

Cortico-striatal circuits and the timing of action and perception

Citation for published version (APA):

Kotz, S. A., Brown, R. M., & Schwartze, M. (2016). Cortico-striatal circuits and the timing of action and perception. *Current Opinion in Behavioral Sciences*, 8, 42-45.
<https://doi.org/10.1016/j.cobeha.2016.01.010>

Document status and date:

Published: 01/04/2016

DOI:

[10.1016/j.cobeha.2016.01.010](https://doi.org/10.1016/j.cobeha.2016.01.010)

Document Version:

Publisher's PDF, also known as Version of record

Document license:

Taverne

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

Cortico-striatal circuits and the timing of action and perception

Sonja A Kotz^{1,2}, Rachel M Brown¹ and Michael Schwartz^{1,2}

Reciprocal connections between cortical and striatal regions of the brain form neuro-functional circuits that are recruited in a wide range of behaviors. One of the basic functions of these circuits is the encoding and decoding of temporal structure. Here we discuss recent evidence on temporal processing, focusing on structural and functional data that inform our understanding of specialization within these circuits and motivate future research avenues on the basis of an integrative temporal processing network.

Addresses

¹Department of Neuropsychology and Psychopharmacology, Maastricht University, Maastricht, The Netherlands

²Department of Neuropsychology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Corresponding author: Kotz, Sonja A
(sonja.kotz@maastrichtuniversity.nl)

Current Opinion in Behavioral Sciences 2016, 8:42–45

This review comes from a themed issue on **Time in perception and action**

Edited by **Warren H Meck** and **Richard B Ivry**

For a complete overview see the [Issue](#) and the [Editorial](#)

Available online 3rd February 2016

<http://dx.doi.org/10.1016/j.cobeha.2016.01.010>

2352-1546/© 2016 Elsevier Ltd. All rights reserved.

Organization of cortico-striatal circuits

To fully understand the neurophysiological, neuroanatomical, and behavioral bases of temporal processing in action and perception a detailed description of cortico-striatal connectivity and circuits is necessary. Over the last two decades several models describing the nature of cortico-striatal connections have emerged and there is general agreement that these connections are topographic. However, it remains a matter of debate whether cortical input to the striatum is diverse or region specific. On the one hand, one basal ganglia region can receive input from many cortical areas [1], while on the other hand one topographically mapped cortical area can project to one basal ganglia region [2,3]. The latter idea in particular has led to diverse closed loop or circuit models describing specific functional connections between cortical and subcortical brain regions [4–6,7**]. However, early on Middleton and Strick [8] argued that the striatum projects back to multiple cortical sites, so a simple closed

loop idea may not suffice. The split circuit model by Joel and Weiner [9] provides a possible solution. The model combines closed and open loops, where open loops moderate striatal projections to a cortical output area that does not project to the striatum itself and also supports communication between closed loops. Thus the split circuit model may best explain why damage to a specific topographic region within a closed loop may nevertheless lead to multifunctional deficits including sensory and motor timing deficits [10].

The nature of cortical–striatal circuits parallels the scientific discussion of how action and perception relate to each other and why temporal processing may play a comparable role in both domains. In a recent review Herwig [11] talked about whether the link between perception and action is structure or process-based. Seminal structure-based accounts postulate that action and perception are intrinsically linked [12,13]. Process-based accounts such as the common coding theory [14,15] propose that action is represented via its perceived sensory consequences and therefore relies on common ground or similarities between the two domains while other process-based accounts link action and perception through a common attentional process (e.g. [16]). Although further elaboration of these concepts is beyond the scope of the current review, both the common ground perspective and the attention perspective of action and perception invite a number of important questions: Are motor structures that also encompass the premotor cortex, supplementary motor area (SMA), basal ganglia and the cerebellum tightly connected to temporal processing, sensory prediction, and the allocation of attention to name a few (for an extensive elaboration see [17])? And if so, do we have to consider dynamic contributions of domain-general motor mechanisms to perception? Could we then conceive of a cortico-striatal circuit in which the basal ganglia bind events in time in both perception and action?

The basal ganglia in motor and perceptual timing

The basal ganglia are classically viewed as responsible for controlling motor behavior in time. This view has been largely driven by the study of Parkinson's disease, a disorder marked by striatal neurodegeneration and motor impairments such as freezing and tremors. Although there is a diverse body of evidence on Parkinson's disease [18,19], it has been suggested that the basal ganglia maintain temporal regularity in repetitive action, such as self-paced finger tapping or walking [20,21]. Further,

several lines of work also suggested a role for the basal ganglia in guiding timed actions based on external sensory information [22], as well as temporal perception in the absence of motor behavior [23]. This early work, along with later observations of increased gait regularity in the presence of a regular auditory stimulus [24], suggested that the basal ganglia may be important for regulating motor timing based on sensory input, a necessary component of motor behavior, and possibly perceptual temporal processing without the need or intention to move.

Recent evidence from patients and healthy adults lends further support to the idea that cortico-striatal circuits play a role in perceptual temporal processing. Patients with Multiple System Atrophy (MSA) and Huntington's disease, both of which involve atrophy of the caudate and putamen among other regions, demonstrated impaired temporal interval and temporal sequence discrimination relative to patients with peripheral nervous system disorders [25]. The link between the basal ganglia and perceptual temporal processing was further strengthened by work involving patients with lesions mainly of the caudate and putamen. Electrophysiological recordings in these patients showed reduced sensitivity to temporal regularity present in auditory sequences relative to healthy controls who were able to differentiate between temporally regular and irregular auditory sequences [26].

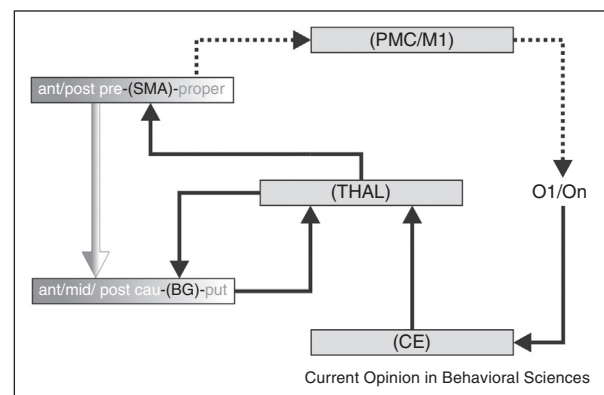
Complementary evidence from healthy adults has further linked individual variability and stimulus- and task demands to cortico-striatal activity in perceptual temporal processing. Individuals who more accurately discriminated visual stimulus durations also showed greater hemodynamic responses in the putamen and prefrontal cortex during temporal discrimination. In addition, individuals who expressed a genetic polymorphism associated with reduced striatal dopamine receptors showed reduced temporal discrimination accuracy and greater hemodynamic response in the caudate during temporal discrimination [27]. Basal ganglia and prefrontal BOLD responses also varied as a function of attention to temporal features, and the degree of discriminability between temporal features [28**]. Participants differentiated bursts of amplitude-modulated noise based on either their total duration or modulation rate. Response in the basal ganglia, along with SMA/pre-SMA and parietal regions among others, co-varied according to the degree of discriminability between the noise bursts based on the task-relevant temporal feature. In sum, there is now considerable evidence that the basal ganglia can contribute specifically to perceptual timing, in addition to timed movement.

Differentiation of uniform cortico-striatal circuits

The functional differentiation of the basal ganglia is paralleled by increasing evidence for functional and structural differentiation in other regions associated with

motor and perceptual timing such as the SMA, premotor cortex, and the cerebellum. In addition, new work suggests complex interactions between these structures and the basal ganglia and substantiates speculations about the nature of these interactions in perceptual temporal processing [29,30]. This knowledge is in part obtained through a combination of recent methodological developments such as MRI resting-state analyses [31–34] or meta-analytic connectivity in humans [35,36] as well as classic approaches such as single-unit recordings or viral tracing in animals [37*,38]. In addition to a more differentiated characterization of cortico-striatal circuits, including the connections between the supplementary motor area and the striatum, these studies provide evidence for direct subcortical pathways linking the cerebellum and the basal ganglia [33,38,39]. These reciprocal connections between core temporal proces-

Figure 1



Sensorimotor temporal processing. Cortico-striato-thalamo-cortical circuits engage in temporal processing in the hundreds-of-milliseconds to seconds range [40**,46]. The sequencing of motor actions probably relies on connections between the supplementary motor area (SMA) and the basal ganglia to encode the temporal structure of successive actions. Targets of this cortico-striatal 'pacing' signal may include the SMA-proper and its connections to premotor (PMC) and primary motor (M1) regions, thus guiding the actual implementation (dotted lines) of successive actions. Production of a motor action generates sensory feedback, that is, a sensory object (O1), thereby initiating a circular process in which a sequence of successive motor actions generates a temporally structured sequence of sensory objects (On). Decoding of the temporal structure of these sensory objects may rely on afferents from early stages of sensory processing to the cerebellum (CE) [30], and 'rapid cerebellar transmission' of an adaptively filtered representation of temporal structure (effectively a sensory 'pacing' signal) to the SMA via the thalamus (THAL). One of the advantages of this network architecture may be the precise automatic encoding of timing errors and their subsequent correction already at early processing stages like the cerebellum. However, simultaneous motor production and sensory processing of temporal structure ultimately requires a more fine-grained differentiation of the core components of the network. For example, structural subdivisions or connectivity patterns of the pre-SMA (into anterior and posterior parts) or the caudate nucleus of the striatum (into anterior, middle, and posterior parts) may map onto specific temporal processing demands and potentially foreshadow an even more detailed, gradual differentiation of a caudal–rostral axis within these structures and their connections.

sing regions (see Figure 1) effectively instantiate a distributed temporal processing network [40**], which may interface with sensory afferent pathways in order to establish a time-optimal perceptual processing mode [30].

It is important to note that the temporal processing function of this network may be activated simultaneously in perception and action as the temporal sequencing and implementation of motor behavior inevitably entails sensory feedback, which in turn may recruit perceptual temporal processing mechanisms. However, the premise of simultaneous action-related and perceptual temporal processing in the same brain regions suggests further structural and functional differentiation of micro regions within the respective macro regions. Despite the progress in dissociating such micro regions and their connectivity for each of the core temporal processing regions, it is difficult to define the criteria that lead to a match between the granularity of these subdivisions and the current concepts of temporal processing. For example, experimental data from perceptual and sensorimotor temporal processing studies are largely compatible with the classic two-part division of the SMA into the rostral pre-SMA and the more caudal SMA-proper along a vertical line intersecting the anterior commissure [41,42]. Via the thalamus, these SMA sub regions also receive concurrent projections from two dissociable non-motor and motor parts of the cerebellar dentate nucleus [43,44].

One of the challenges for conceptual models of temporal processing concerns the time-course and the structural level of the interactions between the core temporal processing regions, which, depending on the ‘entry point’ into the respective processing loops, can be described as cortical–striatal, cerebellar–cortical or vice versa. However, another challenge arises from recent resting-state functional connectivity data, which indicate a three-part division comprising anterior and posterior parts of the pre-SMA, defined in part by specific connections to the caudate nucleus and the putamen of the basal ganglia [33]. Additional criteria such as the specific temporal characteristics of the experimental task may hence have to be considered in order to match these levels of structural differentiation levels of conceptual differentiation in temporal processing models. However, diffusion MRI reveals a three-part division along an anterior–posterior axis also of the caudate nucleus [45] and the question arises whether a gradual differentiation will be required, potentially reflecting striatal micro regions that are defined by their links to cortical networks engaged in specific functions rather than by their links to discrete cortical regions [32].

Outlook

The aim of the current review was to connect recent and classical neuroanatomical and behavioral findings on the

role of cortico-striatal circuits in the timing of perception and action. While a number of central aspects such as the nature of the circuits (e.g. closed versus split), the essential sensorimotor rather than motor only function of the cortico-subcortical interface (e.g. SMA-basal ganglia), and the structural differentiation (e.g. rostral–caudal gradients) have been elucidated, at least two additional issues deserve further consideration: (1) One recent finding confirms the existence of direct subcortical pathways connecting the cerebellum to the basal ganglia via the thalamus. This connection allows direct short-latency modulation of the basal ganglia by the cerebellum [37*]. One intriguing possibility is that this direct connection supports small-scale automatic adjustments of sensorimotor timing errors. (2) To address temporal processing dysfunction and to better understand expertise, one needs to account for individual differences in the structure of these circuits and how these translate into functional differences in simple and complex temporal sequencing behavior.

Conflict of interest statement

Nothing declared.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Graybiel AM: **The basal ganglia.** *Curr Biol* 2000, **10**:R509-R511.
2. Alexander GE, DeLong MR, Strick PL: **Parallel organization of functionally segregated circuits linking basal ganglia and cortex.** *Ann Rev Neurosci* 1986, **9**:357-381.
First and seminal paper on functional cortico-striatal loops.
3. Strick PL, Dum RP, Picard N: **Motor areas on the medial wall of the hemisphere.** *Novartis Found Symp* 1995, **218**:64-75.
4. Middleton FA, Strick PL: **Basal-ganglia, projections' to the prefrontal cortex of the primate.** *Cereb Cortex* 2002, **12**:926-935.
5. Parent A, Hazrati LN: **Functional anatomy of the basal ganglia. I. The cortico-basal ganglia-thalamo-cortical loop.** *Brain Res Rev* 1995, **20**:91-127.
6. Parent A, Hazrati LN: **Functional anatomy of the basal ganglia. II. The place of subthalamic nucleus and external pallidum in basal ganglia circuitry.** *Brain Res Rev* 1995, **20**:128-154.
7. Draganski B, Kherif F, Klöppel S, Cook PA, Alexander DC, Parker GJM, Deichmann R, Ashburner J, Frackowiak RSJ: **Evidence for segregated and integrative connectivity patterns in the human basal ganglia.** *J Neurosci* 2008, **28**:7143-7152.
A methodologically advanced and outstanding view of functional cortico-striatal loops that considers connectivity patterns and parcellation.
8. Middleton FA, Strick PL: **Basal ganglia output and cognition: evidence from anatomical, behavioral, and clinical studies.** *Brain Cogn* 2000, **42**:183-200.
9. Joel D, Weiner I: **The connections of the dopaminergic system with the striatum in rats and primates: an analysis with respect to the functional and compartmental organization of the striatum.** *Neuroscience* 2001, **93**:451-474.
10. Dalla Bella S, Benoit C, Farrugia N, Schwartze M, Kotz SA: **Effects of auditory cuing in Parkinson's disease: beyond a motor benefit.** *Ann N Y Acad Sci* 2015, **1337**:77-85.

11. Herwig A: **Linking perception and action by structure or process? Toward an integrative perspective.** *Neurosci Biobehav Rev* 2015, **52**:105-116.
 12. James W: *The principles of psychology.* New York: Dover Publications; 1890.
 13. Sperry RW: **Neurology and the mind-body problem.** *Am Sci* 1991, **40**:291-312.
 14. Prinz W: **Perception and action planning.** *Eur J Cogn Psychol* 1997, **9**:129-154.
 15. Hommel B, Müsseler J, Aschersleben G, Prinz W: **The theory of event coding (TEC): a framework for perception and action planning.** *Behav Brain Sci* 2001, **24**:849-878.
 16. Schneider WX, Einhäuser W, Horstmann G: **Attentional selection in visual perception, memory, and action: a quest for cross-domain integration.** *Philos Trans R Soc Lond B Biol Sci* 2013, **368**:1-7.
 17. Press C, Cook R: **Beyond action-specific simulation: domain-general motor contributions to perception.** *Trends Cogn Sci* 2015, **19**:176-178.
 18. Merchant H, Luciana M, Hooper C, Majestic S, Tuite P: **Interval timing and Parkinson's disease: heterogeneity in temporal performance.** *Exp Brain Res* 2008, **184**:233-248.
 19. Jones C, Jahanshahi M: **Contributions of the basal ganglia to temporal processing: evidence from Parkinson's disease.** *Timing Time Percept* 2014, **2**:87-127.
 20. O'Boyle DJ, Freeman JS, Cody FWJ: **The accuracy and precision of timing of self-paced, repetitive movements in subjects with Parkinson's disease.** *Brain* 1996, **119**:51-70.
 21. Hausdorff JM, Cudkowicz ME, Firtion R, Wei JY, Goldberger AL: **Gait variability and basal ganglia disorders: stride-to-stride variations of gait cycle timing in Parkinson's disease and Huntington's disease.** *Mov Disord* 1998, **13**:428-437.
 22. Khudados E, Cody FWJ, O'Boyle: **Proprioceptive regulation of voluntary ankle movements, demonstrated using muscle vibration, is impaired by Parkinson's disease.** *J Neurol Neurosurg Psychiatry* 1999, **67**:504-510.
 23. Artieda J, Pastor MA, Lacruz F, Obeso JA: **Temporal discrimination is abnormal in Parkinson's disease.** *Brain* 1992, **115**:199-210.
 24. Baker K, Rochester L, Nieuwboer A: **The effect of cues on gait variability – reducing the attentional cost of walking in people with Parkinson's disease.** *Parkinsonism Relat Disord* 2008, **14**:314-320.
 25. Cope TE, Grube M, Singh B, Burn DJ, Griffiths TD: **The basal ganglia in perceptual timing: timing performance in Multiple System Atrophy and Huntington's disease.** *Neuropsychologia* 2014, **52**:73-81.
 26. Schwartz M, Stockert A, Kotz SA: **Striatal contributions to sensory timing: voxel-based lesion mapping of electrophysiological markers.** *Cortex* 2015, **71**:332-340.
 27. Wiener M, Lee Y-S, Lohoff FW, Coslett B: **Individual differences in the morphometry and activation of time perception networks are influenced by dopamine genotype.** *Neuroimage* 2014, **89**:10-22.
 28. Henry MJ, Hermann B, Obleser J: **Selective attention to temporal features on nested time scales.** *Cereb Cortex* 2015, **25**:450-459.
- This study provides evidence that striatal-cortical circuits play a role in the perception of auditory temporal features using an elegant temporal discrimination task in which stimuli are kept constant while the task-relevance of particular features of the stimuli was systematically varied.
29. Teki S, Grube M, Griffith TD: **A unified model of time perception accounts for duration-based and beat-based timing mechanisms.** *Front Integr Neurosci* 2012, **5**:90.
 30. Schwartz M, Kotz SA: **A dual-pathway neural architecture for specific temporal prediction.** *Neurosci Biobehav Rev* 2013, **37**:2587-2596.
 31. Di Martino A, Scheres A, Margulies DS, Kelly AMC, Uddin LQ, Shehzad Z, Biswal B, Walters JR, Castellanos FX, Milham MP: **Functional connectivity of human striatum: a resting state fMRI study.** *Cereb Cortex* 2008, **18**:2735-2747.
 32. Jung WH, Jang JH, Park JW, Kim E, Goo E, Im O, Kwon JS: **Unraveling the intrinsic functional organization of the human striatum: a parcellation and connectivity study based on resting-state fMRI.** *PLoS One* 2014, **9**:e106768.
 33. Zhang S, Ide JS, Li CR: **Resting-state functional connectivity of the medial superior frontal cortex.** *Cereb Cortex* 2012, **22**:99-111.
 34. Bernard JA, Peltier SJ, Benson BL, Wiggins JL, Jaeggi SM, Buschkuhl M, Jonides J, Monk CS, Seidler RD: **Dissociable functional networks of the human dentate nucleus.** *Cereb Cortex* 2014, **24**:2151-2159.
 35. Robinson JL, Laird AR, Glahn DC, Blangero J, Sanghera MK, Pessoa L, Fox PM, Uecker A, Friehs G, Young KA, Griffin JL, Lovaglio WR, Fox PT: **The functional connectivity of the human caudate: an application of meta-analytic connectivity modeling with behavioral filtering.** *Neuroimage* 2012, **60**:117-129.
 36. Riedel MC, Ray KL, Dick AS, Sutherland MT, Hernandez Z, Fox PM, Eickhoff SB, Fox PT, Laird AR: **Meta-analytic connectivity and behavioral parcellation of the human cerebellum.** *Neuroimage* 2015, **117**:327-342.
 37. Chen CH, Fremont R, Artega-Bracho EE, Khodakhah K: **Short latency cerebellar modulation of the basal ganglia.** *Nat Neurosci* 2014, **17**:1767-1775.
- This study provides evidence for a disynaptic pathway between the cerebellum and the striatum in mice, thus establishing a basis for rapid communication between the two regions and a cerebellar modulation of striatal activity.
38. Bostan AC, Dum RP, Strick PL: **The basal ganglia communicate with the cerebellum.** *Proc Natl Acad Sci U S A* 2010, **107**:8452-8456.
 39. Bostan AC, Dum RP, Strick PL: **Cerebellar networks with the cerebral cortex and basal ganglia.** *Trends Cogn Sci* 2013, **17**:241-254.
 40. Merchant H, Harrington DL, Meck WH: **Neural basis of the perception and estimation of time.** *Annu Rev Neurosci* 2013, **36**:313-336.
- This article provides an excellent overview of the current research into temporal processing and it details the notion of a distributed temporal processing network.
41. Picard N, Strick PL: **Imaging the premotor areas.** *Curr Opin Neurobiol* 2001, **11**:663-672.
 42. Schwartz M, Rothermich K, Kotz SA: **Functional dissociation of pre-SMA and SMA-proper in temporal processing.** *Neuroimage* 2012, **60**:290-298.
 43. Akkal DA, Dum RP, Strick PL: **Supplementary motor area and presupplementary motor area: targets of basal ganglia and cerebellar output.** *J Neurosci* 2007, **27**:10659-10673.
 44. Dum RP, Strick PL: **An unfolded map of the cerebellar dentate nucleus and its projections to the cerebral cortex.** *J Neurophysiol* 2003, **89**:634-639.
 45. Kotz SA, Anwender A, Axer H, Knösche TR: **Beyond cytoarchitectonics: the internal and external connectivity structure of the caudate nucleus.** *PLoS One* 2013, **8**:e70141.
 46. Buhusi CV, Meck WH: **What makes us tick? Functional and neural mechanisms of interval timing.** *Nat Rev Neurosci* 2005, **6**:755-765.