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Evaluating the roles of the basal ganglia and the cerebellum in time perception

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I. Timing in the brain

SENSORY CORTEX

HIPPOCAMPUS

PREFRONTAL CORTEX

SMA/PRE-SMA

BASAL GANGLIA

CEREBELLUM

Cerebellum

Neuropsychological work in patients with cerebellar degeneration:

- **Patient groups:** Unilateral/bilateral CB lesions; Parkinson's patients; Ataxics
- **Timing tasks:** Motor: Finger tapping, circle drawing
  Perceptual: duration discrimination
- **Response Measure:** Variability – motor vs. clock (cf. Wing & Kristofferson, 73)
- **Timing mechanisms:** Event-based (tapping) vs. Emergent (cont. circle) timing
- **Results:** CB patients impaired on event-based timing tasks
  PD patients impaired on emergent timing tasks

Cerebellum and Timing

- Involved in sub-second and not supra-second time perception
- Critical for behaviour requiring real-time prediction
- CB: error-based learning (climbing fiber as teaching signal)
- CB: instantiates an internal forward model

➢ **CB as a dedicated (event-based) timing system**

Basal ganglia

Neuropsychological work in patients (Artieda/Pastor/Harrington):

Parkinson's patients impaired on time perception and production tasks, implicating the nigrostriatal dopaminergic system.

Neurophysiological work in animal models with lesions/pharmacology (Meck):

- **Timing tasks:** Peak-interval timing
- **Response Measure:** Gaussian PI response function (mean & precision)
- **Timing mechanisms:** Striatal Beat Frequency model (Matell and Meck, 2004)
- **Results:** PI response function shifts horizontally with DA +/- (i.e., internal clock speeds up or down)

Magnitude of leftward shift α DA (+) dose
Magnitude of rightward shift α DA (-) affinity to D2 receptor

Basal ganglia and Timing

- Dorsal striatum (putamen and caudate) key for time perception
- Role of striatum in timing is dopamine dependent (nigrostriatal dopamine)
- Striato-frontal network (BG-SMA-PMC-DLPFC) key for timing
- BG computations based on dopamine-dependent reinforcement learning

➢ **Dorsal striatum as a possible substrate for an internal clock**

II. Timing mechanisms

- **Sub-second** **vs.** **Supra-second timing**
- **Event-based timing** **vs.** **Emergent timing**

Ivry et al.

- **Implicit** **vs.** **Explicit timing**

Coull et al.

- **Automatic** **vs.** **Cognitive timing**

Lewis and Miall

- **Duration-based** **vs.** **Beat-based timing**

Griffiths et al.

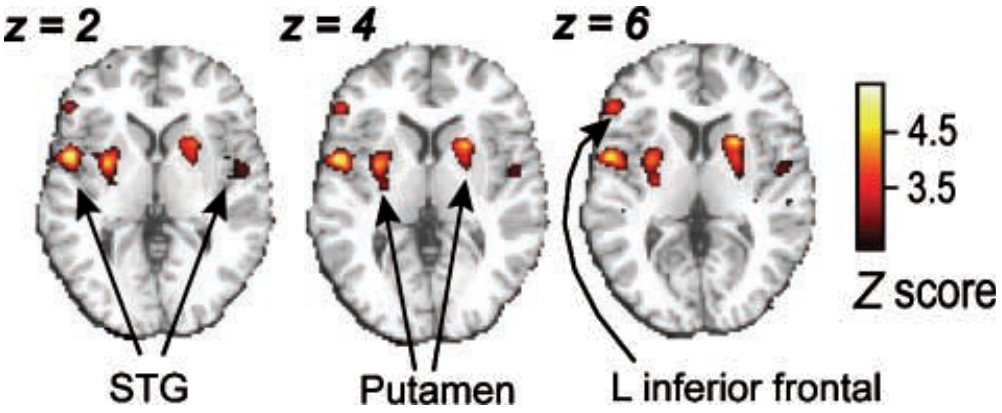
Beat-based timing

A regular beat offers beneficial temporal cues in perceptual timing

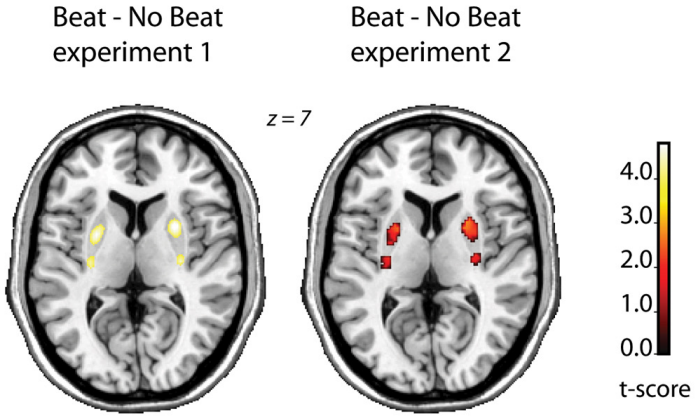
(Povel & Essen, 1985)

Parkinson's patients show deficits in perceptual timing tasks.

(Artieda et al. 1992, Harrington et al. 1998, Grahn & Brett, 2009)



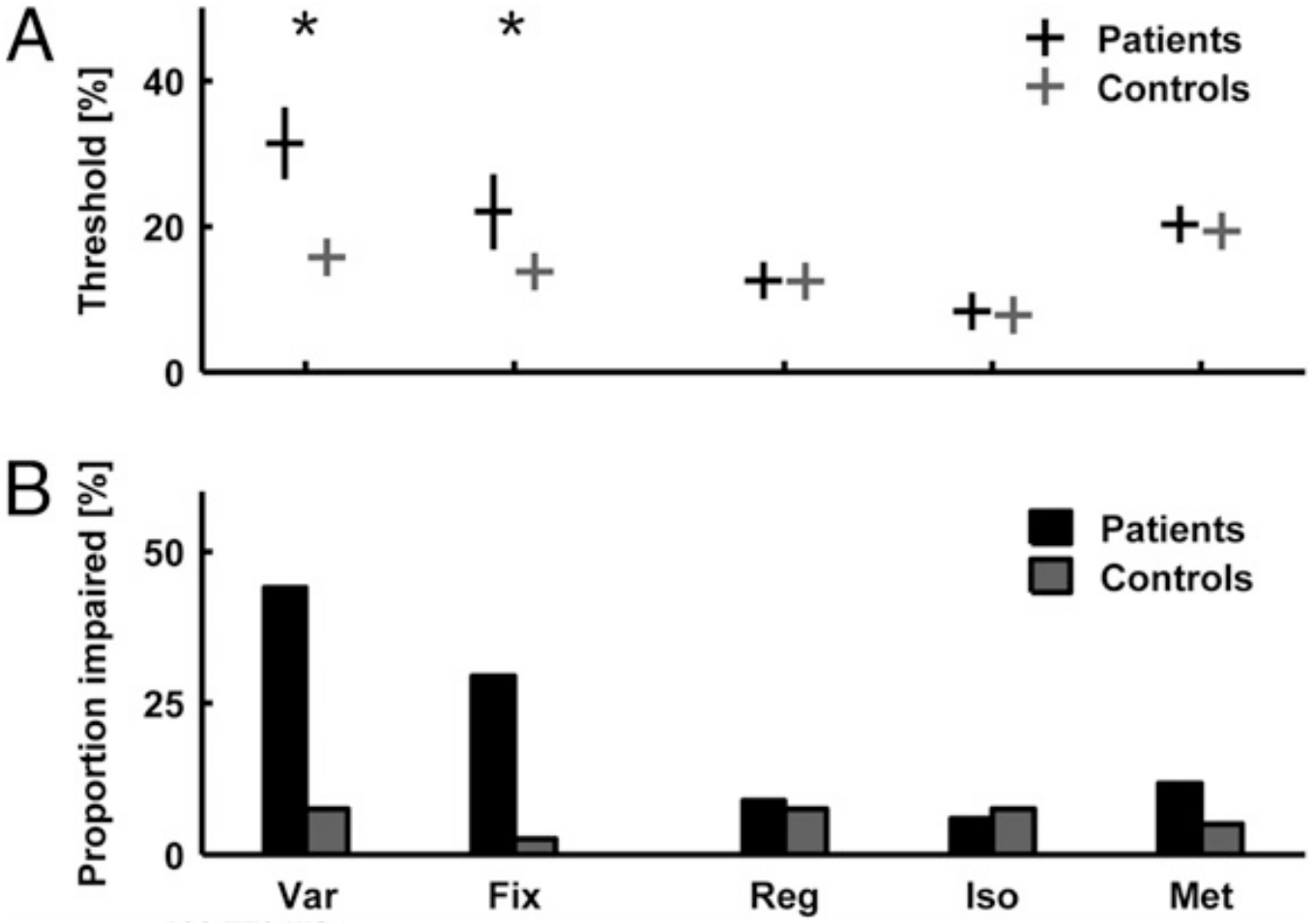
Grahn and Brett, 2007



Grahn and Rowe, 2009

Duration-based timing

Patients with Spino Cerebellar Ataxia type 6:



(Grube et al., 2010: PNAS)

III. Functional MRI study

Aim: Test for dissociation between the timing functions of cerebellum and basal ganglia according to the rhythmic context of time intervals.

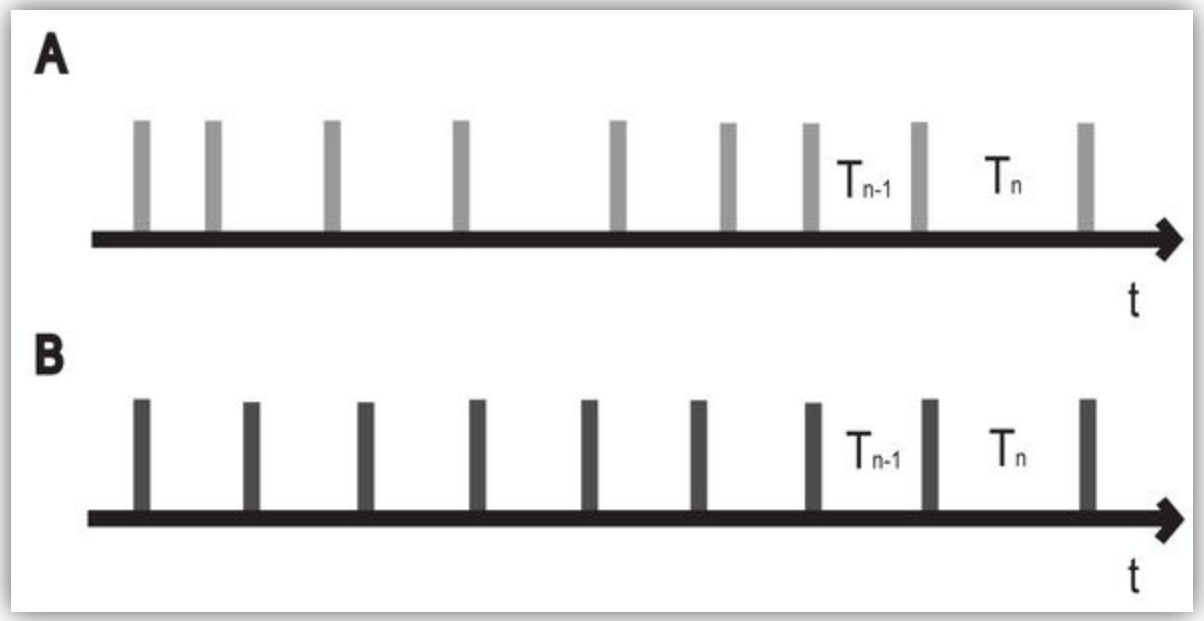
Hypotheses:

H1: Beat-based timing more accurate than duration-based timing

H2: Cerebellum more involved in absolute, duration-based timing

H3: Basal ganglia more involved in relative, beat-based timing

Stimulus and Task

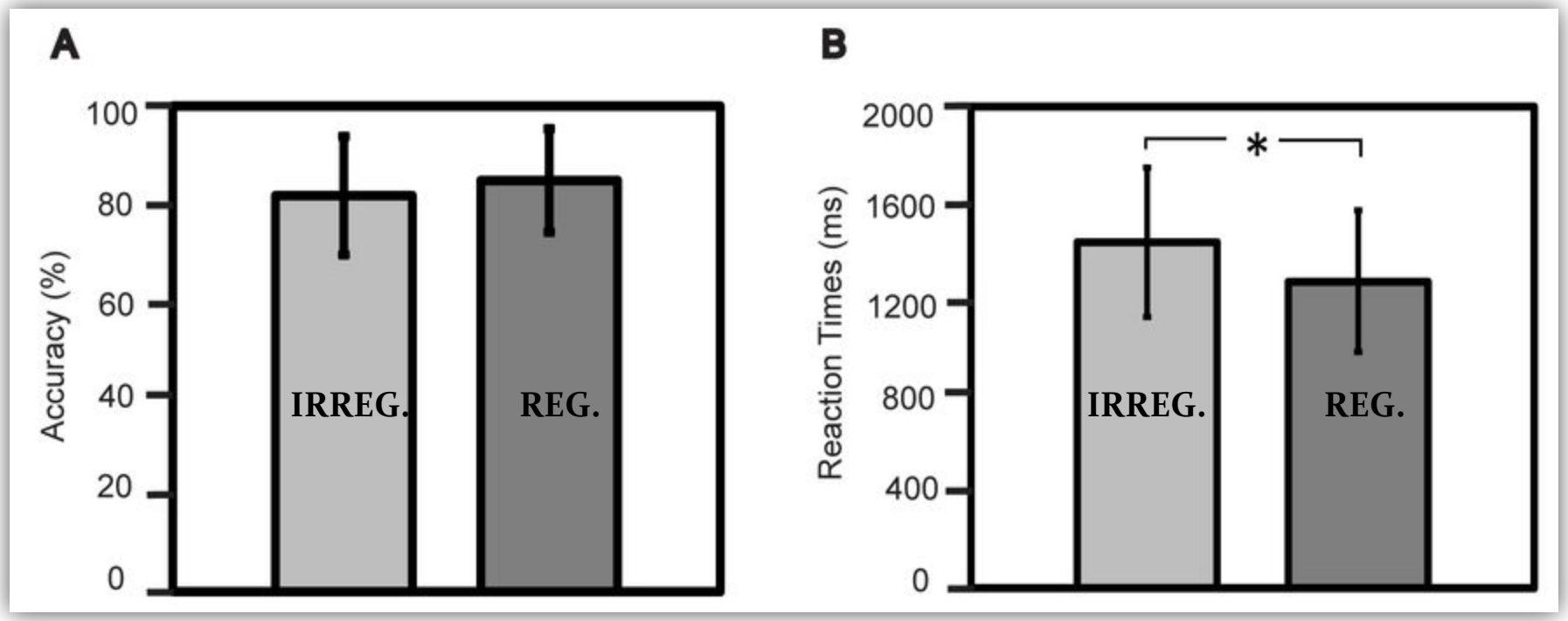


- ***Judge the duration of the final compared to the penultimate interval***
  T_n > / < T_{n-1}

Sequence A: Irregular with 15% average jitter

Sequence B: Regular with an isochronous beat

Behaviour in scanner



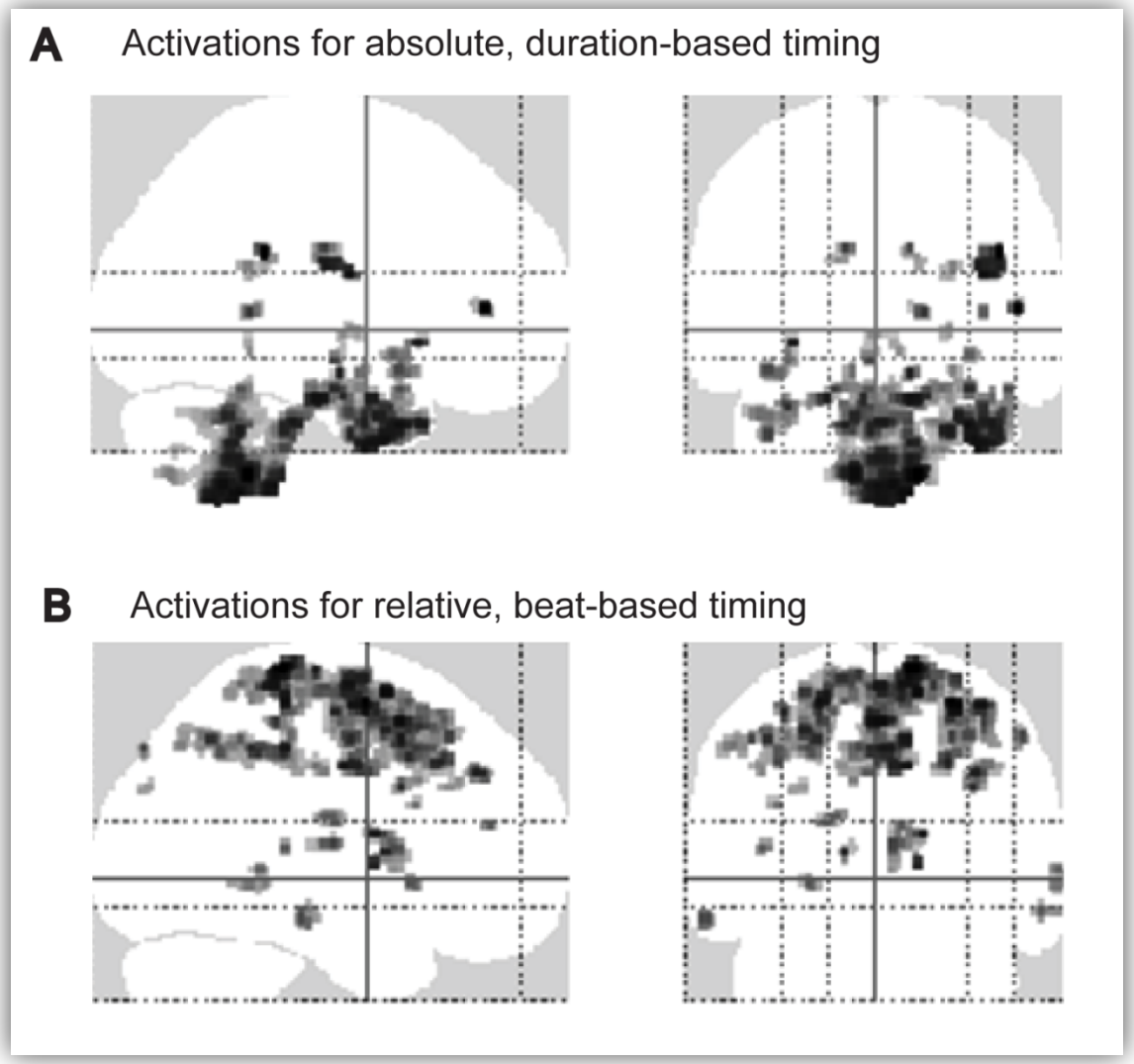
81.53% ± 12.28%

84.72% ±10.64%

1438 ± 297 ms

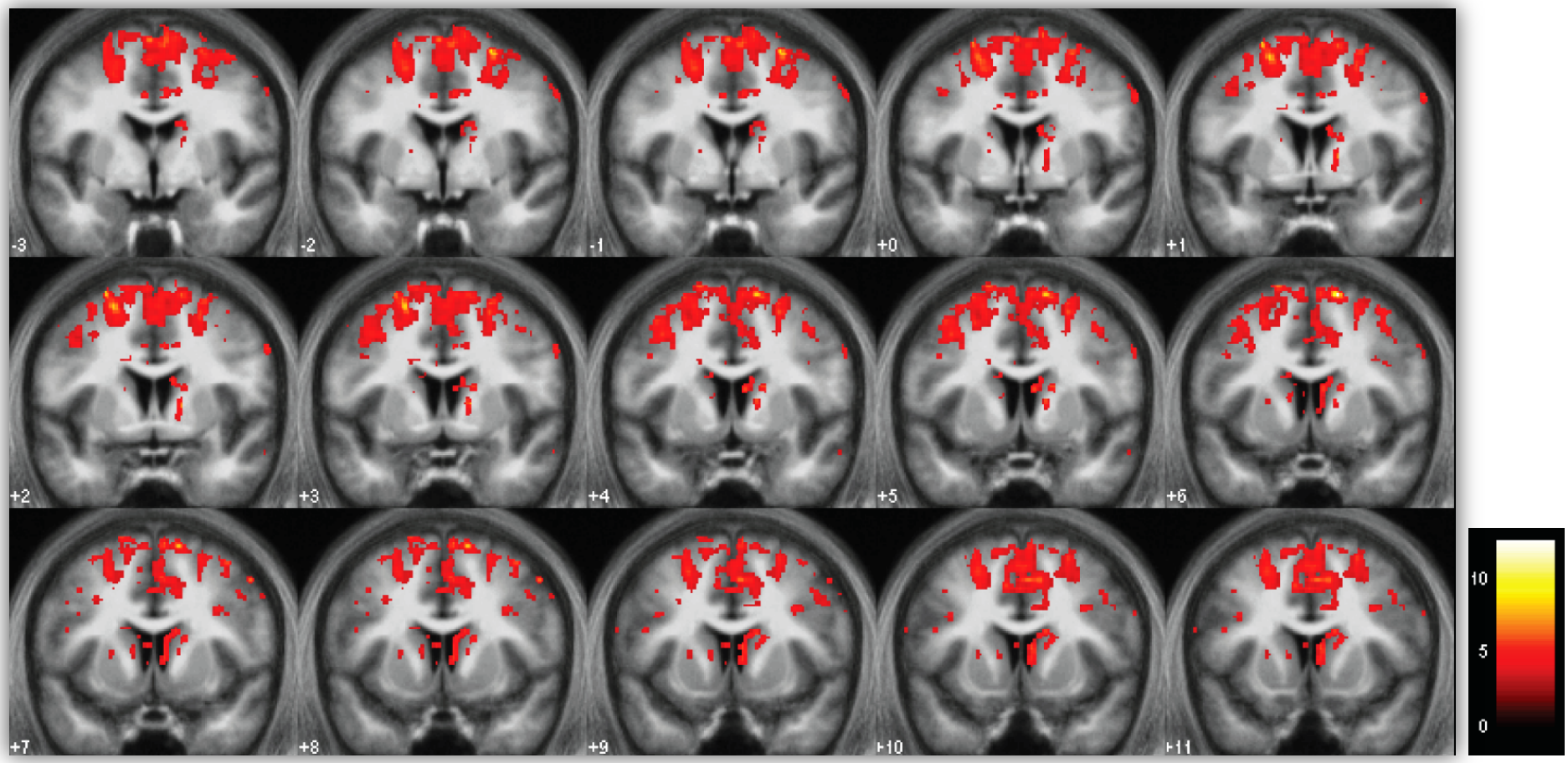
1275 ± 312 ms

fMRI results



MNI space; t-value > 4.00 and extent threshold > 10 voxels

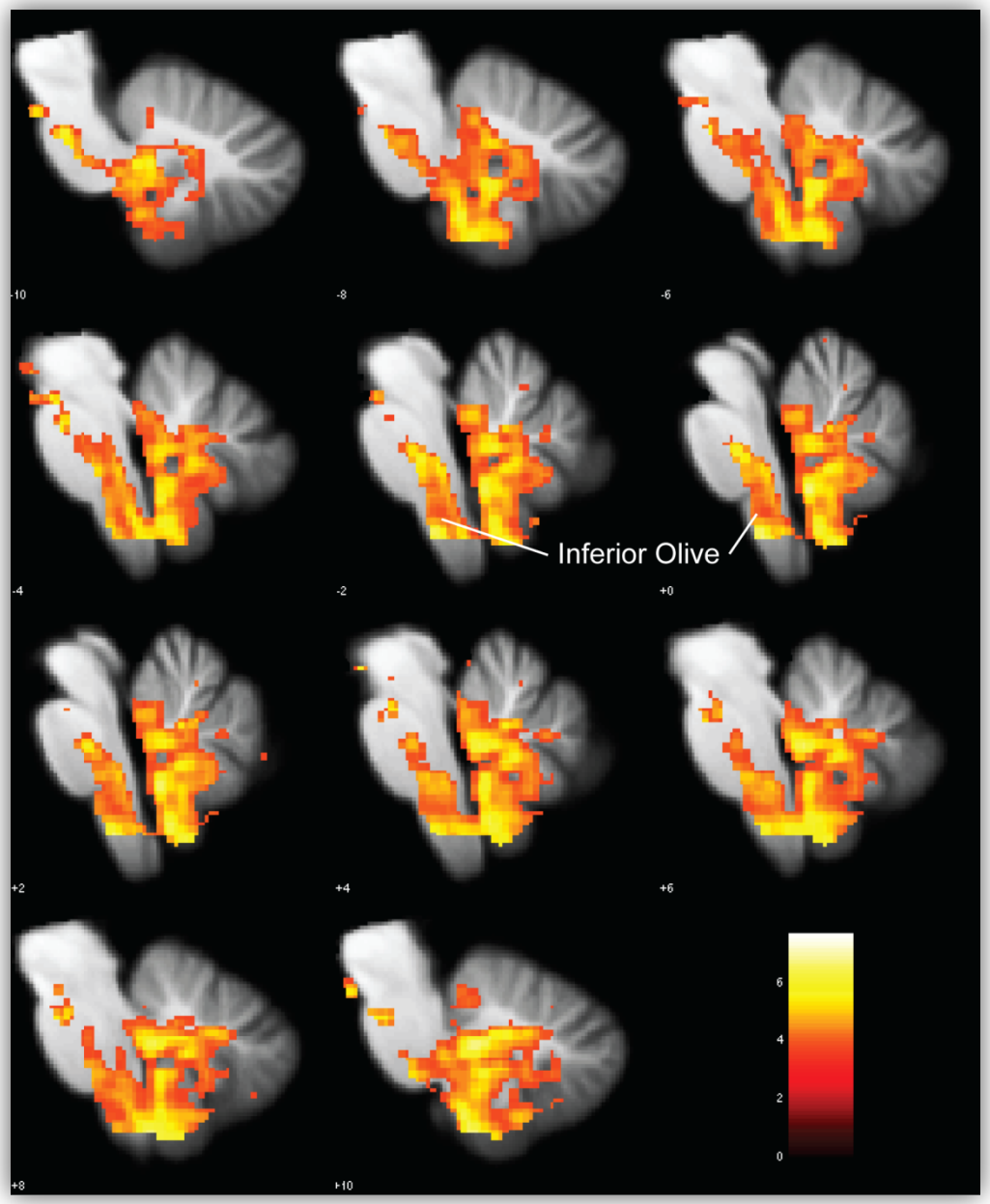
Fronto-striatal activations



x = -3 mm to + 11 mm

p < 0.001 (unc.)

Olivocerebellar activations

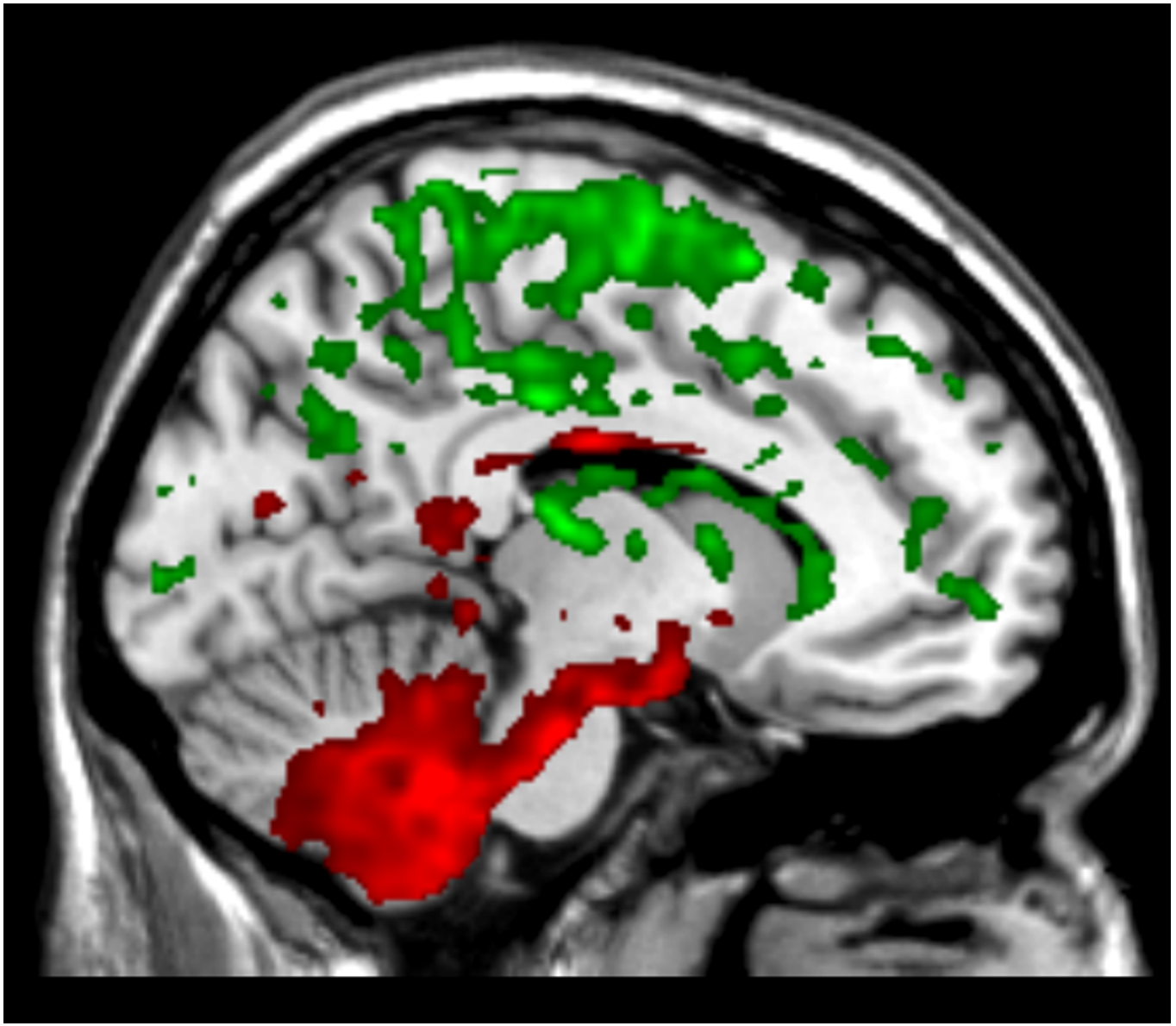


p < 0.001 (unc.)

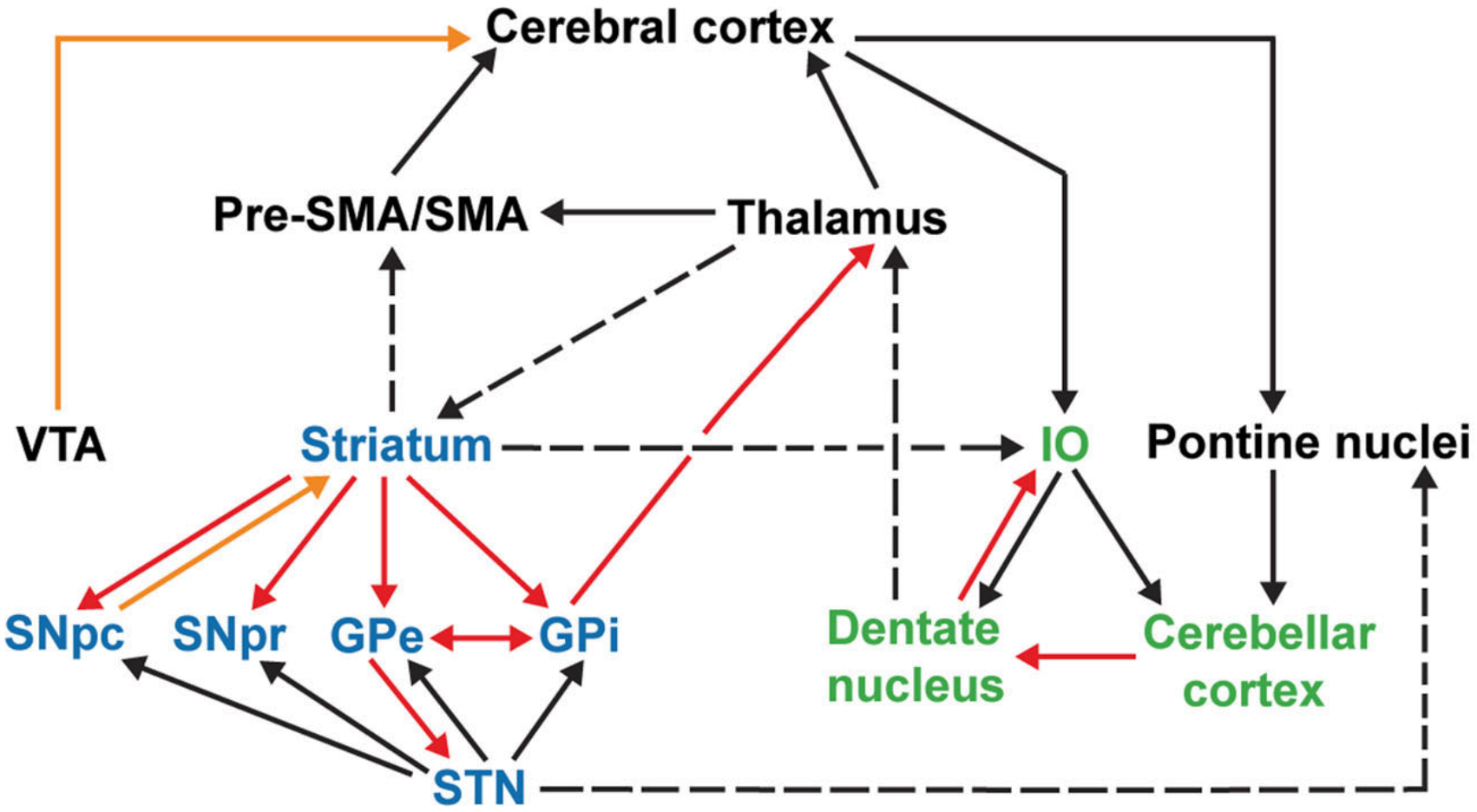
x = -10 to +10 mm

Teki et al., 2011
J Neurosci

Functional dissociation



IV. Unified model



Teki et al., 2012
Frontiers

Unified model: features

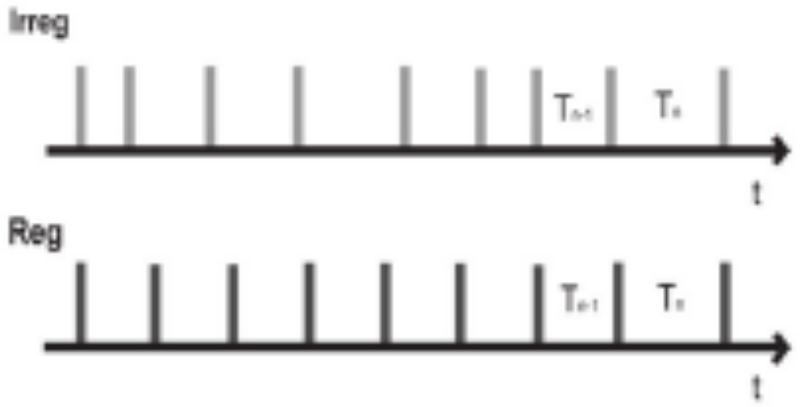
- Motor structures specialized for timekeeping in the brain
- Timing functions of BG and CB not necessarily independent
- BG network timing signal based on SBF model
- CB network timing signal based on known neurophysiology
- The two key networks interact to improve the accuracy of the timing signal

Assumptions:

- Striatum serves as default/central timekeeper
- Beat-based clock operates for timing stimuli in predictable, beat-based context
- Duration-based clock more active for stimuli in irregular, isolated context

Unified model: mechanism

- **Function**: beat-based timing with error-correction by duration-based clock



Regular context:
beat-based clock produces less errors in predicting next time intervals =>
less error-correction required and lesser contribution of CB clock

Irregular context:
beat-based clock produces larger errors in predicting next time intervals =>
greater error-correction required and more contribution by CB clock

Unified model: support

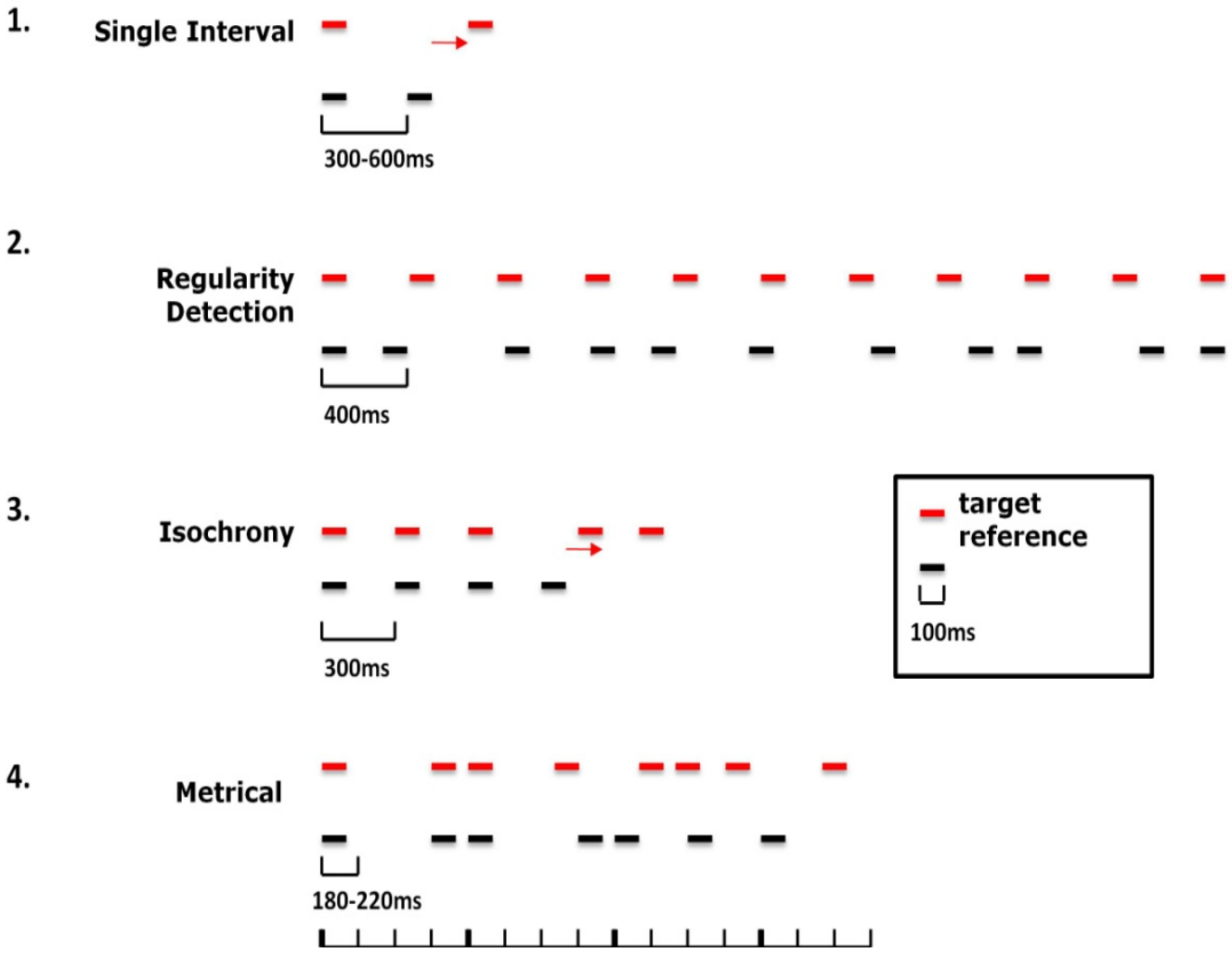
Is a functional dissociation possible?

- CB lesions do not affect relative timing (Grube) or emergent timing (Ivry)
- Striatal lesions affects both relative and absolute timing:

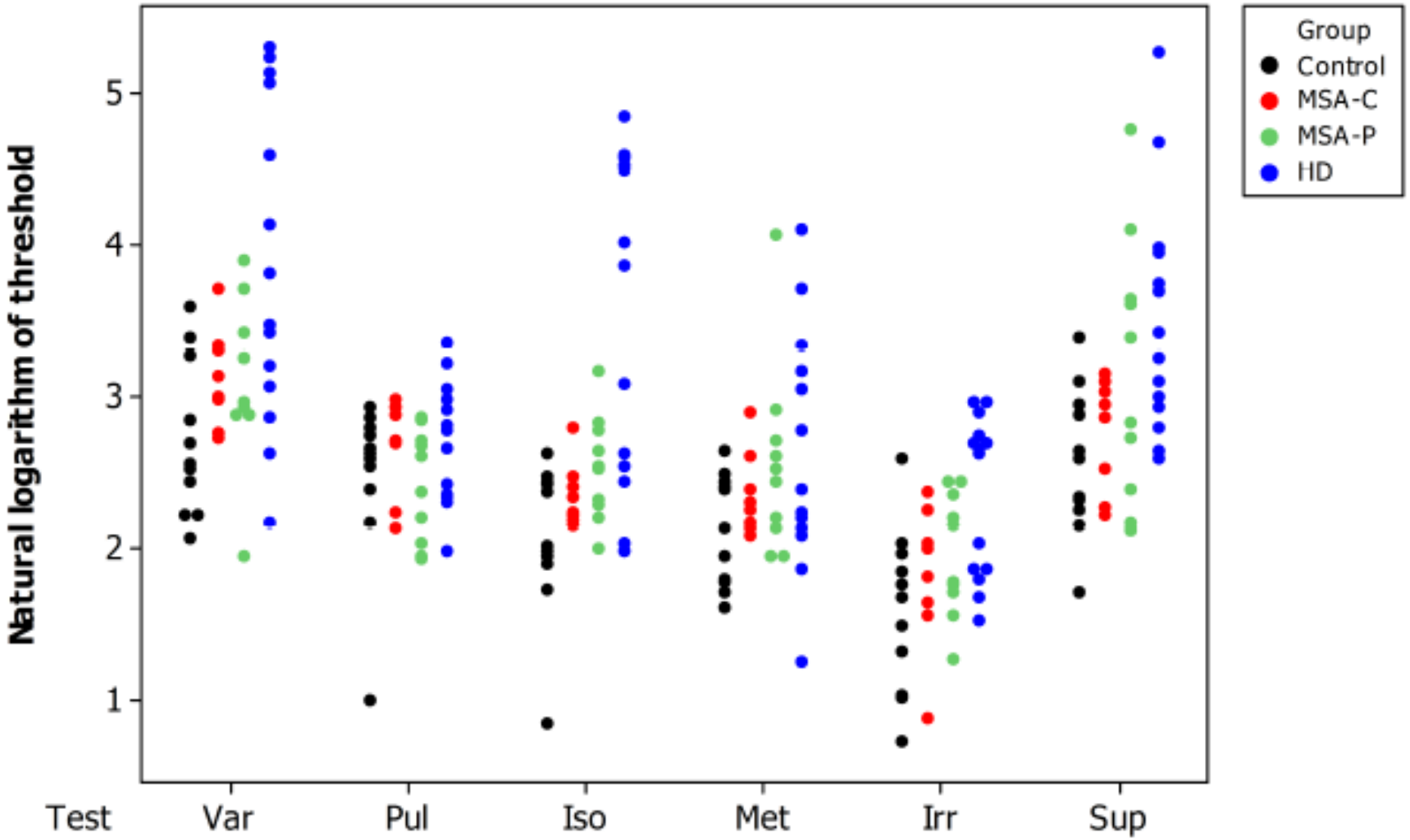
    1) **Parkinson's disease**

    2) **Huntington's disease and Multiple Systems Atrophy**

I. Parkinson's patients



II. Huntington's and MSA patients



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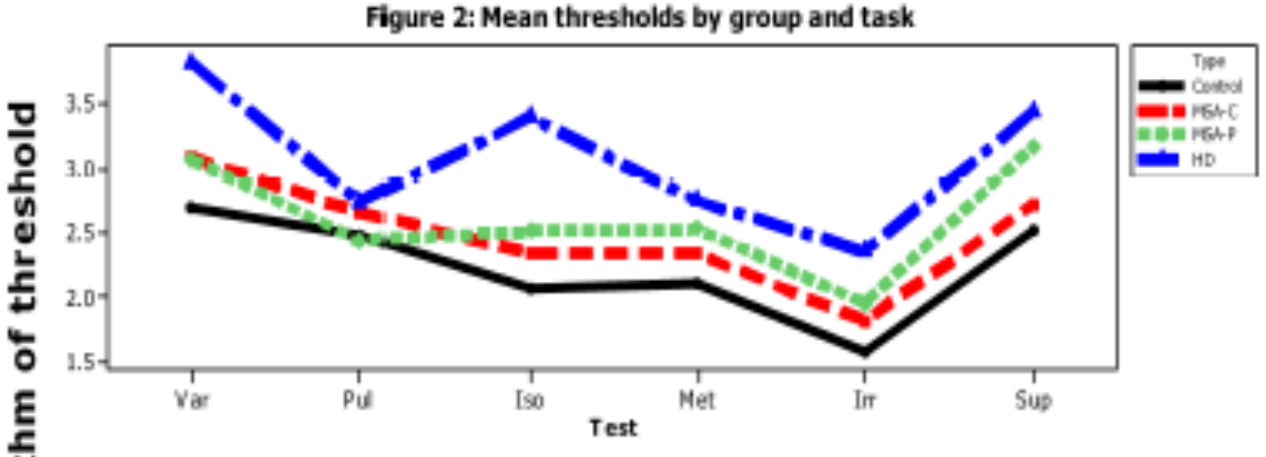

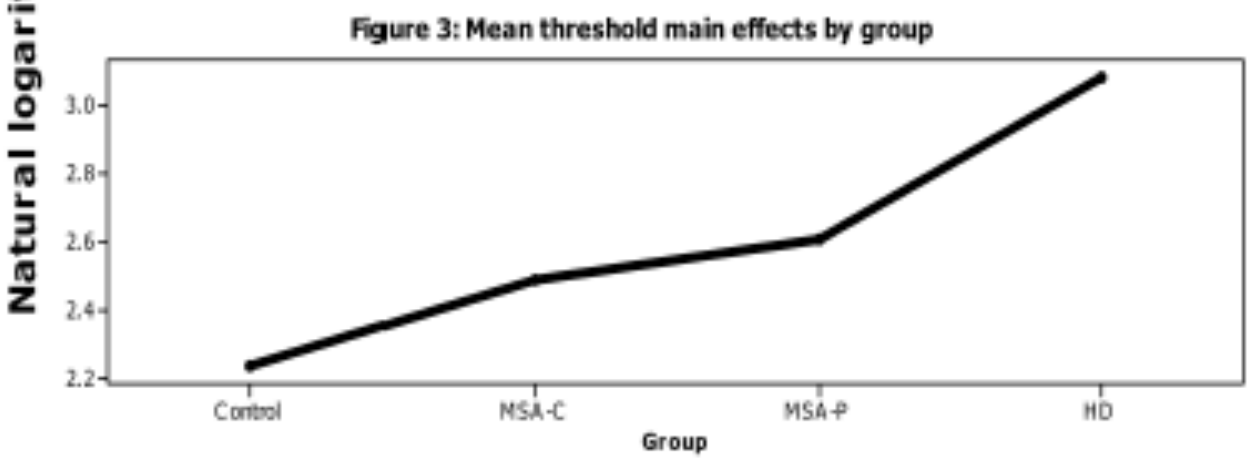

- HD patients significantly worse than controls on absolute and relative timing tasks
- MSA-P also significantly worse than controls on absolute and relative timing tasks

Cope et al., 2013 (in press)

Unified model: summary

- Unified model emphasizes projections between CB and BG which were earlier looked at in isolation wrt interval timing
- Model is asymmetrical in that BG clock (and relative timing) is default mode
- Patients with striatal lesions (PD, HD, MSA-P) impaired on both absolute and relative timing tasks
- Patients with CB lesions impaired only on event-based and not emergent timing tasks
- Understanding timing through such disorders may provide key insights.

Overall summary

Time is a distributed property of brain circuits but certain structures are specialized for temporal processing.

Rhythmic structure of time intervals is an important dimension in the analysis of time intervals, especially in auditory domain for signals such as speech and music.

Substrates involved in timing may have separate roles (attention/memory) but the dorsal striatum appears to be vital for supporting core timing functions.

Disorders that are associated with impairment in timing analysis can give us a view into the systems level deficits.

Acknowledgments

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http://www.fil.ion.ucl.ac.uk/~steki

http://www.fil.ion.ucl.ac.uk/~tgriff