howe et al. 2011; Takahashi et al. 2015) and across brain structures (Kay and Beshel 2010; Leventhal et al. 2012). Indeed, discrete bursts of beta oscillations occur almost simultaneously throughout different nuclei of the mCBGT on normal behaving rats. Notably, this state of elevated beta power reflects not simply sensory processing, or motor output, but rather occurs as subjects use sensory cues to determine voluntary actions (Leventhal et al. 2012). The highly regulated and transient nature of beta oscillations throughout mCBGT circuit is linked directly with a clear engagement of an animal in a particular task, whereas beta oscillations are less prominent during spontaneous behavior (Mallet et al. 2008). Consequently, it has been suggested that beta oscillations reflect a stabilized state of the mCBGT networks that reduces interference from alternative potential actions, and allows to focus on a paradigm (Engel and Fries 2010).

On the other hand, abnormally strong beta-oscillations have been found in the CBGT circuit of Parkinson's disease (PD) patients (Levy et al. 2002; Weinberger et al. 2009). In contrast, beta-power is reduced by treatments that improve bradykinesia and rigidity, such as dopamine replacement therapy (Brown et al. 2001; Levy et al. 2002) and deep brain stimulation (Kühn et al. 2008). The current

hypothesis is that the increased beta power in PD, resulting from low dopamine levels, may reflect over-stabilization of the mCBGT network, producing an extreme persistence of the current motor state (Hammond et al. 2007). Therefore, the pathological enhancement of beta-oscillations in PD results in an almost complete inability to modify their motor behavior. There are two additional lines of evidence supporting the notion that dopamine plays a critical role in the maintenance of an ongoing functional state. First, it has been shown that antagonists of dopaminergic receptors produce an elongation of produced intervals (see Buhusi and Meck 2005). Second, it has been shown that activation of D2 receptors promotes functional reconfiguration of the striatal microcircuit (Carrillo-Reid et al. 2011), whereas dopamine depletion promotes the emergence of a dominant state (Jaidar et al. 2010). Nevertheless, there is evidence against a causal role of beta-band oscillations in this disease (see Eusebio and Brown 2009 for a review). Furthermore, the large increase in beta-band spiking oscillations in MPTP-treated parkinsonian monkeys is present in neurons from many nuclei across the CBGT circuit, but not in medium spiny neurons of the neostriatum (Deffains et al. 2016).

Overall, these studies support the hypothesis that beta oscillations are part of a brain mechanism engaged in maintaining the status quo across large portions of the motor system (Engel and Fries 2010).

Human beat-based timing and beta oscillations

Beat perception is a cognitive ability that allows the detection of a regular pulse (or beat) in music and permits synchronous entrainment to this pulse during dancing and musical group playing (Merchant et al. 2015a). Thus, beat-based timing can be considered a fundamental musical trait that, arguably, played a crucial role in the origins of music (Honing 2013; Mendoza and Merchant 2014). Beat-based timing occurs within a specific frequency range corresponding to the musical tempo between 0.5 and 5 Hz.

In order to move in synchrony to a musical rhythm, the brain must extract the regularity in the incoming temporal information and predict when the next beat will occur. There is increasing evidence that beat perception involves tight interactions between auditory and motor systems (Merchant and Yarrow 2016). The bottom-up and top-down interactions between the auditory system and mCBGT seem to be accomplished by means of the oscillatory behavior of across these circuits (Merchant and Yarrow 2016). Specifically, it has been suggested that temporal prediction is accomplished in the motor system, through some sort of movement simulation (Arnal and Giraud 2012; Morillon and Schroeder 2015). This

predictive information is provided to sensory areas through an oscillatory corollary discharge, in order to enhance processing of incoming information at particular points in time (Schroeder and Lakatos 2009; Morillon et al. 2014).

Induced beta oscillations correspond to changes in power that are not phase locked to sensory or motor events. Interestingly, the amplitude fluctuations of induced beta constitute a large part of the predictive signal needed to perceive and entrain to a beat (Merchant et al. 2015a). Human EEG or MEG recordings during isochronous auditory sequences exhibit an induced beta power that initially decreases following each tone in the sequence, and is followed by an increase rebound prior the onset of the next tone (Fujioka et al. 2009). The timing of the induced beta rebound has a periodic timing that predicts the tempo of the stimulus beat, which is disrupted when a stimulus in the sequence is omitted. For example, when human participants are instructed to extract the beat from a rhythmic pattern of ambiguous metrics (i.e. weak vs strong), a peak of induced beta activity was observed just before the stimulus corresponding to the perceived downbeat (Iversen et al. 2009). Furthermore, enhanced beta activity was observed in the auditory cortex of participants passively listening to isochronous sequences of auditory stimuli, but not when sequences were irregular (Fujioka et al. 2012). Interestingly, beta activity also occurred in motor areas, including the MPC during passive listening to isochronous stimuli, with an opposite phase compared to auditory cortical areas. These findings suggest that beta oscillatory activity provides a top-down motor expectation signal of the beat structure to the auditory system (Fujioka et al. 2012).

Recently, Fujioka et al. (2015) investigated the role of induced beta oscillations in representing “what” and “when” information in musical sequences with different metrical contexts, namely, a march (one-two, one-two) and a waltz (one-two-three, one-two-three). Musically trained subjects listened to beat sequences of metrically accented beats, where every second (march) or third (waltz) beat was louder, along with similar unaccented beats. The task consisted of an initial perception phase where accented beats were presented in march or waltz contexts, where subjects required to actively perceive the meter, followed by an imagery phase where unaccented beats were presented at a softer intensity and participants had to subjectively imagine the meter. The results showed an induced beta power with a sharp decrease after the stimulus and a subsequent recovery with a shallow slope that could distinguish between accented beat positions (march vs waltz) in the metrical sequences.

Summarizing, the human audiomotor system during beat perception is tightly coordinated through beta oscillations, which produce a predictive signal from the motor to the

auditory system that controls the influx of information of the next beat in a sequence of rhythmic stimuli.

Putaminal beta oscillations increase during internally driven rhythmic tapping

For long, beat perception and rhythm entrainment have been considered unique human abilities (Fitch 2013; Patel 2014; Honing et al. 2012). Nevertheless, recent behavioral and electrophysiological findings have demonstrated that monkeys can entrain to an isochronous metronome (Zarco et al. 2009; Merchant et al. 2015a, b). Indeed, the gradual audiomotor evolution hypothesis (Merchant and Honing 2014; Honing and Merchant 2014) suggests beat-based timing to be omnipresent in humans, but only present in nonhuman primates when processing regular sequences (Honing et al. 2017; García-Garibay et al. 2016). Consequently, we studied the changes in beta oscillations in the LFPs of the dorsal putamen of monkeys performing the SCT. This task includes tapping to an isochronous metronome, followed by an internally driven tapping behavior.

We found tuning for interval and/or serial order as an orderly change in the power of transient modulations in the beta-band across putaminal LFPs during the execution of the SCT (Bartolo et al. 2014). These are sharp beta increases with a preferred interval or serial order, similarly to the temporal or sequential tuning observed in single cell discharge rate (Merchant et al. 2013b). In the case of interval tuned beta oscillations, we found that all the tested durations were represented across LFPs. However, there was a bias in the distribution of preferred durations toward intervals 800 ms, which is similar to the bias of preferred durations for single cells in the medial premotor cortex (MPC) (Merchant et al. 2013b). This bias could be associated with the preferred tempo in Rhesus monkeys. Indeed, the preferred tempo in humans is 600 ms (Fraisse 1982; Collyer et al. 1994).

Notably, there was a strong bias in the serial order tuned LFPs toward the continuation phase for the beta-band when the activity was aligned to the taps (Fig. 2); whereas in gamma-band, the bias was toward the synchronization phase of the SCT, especially when the spectrograms were aligned to the stimuli (Bartolo et al. 2014). Gamma and beta band bursts rarely co-occurred in the same recording site. These results suggest a division of labor where gamma oscillations are linked with the stimulus processing of the metronome, whereas the beta oscillations are engaged in the control of internally driven tapping. In addition, an analysis of coherence between simultaneously recorded LFPs tuned to serial order showed that beta-oscillations were largely coherent and in-phase at large recording distances, suggesting that beta oscillations are used for high-

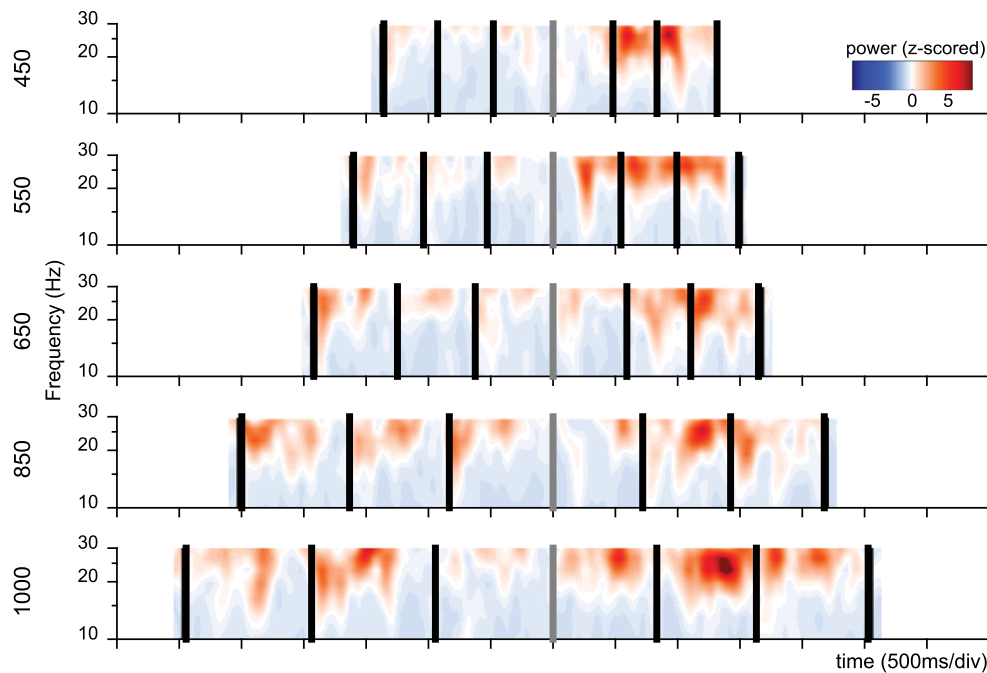


Fig. 2 Spectrograms of the LFP oscillatory activity of one recording site. Each panel is the average beta-band spectrogram (n trials = 5) during the execution of the SCT for different target intervals, as indicated on the left. Spectrograms are aligned to the last tap of the

synchronization phase of the SCT (gray vertical bars). Black bars represent the tapping times. The color code is the normalized spectral power in the beta-band frequencies (z scored with respect to the mean and SD power during the whole recording session)

level interactions involving large areas of the putamen, and probably also other elements of the CBGT circuit, during the execution of internally driven rhythmic behaviors. In contrast, gamma-band oscillations were local. These results suggest that beta bursts reflect stable and sustained activity of a broad network involved in top-down control of internally driven isochronous tapping (Bartolo et al. 2014).

It is important to consider that putaminal neurons recorded with the same electrode as the LFPs became entrained to beta-oscillations, indicating that this band is driving the firing patterns of putaminal cells, and that the tuning to duration and/or serial order in the rhythmic activity of LFPs were generated, at least in part, within the putamen.

In this regard, PD patients have clear deficiencies in the organization of sequential and temporal aspects of motor behavior (Harrington et al. 1998; Helmuth et al. 2000; Merchant et al. 2008c). MPC is strongly connected with the putamen and is a critical node of the CBGT circuit (Parent and Hazrati 1995; Middleton and Strick 2000). Hence, these previous observations and the current data suggest that tuning to duration and serial order is an encoding strategy used along the CBGT circuit to represent the temporal and sequential structure of rhythmic movements.

Based on all this evidence, it seems reasonable to consider that the mCBGT circuit is part of the beat-based timing mechanism that exhibits a global entrainment in the beta band during the production of internally timed movements in the SCT (Teki 2014). The network

entrainment in the beta band during internally driven rhythmic movements reduces interference from sensory inputs, permitting the internal clock to take control of the timing behavior (Bartolo et al. 2014).

Beta oscillations encode the initiation of motor sequences

We also compared the beta burst modulations in the primate putamen during two sequential tasks. The SCT, described above, that is a regularly paced sequential tapping task; and the RTT that is a reaction time task, where the sequence of taps is irregular, since the interval between the stimuli that drive the tapping is random (Bartolo and Merchant 2015). Again, we found that beta bursts are tuned to the sequential structure of the tasks, decreasing their spectral power around a preferred serial order. The preferred serial-order distribution was strongly biased toward the beginning of the task during the RTT. Concordantly, the same sequence initiation beta signal was observed during the SCT, when LFPs were aligned to the stimulus times. This initiation signal was followed by enhanced beta activity during the internally paced phase of the SCT as seen before (Bartolo et al. 2014).

These findings suggest that striatal activity also plays a role in cueing the initiation of a motor sequence. A general starting signal mediated by beta activity was present during

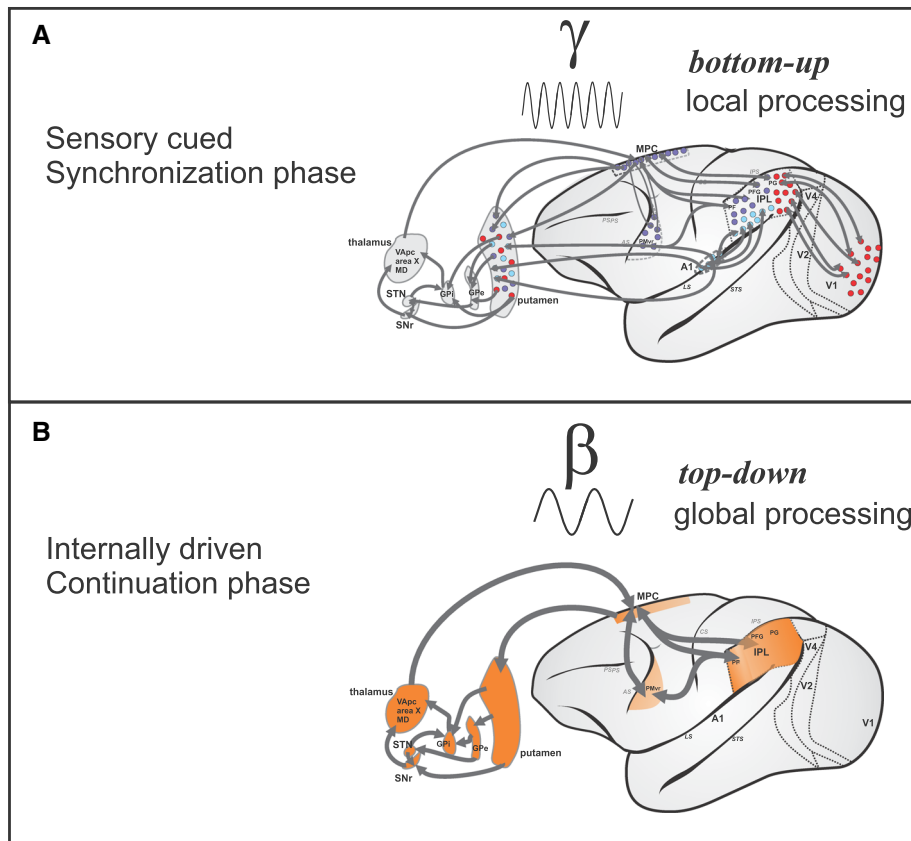


Fig. 3 The motor cortico-basal ganglia-thalamo-cortical circuit (mCBGT) of the monkey is implicated in rhythmic processing during the SCT. **a** During the Synchronization phase, the processing of the sensory metronome is accomplished through local gamma oscillations defining a bottom-up flow of information, starting from the corresponding primary sensory area to the parietal and then premotor areas, as well as by the mCBGT. In turn the mCBGT drives the tapping behavior. Visual (*red*) and auditory (*blue*) dorsal stream inputs are depicted as well as bimodal regions (*purple*). *Small circles* across the areas represent neurons responsive to the corresponding *color coded* modality. **b** During the continuation phase, the internally driven motor behavior is due to a top-down signal that depends on the

global beta oscillation entrainment across all the mCBGT depicted in orange. *A1* primary auditory area, *AS* arcuate sulcus, *CS* central sulcus, *GPe* globus pallidus externus, *GPI* globus pallidus internus, *IPL* inferior parietal lobe, *IPS* intraparietal sulcus, *LS* lateral sulcus, *MPC* medial premotor cortex, *MD* nucleus medialis dorsalis, *PF* part of rostral inferior parietal convexity, *PFg* part of rostral inferior parietal convexity, caudal to PF, *PG* part of caudal inferior parietal convexity, caudal to PFG, *PMvr* rostral ventral premotor area, *PS* principal sulcus, *SNr* substantia nigra pars reticulata, *STN* subthalamic nucleus, *STS* superior temporal sulcus, *VAp* nucleus ventralis anterioris pars parvocellularis, *V1* primary visual area, *V2* secondary visual area

isochronous tapping, as well as during irregular tapping, particularly when spectrograms were aligned to stimulus times (Bartolo and Merchant 2015). This pattern is consistent with the idea that beta activity reflects the utilization of a cue to initiate or cancel an action (Leventhal et al. 2012). Thus, the observed initial and stimulus-driven beta bursts may reset the entire mCBGT circuit to engage in different sequential behaviors. Indeed, previous studies suggest that cell activity in the basal ganglia encode the first and last elements of behavioral sequences, allowing the concatenation of single movements into integrated sequential actions (Jin and Costa 2010). Consequently, these results support the role of beta oscillations in sequence bounding that may reflect a general brain mechanism for packing individual behavioral elements as a sequential entity (Fujii and Graybiel 2003).

Concluding remarks

Recently, a canonical microcircuit for predictive coding has been proposed. Prediction in this circuit emerges from the iterative communication between (1) bottom-up processing in the superficial cortical neurons that represent stimulus properties using gamma oscillations and (2) top-down coding of predictive signals by deep cortical cells oscillating in the beta band (Bastos et al. 2012). We can attempt to generalize this idea on how the intrinsic interaction within the mCBGT shapes the SCT execution. First, the bottom-up processing of the metronome in the gamma band gives access to the sensory information to the mCBGT (Fig. 3a). This local sensory signal then is transformed into a perceived beat model of the metronome, that now is predictive and is used to trigger the taps during the

synchronization (Merchant et al. 2015b). When the metronome is turned off, the internal predictive machinery across all the mCBGT is turned on, where the beta oscillations take the lead and plays the simultaneous role of: (1) acting as a bonding signal across all this circuit, and (2) controlling the temporal behavior during the continuation phase of the SCT (Fig. 3b). Fortunately, this model is in accordance with all the beat-based timing research performed in humans. Nevertheless, it is evident that extensive experiments are needed to have a better understanding of the neural mechanisms of beat-based timing during the SCT in non-human primates. Of critical importance is the simultaneous recordings of the auditory areas, the MPC, and the basal ganglia to determine in real time the bottom-up and top-down interactions between the critical elements of the circuit engaged during this classical task of motor timing (Mendoza et al. 2016).

To end, the study of the neural underpinnings of beat perception and entrainment in monkeys is critical to understand how the audiomotor system in humans can predict the regular pulse of music and then respond in synchrony to this beat during dancing and musical ensemble playing. Beat perception and synchronization can be considered fundamental musical element that played a decisive role in the origins of music (Merchant et al. 2015a). Indeed, these abilities were gradually developed in the primate order, with all the basic elements present in macaques (Merchant and Honing 2014). Consequently, the recording of single cells, neural populations, and LFPs in different areas of the audiomotor system will be of crucial value to understand the dynamical processing of sensory information, the prediction of sensory and motor events, and the control of movements with precise timing during tasks such as the SCT.

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References

- Arnal LH, Giraud AL (2012) Cortical oscillations and sensory predictions. *Trends Cogn Sci* 16(7):390–398
- Baker SN, Olivier E, Lemon RN (1997) Coherent oscillations in monkey motor cortex and hand muscle EMG show task-dependent modulation. *J Physiol* 501(1):225–241
- Bartolo R, Merchant H (2009) Learning and generalization of time production in humans: rules of transfer across modalities and interval durations. *Exp Brain Res* 197(1):91–100
- Bartolo R, Merchant H (2015) β oscillations are linked to the initiation of sensory-cued movement sequences and the internal guidance of regular tapping in the monkey. *J Neurosci* 35(11):4635–4640
- Bartolo R, Prado L, Merchant H (2014) Information processing in the primate basal ganglia during sensory guided and internally driven rhythmic tapping. *J Neurosci* 34(11):3910–3923
- Bastos AM, Usrey WM, Adams RA, Mangun GR, Fries P, Friston KJ (2012) Canonical microcircuits for predictive coding. *Neuron* 76(4):695–711
- Brown P, Oliviero A, Mazzone P, Insola A, Tonali P, Di Lazzaro V (2001) Dopamine dependency of oscillations between subthalamic nucleus and pallidum in Parkinson's disease. *J Neurosci* 21(3):1033–1038
- Buhusi CV, Meck WH (2005) What makes us tick? Functional and neural mechanisms of interval timing. *Nat Rev Neurosci* 6:755–765
- Buzsaki G (2006) *Rhythms of the brain*. Oxford University Press, Oxford
- Buzsaki G, Draguhn A (2004) Neuronal oscillations in cortical networks. *Science* 304:1926–1929
- Carrillo-Reid L, Hernandez-Lopez S, Tapia D, Galarraga E, Bargas J (2011) Dopaminergic modulation of the striatal microcircuit: receptor-specific configuration of cell assemblies. *J Neurosci* 31(42):14972–14983
- Collyer CE, Broadbent HA, Church RM (1994) Preferred rates of repetitive tapping and categorical time production. *Attent Percept Psychophys* 55(4):443–453
- Courtemanche R, Fujii N, Graybiel AM (2003) Synchronous, focally modulated β -band oscillations characterize local field potential activity in the striatum of awake behaving monkeys. *J Neurosci* 23(37):11741–11752
- Crowe DA, Zarco W, Bartolo R, Merchant H (2014) Dynamic representation of the temporal and sequential structure of rhythmic movements in the primate medial premotor cortex. *J Neurosci* 34(36):11972–11983
- Deffains M, Iskhakova L, Katabi S, Haber SN, Israel Z, Bergman H (2016) Subthalamic, not striatal, activity correlates with basal ganglia downstream activity in normal and parkinsonian monkeys. *Elife* 5:e16443
- Diehl RL, Lotto AJ, Holt LL (2004) Speech perception. *Annu Rev Psychol* 55:149–179
- Donnet S, Bartolo R, Fernandes JM, Cunha JPS, Prado L, Merchant H (2014) Monkeys time their pauses of movement and not their movement-kinematics during a synchronization-continuation rhythmic task. *J Neurophysiol* 111(10):2138–2149
- Engel AK, Fries P (2010) Beta-band oscillations—signalling the status quo? *Curr Opin Neurobiol* 20(2):156–165
- Engel AK, Fries P, Singer W (2001) Dynamic predictions: oscillations and synchrony in top-down processing. *Nat Rev Neurosci* 2:704–716
- Eusebio A, Brown P (2009) Synchronisation in the beta frequency-band—the bad boy of parkinsonism or an innocent bystander? *Exp Neurol* 217(1):1–3
- Fitch W (2013) Rhythmic cognition in humans and animals: distinguishing meter and pulse perception. *Front Syst Neurosci* 7:68
- Fraisse P (1982) Rhythm and tempo. In: Deutsch D (ed) *Psychology of music*. Academic, New York, pp 149–180
- Fujii N, Graybiel AM (2003) Representation of action sequence boundaries by macaque prefrontal cortical neurons. *Science* 301(5637):1246–1249
- Fujioka T, Trainor LJ, Large EW, Ross B (2009) Beta and gamma rhythms in human auditory cortex during musical beat processing. *Ann N Y Acad Sci* 1169(1):89–92
- Fujioka T, Trainor LJ, Large EW, Ross B (2012) Internalized timing of isochronous sounds is represented in neuromagnetic beta oscillations. *J Neurosci* 32(5):1791–1802

- Fujioka T, Ross B, Trainor LJ (2015) Beta-band oscillations represent auditory beat and its metrical hierarchy in perception and imagery. *J Neurosci* 35(45):15187–15198
- Gamez J, Bartolo R, Mendoza G, Prado L, Merchant H (2017) Coupling of periodic neural state trajectories during rhythmic tapping. *Nat Commun* (**submitted**)
- García-Garibay O, Cadena-Valencia J, Merchant H, de Lafuente V (2016) Monkeys share the human ability to internally maintain a temporal rhythm. *Front Psychol* 7:1971. doi:10.3389/fpsyg.2016.01971
- Gouvêa TS, Monteiro T, Motiwala A, Soares S, Machens C, Paton JJ (2015) Striatal dynamics explain duration judgments. *eLife* 4:e11386
- Grahn JA, Brett M (2007) Rhythm and beat perception in motor areas of the brain. *J Cogn Neurosci* 19(5):893–906
- Grahn JA, Rowe JB (2009) Feeling the beat: premotor and striatal interactions in musicians and nonmusicians during beat perception. *J Neurosci* 29(23):7540–7548
- Grube M, Cooper FE, Chinnery PF, Griffiths TD (2010) Dissociation of duration-based and beat-based auditory timing in cerebellar degeneration. *Proc Natl Acad Sci* 107(25):11597–11601
- Gupta DS, Merchant H (2017) Editorial: understanding the role of the time dimension in the brain information processing. *Front Psychol* 8:240
- Hammond C, Bergman H, Brown P (2007) Pathological synchronization in Parkinson's disease: networks, models and treatments. *Trends Neurosci* 30(7):357–364
- Harrington DL, Haaland KY, Hermanowitz N (1998) Temporal processing in the basal ganglia. *Neuropsychologia* 12(1):3
- Helmuth LL, Mayr U, Daum I (2000) Sequence learning in Parkinson's disease: a comparison of spatial-attention and number-response sequences. *Neuropsychologia* 38(11):1443–1451
- Honing H (2013) Structure and interpretation of rhythm in music. In: Deutsch D (ed) *Psychology of Music*, 3rd edn. Academic press, London, pp 369–404
- Honing H, Merchant H (2014) Differences in auditory timing between human and nonhuman primates. *Behav Brain Sci* 37(06):557–558
- Honing H, Merchant H, Háden GP, Prado L, Bartolo R (2012) Rhesus monkeys (*Macaca mulatta*) detect rhythmic groups in music, but not the beat. *PLoS One* 7(12):e51369
- Honing H, Bouwer FL, Prado L, Merchant H (2017). Rhesus monkeys (*Macaca mulatta*) detect isochrony in rhythm, but not the beat. *Cortex* (**submitted**)
- Howe MW, Atallah HE, McCool A, Gibson DJ, Graybiel AM (2011) Habit learning is associated with major shifts in frequencies of oscillatory activity and synchronized spike firing in striatum. *Proc Natl Acad Sci* 108(40):16801–16806
- Iversen JR, Repp BH, Patel AD (2009) Top-down control of rhythm perception modulates early auditory responses. *Ann N Y Acad Sci* 1169(1):58–73
- Jaidar O, Carrillo-Reid L, Hernandez A, Drucker-Colín R, Bargas J, Hernandez-Cruz A (2010) Dynamics of the parkinsonian striatal microcircuit: entrainment into a dominant network state. *J Neurosci* 30(34):11326–11336
- Janata P, Grafton ST (2003) Swinging in the brain: shared neural substrates for behaviors related to sequencing and music. *Nat Neurosci* 6:682–687
- Jazayeri M, Shadlen MN (2015) A neural mechanism for sensing and reproducing a time interval. *Curr Biol* 25(20):2599–2609
- Jin X, Costa RM (2010) Start/stop signals emerge in nigrostriatal circuits during sequence learning. *Nature* 466(7305):457–462
- Kay LM, Beshel J (2010) A beta oscillation network in the rat olfactory system during a 2-alternative choice odor discrimination task. *J Neurophysiol* 104(2):829–839
- Knudsen EB, Powers ME, Moxon KA (2014) Dissociating movement from movement timing in the rat primary motor cortex. *J Neurosci* 34(47):15576–15586
- Kühn AA, Kempf F, Brücke C, Doyle LG, Martinez-Torres I, Pogosyan A, Vandenberghe W (2008) High-frequency stimulation of the subthalamic nucleus suppresses oscillatory β activity in patients with Parkinson's disease in parallel with improvement in motor performance. *J Neurosci* 28(24):6165–6173
- Kung SJ, Chen JL, Zatorre RJ, Penhune VB (2013) Interacting cortical and basal ganglia networks underlying finding and tapping to the musical beat. *J Cogn Neurosci* 25(3):401–420
- Large EW, Herrera JA, Velasco MJ (2015) Neural networks for beat perception in musical rhythm. *Front Syst Neurosci* 9:159. 2015, doi:10.3389/fnsys.2015.00159 (**eCollection**)
- Leventhal DK, Gage GJ, Schmidt R, Pettibone JR, Case AC, Berke JD (2012) Basal ganglia beta oscillations accompany cue utilization. *Neuron* 73(3):523–536
- Levy R, Ashby P, Hutchison WD, Lang AE, Lozano AM, Dostrovsky JO (2002) Dependence of subthalamic nucleus oscillations on movement and dopamine in Parkinson's disease. *Brain* 125(6):1196–1209
- Mallet N, Pogosyan A, Márton LF, Bolam JP, Brown P, Magill PJ (2008) Parkinsonian beta oscillations in the external globus pallidus and their relationship with subthalamic nucleus activity. *J Neurosci* 28(52):14245–14258
- Matell MS, Meck WH (2004) Cortico-striatal circuits and interval timing: coincidence detection of oscillatory processes. *Cogn Brain Res* 21(2):139–170
- Mello GB, Soares S, Paton JJ (2015) A scalable population code for time in the striatum. *Curr Biol* 25(9):1113–1122
- Mendez JC, Prado L, Mendoza G, Merchant H (2011) Temporal and spatial categorization in human and non-human primates. *Front Integr Neurosci* 5:50
- Méndez JC, Pérez O, Prado L, Merchant H (2014) Linking perception, cognition, and action: psychophysical observations and neural network modelling. *PLoS One* 9(7):e102553
- Mendoza G, Merchant H (2014) Motor system evolution and the emergence of high cognitive functions. *Prog Neurobiol* 122:73–93
- Mendoza G, Peyrache A, Gámez J, Prado L, Buzsáki G, Merchant H (2016) Recording extracellular neural activity in the behaving monkey using a semichronic and high-density electrode system. *J Neurophysiol* 116(2):563–574
- Merchant H, Averbeck BB (2017) The computational and neural basis of rhythmic timing in medial premotor cortex. *J Neurosci*. doi:10.1523/JNEUROSCI.0367-17.2017
- Merchant H, de Lafuente V (2014a) Introduction to the neurobiology of interval timing. *Adv Exp Med Biol* 829(1):1–13
- Merchant H, de Lafuente V (2014b) *Neurobiology of interval timing*. Springer Editorial System, Berlin
- Merchant H, Georgopoulos AP (2006) Neurophysiology of perceptual and motor aspects of interception. *J Neurophysiol* 95(1):1–13
- Merchant H, Honing H (2014) Are non-human primates capable of rhythmic entrainment? Evidence for the gradual audiomotor evolution hypothesis. *Front Neurosci* 7:274
- Merchant H, Yarrow K (2016) How the motor system both encodes and influences our sense of time. *Curr Opin Behav Sci* 8:22–27
- Merchant H, Battaglia-Mayer A, Georgopoulos AP (2001) Effects of optic flow in motor cortex and area 7a. *J Neurophysiol* 86(4):1937–1954
- Merchant H, Zarco W, Bartolo R, Prado L (2008a) The context of temporal processing is represented in the multidimensional relationships between timing tasks. *PLoS One* 3(9):e3169
- Merchant H, Zarco W, Prado L (2008b) Do we have a common mechanism for measuring time in the hundreds of millisecond range? Evidence from multiple-interval timing tasks. *J Neurophysiol* 99(2):939–949

- Merchant H, Luciana M, Hooper C, Majestic S, Tuite P (2008c) Interval timing and Parkinson's disease: heterogeneity in temporal performance. *Exp Brain Res* 184(2):233–248
- Merchant H, Zarco W, Prado L, Perez O (2009) Behavioral and neurophysiological aspects of target interception. *Adv Exp Med Biol* 629:201–220
- Merchant H, Zarco W, Pérez O, Prado L, Bartolo R (2011) Measuring time with different neural chronometers during a synchronization-continuation task. *Proc Natl Acad Sci USA* 108:19784–19789
- Merchant H, de Lafuente V, Pena-Ortega F, Larriva-Sahd J (2012) Functional impact of interneuronal inhibition in the cerebral cortex of behaving animals. *Prog Neurobiol* 99(2):163–178
- Merchant H, Harrington D, Meck WH (2013a) Neural basis of the perception and estimation of time. *Ann Rev Neurosci* 36(1):313–336
- Merchant H, Pérez O, Zarco W, Gámez J (2013b) Interval tuning in the primate medial premotor cortex as a general timing mechanism. *J Neurosci* 33(21):9082–9096
- Merchant H, Bartolo R, Perez O, Mendez JC, Mendoza G, Gamez J, Yc K, Prado L (2014) Neurophysiology of timing in the hundreds of milliseconds: multiple layers of neuronal clocks in the medial premotor areas. *Adv Exp Med Biol* 829(1):143–154
- Merchant H, Grahn J, Trainer L, Rohrmeier M, Fitch TW (2015a) Finding the beat: a neural perspective across humans and non-human primates. *Philos Trans R Soc Lond B Biol Sci* 370:186–202
- Merchant H, Perez O, Bartolo R, Mendez JC, Mendoza G, Gamez J, Yc K, Prado L (2015b) Sensorimotor neural dynamics during isochronous tapping in the medial premotor cortex of the macaque. *Eur J Neurosci* 41(5):586–602
- Middleton FA, Strick PL (2000) Basal ganglia output and cognition: evidence from anatomical, behavioral, and clinical studies. *Brain Cogn* 42(2):183–200
- Mita A, Mushiaki H, Shima K, Matsuzaka Y, Tanji J (2009) Interval time coding by neurons in the presupplementary and supplementary motor areas. *Nat Neurosci* 12:502–507
- Morillon B, Schroeder CE (2015) Neuronal oscillations as a mechanistic substrate of auditory temporal prediction. *Ann N Y Acad Sci* 1337(1):26–31
- Morillon B, Schroeder CE, Wyart V (2014) Motor contributions to the temporal precision of auditory attention. *Nat Commun* 5:5255. doi:10.1038/ncomms6255
- Murthy VN, Fetz EE (1996) Synchronization of neurons during local field potential oscillations in sensorimotor cortex of awake monkeys. *J Neurophysiol* 76(6):3968–3982
- Parent A, Hazrati LN (1995) Functional anatomy of the basal ganglia. I. The cortico-basal ganglia-thalamo-cortical loop. *Brain Res Rev* 20(1):91–127
- Patel AD (2014) The evolutionary biology of musical rhythm: was Darwin wrong? *PLoS Biol* 12(3):e1001821
- Perez O, Kass R, Merchant H (2013) Trial time warping to discriminate stimulus-related from movement-related neural activity. *J Neurosci Methods* 212(2):203–210
- Petter EA, Merchant H (2016) Temporal processing by intrinsic neural network dynamics. *Timing Time Percept* 4(4):399–410
- Repp BH, Su YH (2013) Sensorimotor synchronization: a review of recent research (2006–2012). *Psychon Bull Rev* 20(3):403–452
- Sanes JN, Donoghue JP (1993) Oscillations in local field potentials of the primate motor cortex during voluntary movement. *Proc Natl Acad Sci* 90(10):4470–4474
- Schroeder CE, Lakatos P (2009) Low-frequency neuronal oscillations as instruments of sensory selection. *Trends Neurosci* 32(1):9–18
- Schwartz M, Keller PE, Patel AD, Kotz SA (2011) The impact of basal ganglia lesions on sensorimotor synchronization, spontaneous motor tempo, and the detection of tempo changes. *Behav Brain Res* 216(2):685–691
- Takahashi K, Kim S, Coleman TP, Brown KA, Suminski AJ, Best MD, Hatsopoulos NG (2015) Large-scale spatiotemporal spike patterning consistent with wave propagation in motor cortex. *Nature Commun* 6:7169. doi:10.1038/ncomms8169
- Teki S (2014) Beta drives brain beats. *Front Syst Neurosci* 8:155
- Teki S, Grube M, Kumar S, Griffiths TD (2011) Distinct neural substrates of duration-based and beat-based auditory timing. *J Neurosci* 31(10):3805–3812
- Teki S, Grube M, Griffiths TD (2012) A unified model of time perception accounts for duration-based and beat-based timing mechanisms. *Front Integr Neurosci* 5:90
- Weinberger M, Hutchison WD, Dostrovsky JO (2009) Pathological subthalamic nucleus oscillations in PD: can they be the cause of bradykinesia and akinesia? *Exp Neurol* 219(1):58–61
- Wing AM (2002) Voluntary timing and brain function: an information processing approach. *Brain Cogn* 48(1):7–30
- Wright BA, Buonomano DV, Mahncke HW, Merzenich MM (1997) Learning and generalization of auditory temporal-interval discrimination in humans. *J Neurosci* 17(10):3956–3963
- Zarco W, Merchant H (2009) Neural temporal codes for representation of information in the nervous system. *Cogn Crit* 1(1):1–30
- Zarco W, Merchant H, Prado L, Mendez JC (2009) Subsecond timing in primates: comparison of interval production between human subjects and rhesus monkeys. *J Neurophysiol* 102(6):3191–3202