A unified model for the neural bases of auditory time perception

Sundeep Teki, PhD (2011-13)
Auditory Group (PI: Tim Griffiths)
Wellcome Trust Centre for Neuroimaging
http://www.fil.ion.ucl.ac.uk/~steki

frontiers
IN INTEGRATIVE NEUROSCIENCE

EDITORIAL ARTICLE » Research Topic

Interval timing and time-based decision making

Warren H. Meck[1], Valérie Doyère[2] and Agnès Gruart[3]*

1 Duke University, Durham, NC, USA
2 CNRS, Université Paris-Sud, Orsay, France
3 University Pablo de Olavide, Seville, Spain

frontiers
IN INTEGRATIVE NEUROSCIENCE

PERSPECTIVE ARTICLE » This article is part of a Research Topic

A unified model of time perception accounts for duration-based and beat-based timing mechanisms

Sundeep Teki[1]*, Manon Grube[2] and Timothy D. Griffiths[1,2]

1 Wellcome Trust Centre for Neuroimaging, University College London, London, UK
2 Institute of Neuroscience, Newcastle University, Newcastle-upon-Tyne, UK

Outline

I. Timing substrates

II. Timing mechanisms

III. Rhythm and Timing

IV. Unified timing model

V. Discussion

I. Timing substrates

SENSORY CORTEX

HIPPOCAMPUS

PREFRONTAL CORTEX

SMA/PMC

BASAL GANGLIA

CEREBELLUM

Cerebellum

Neurophysiological work in animal models

(Braitenberg, Llinas, Cohen, de Zeeuw et al.):

- Cerebellar role in adaptive timing and learning

  e.g. eye-blink conditioning experiments, vestibulo-ocular reflex

- Analysis of basic cerebellar circuitry suggests timing capabilities esp. Inferior olive

Neuropsychological work in patients with cerebellar degeneration (Ivry et al.):

- **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

Basal ganglia

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

Neuropsychological work in patients (Artieda/Pastor/Harrington et al.):

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

Neuroimaging work in humans (Grahn/McAuley et al.):

- Role of striatum in beat (regular time) perception

Emerging consensus...

CEREBELLUM:

- Involved in sub- and not supra-second time perception
- Critical for behavior requiring real-time prediction
- Error-based learning mechanism (climbing fiber input as teaching signal)

BASAL GANGLIA:

- 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

CORTEX/PFC/HIPPOCAMPUS:

- Not critical; modulatory function; mediate working memory/attention
- Auditory cortical areas (e.g. STG) more involved than visual cortex

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 (Absolute) (ΔT_i)** vs. **Beat-based timing (Relative) (ΔT_i / T_{beat})**

Griffiths et al.

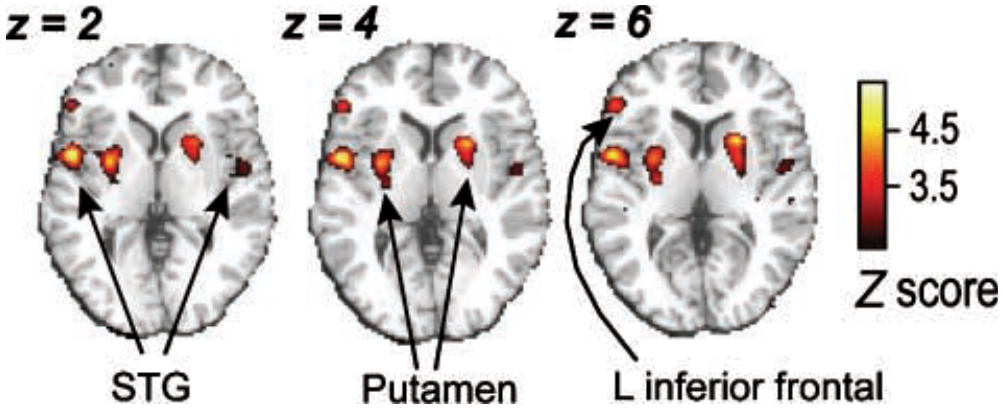
Beat-based timing

A regular beat offers beneficial temporal cues in perceptual timing

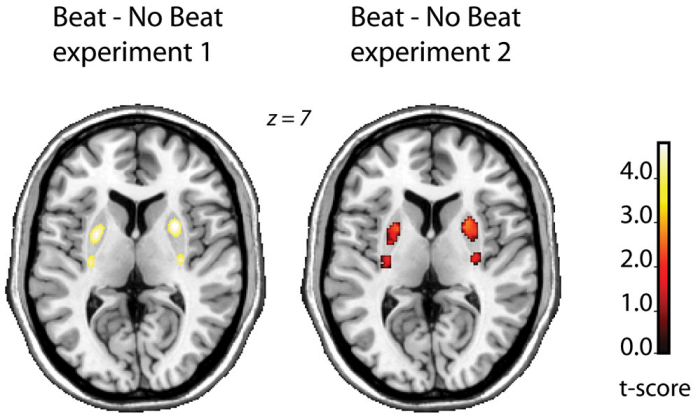
(Povel & Essen, 1985)

Parkinson's patients show deficits in perceptual timing tasks.

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



Grahn and Brett, 2007



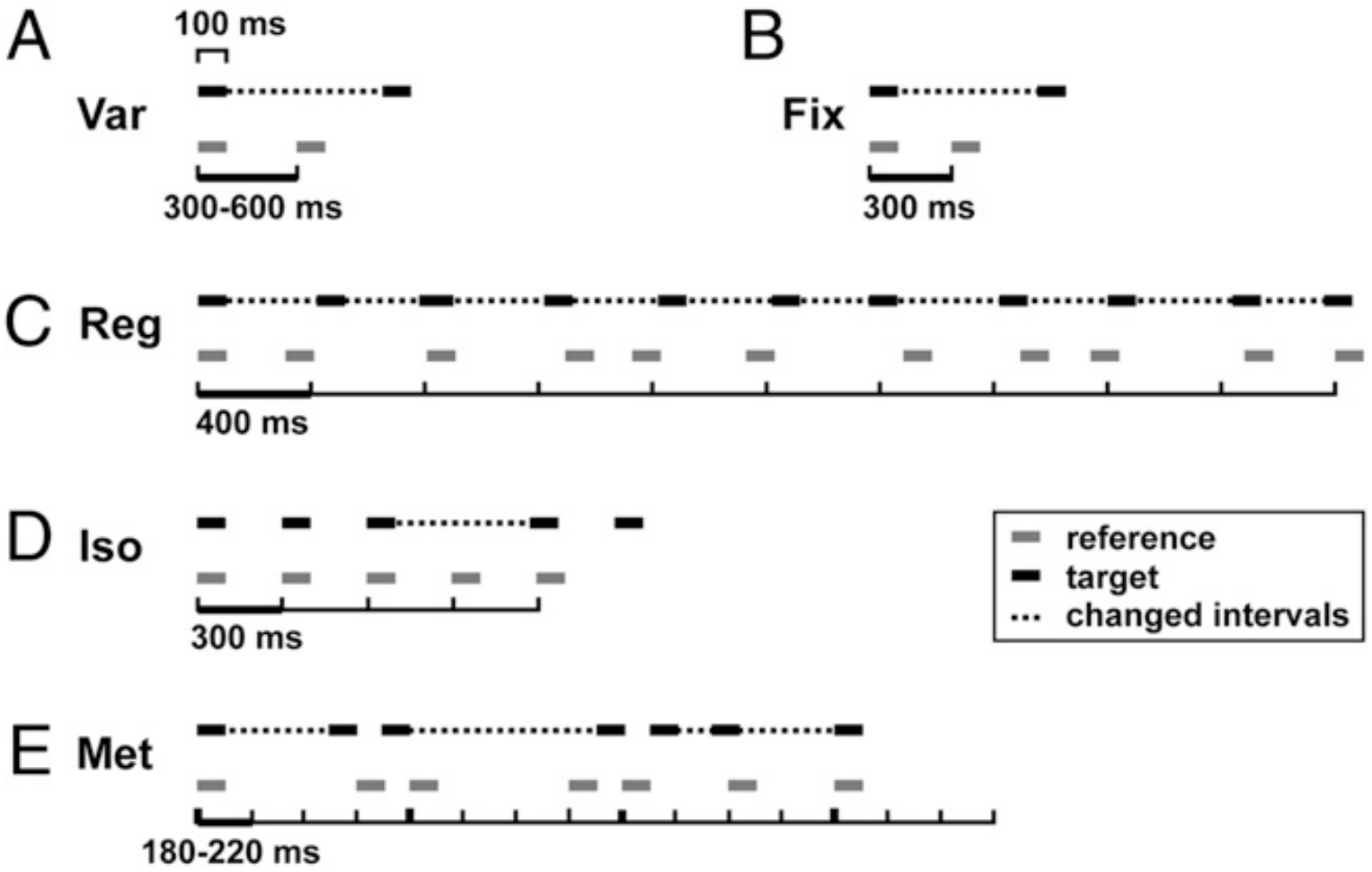
Grahn and Rowe, 2009

Basal ganglia, pre-SMA/SMA, and pre-motor cortex

implicated in perception of beat-based and metrical rhythmic sequences.

Duration-based timing

Patients with Spino Cerebellar Ataxia type 6:



(Grube et al., 2010. PNAS)

III. Rhythm & Timing

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

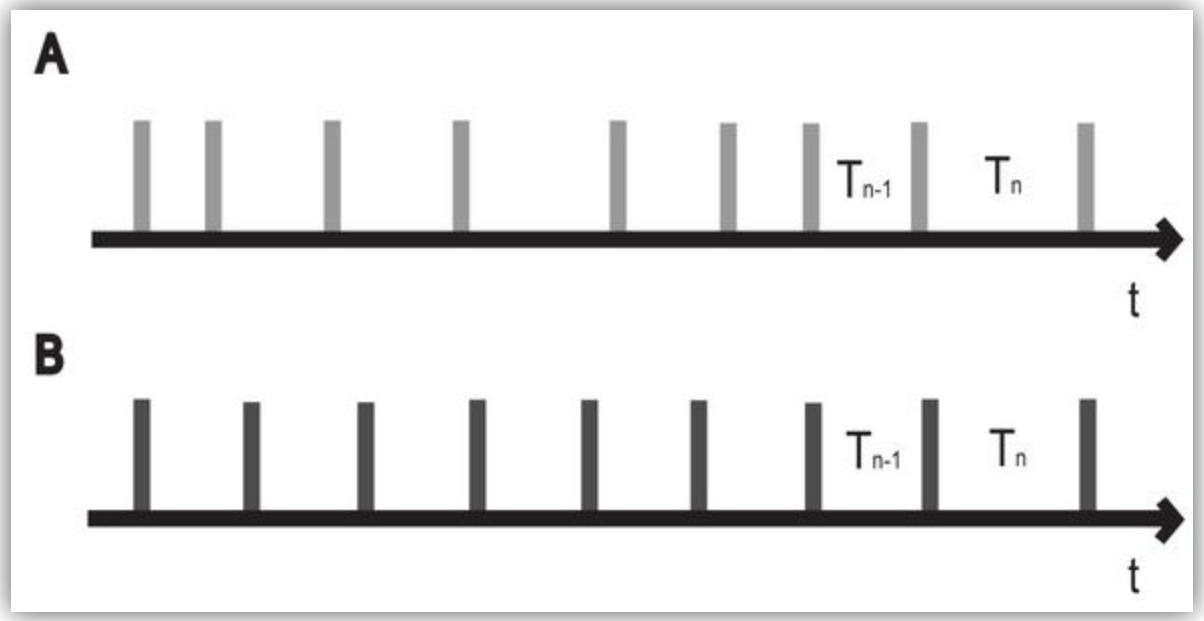
Hypotheses:

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

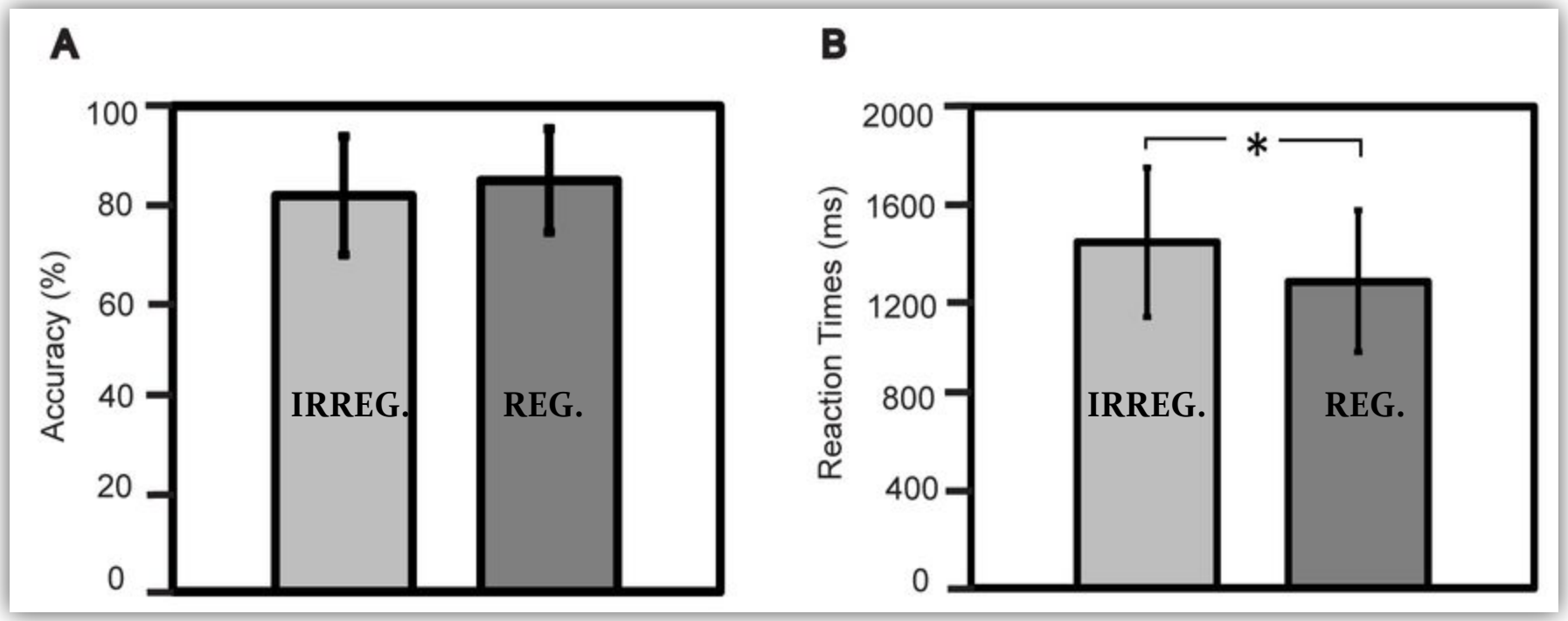


- ***Judge the duration of the final compared to the penultimate interval***
  T_n > / < T_{n-1}

Sequence A: Irregular with 15% average jitter

Sequence B: Regular with an isochronous beat

Behaviour in scanner



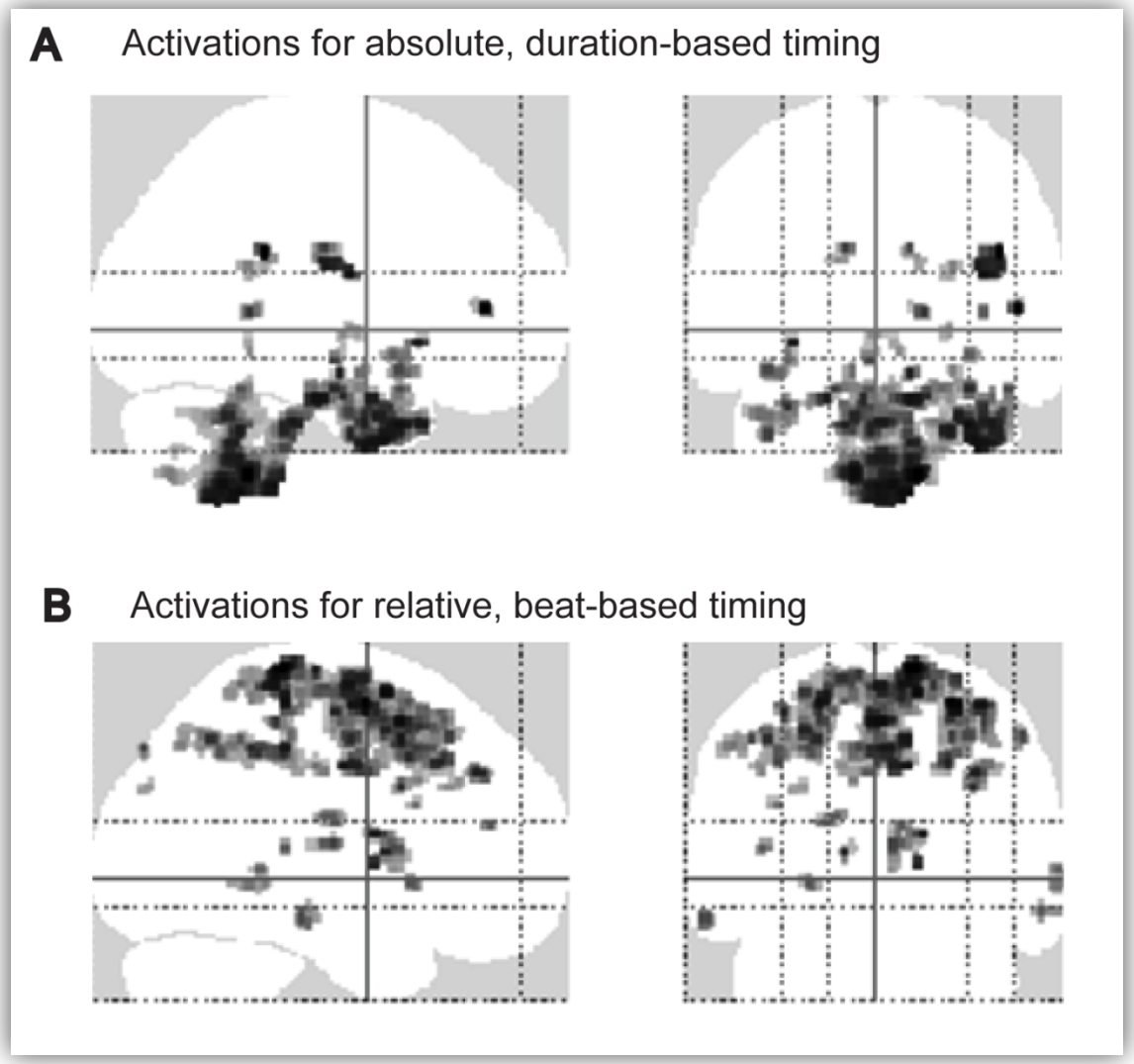
81.53% ± 12.28%

84.72% ±10.64%

1438 ± 297 ms

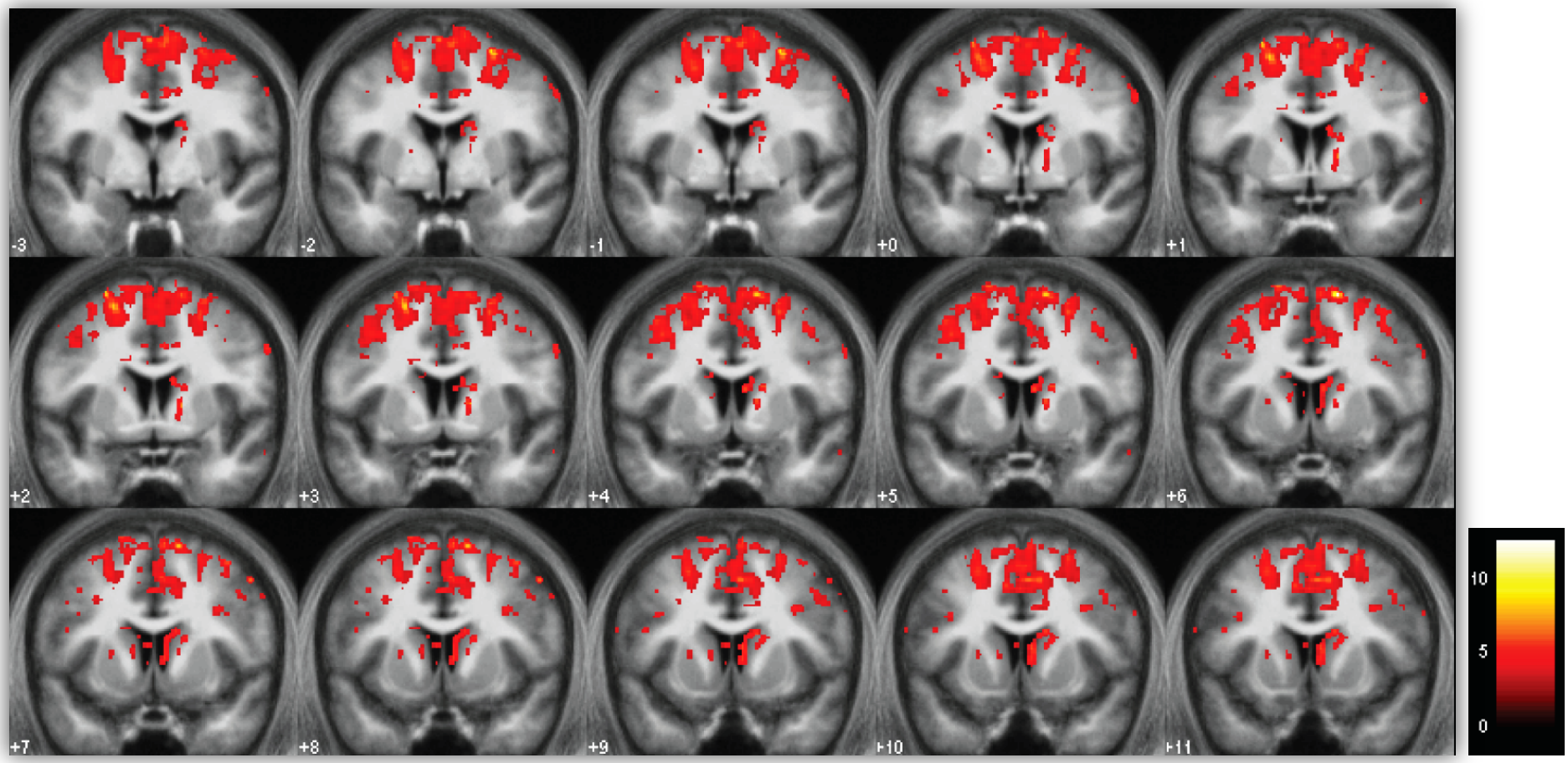
1275 ± 312 ms

fMRI Results



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

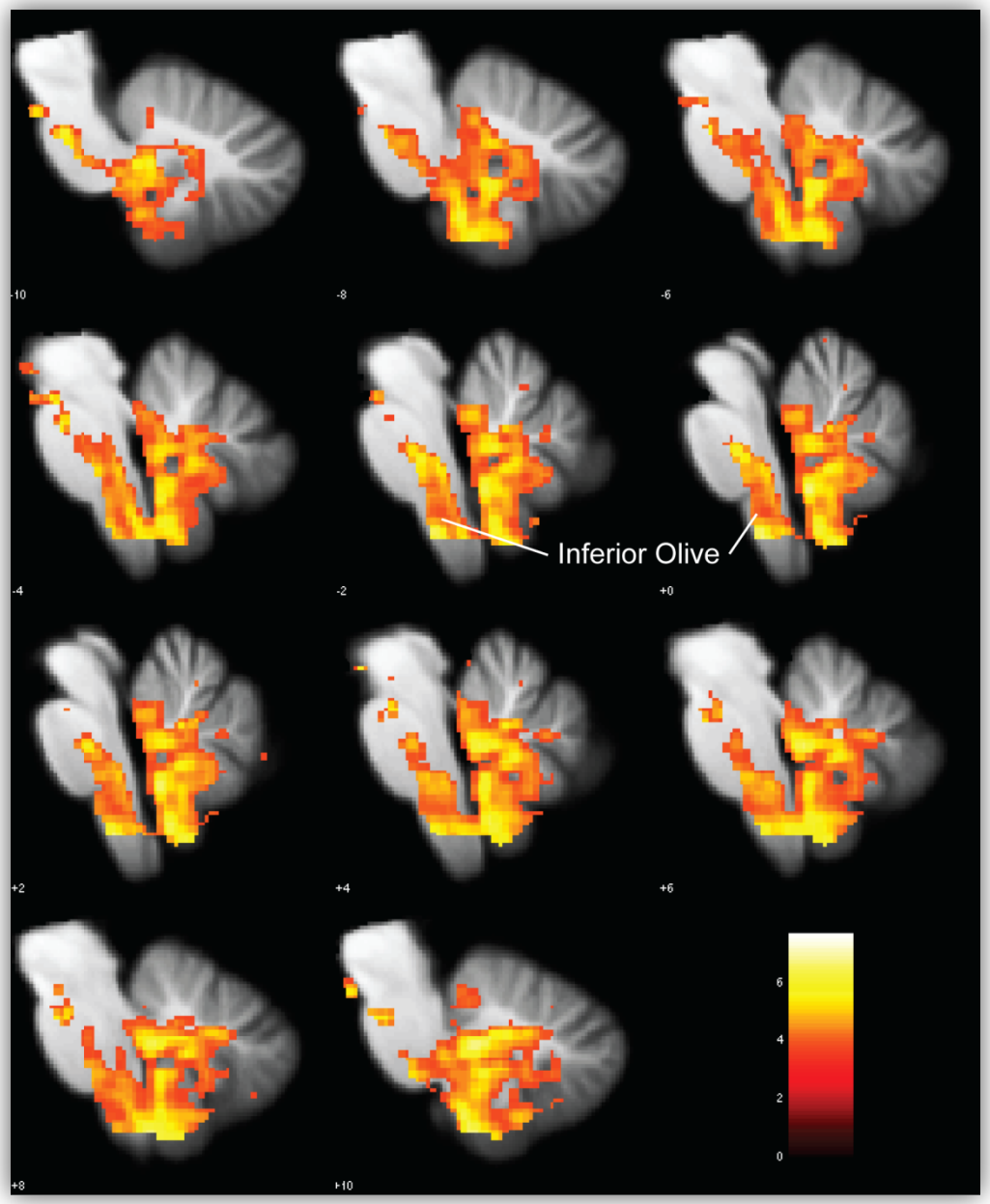
Striatal, premotor and prefrontal activations



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

IV. Unified model

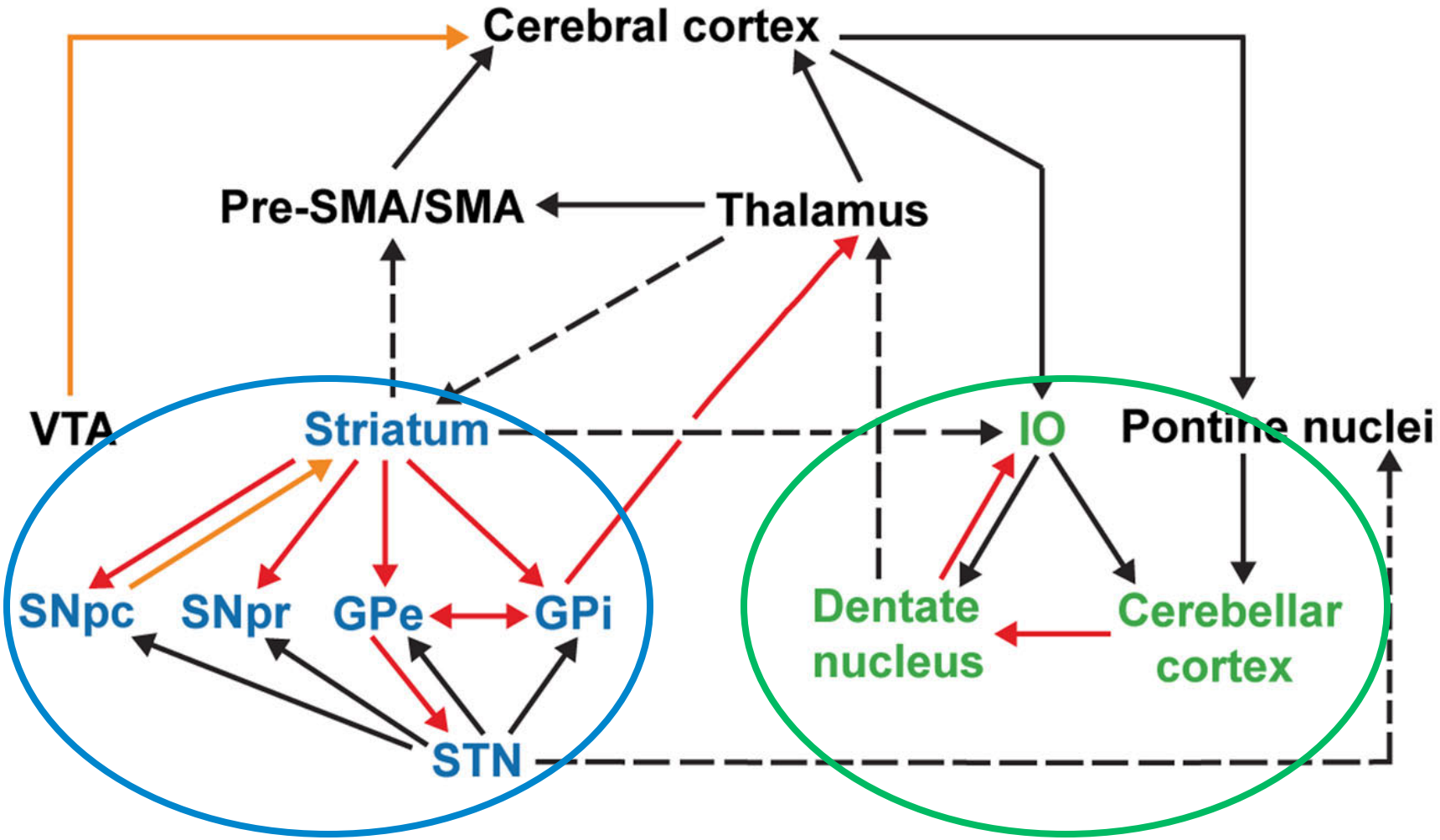
I. Assumptions:

- Motor structures specialized for timekeeping in the brain
- Striatum serves as default/central timekeeper
- Timing functions of BG and CB not necessarily independent
- Beat-based clock operates for timing stimuli in predictable, beat-based context
- Duration-based clock more active for stimuli in irregular, isolated context

II. Features:

- BG network timing signal based on SBF model
- CB network timing signal based on known neurophysiology
- The two key networks interact to improve the precision of the timing signal

Unified model



Exc.

Inh.

DA

Anat.

Teki et al., 2012
Front Int Neurosci

Unified model

III. Anatomy:

- CB and BG networks based on known anatomy

Novel CB⇔BG connections:

Interconnections between striatal and cerebellar networks (cf. Strick lab):

- **Dentate => Thalamus => Striatum** **(Hoshi et al., 2005)**
- **STN => Pontine nuclei => Cerebellar cortex** **(Bostan et al., 2010)**

Sensory input:

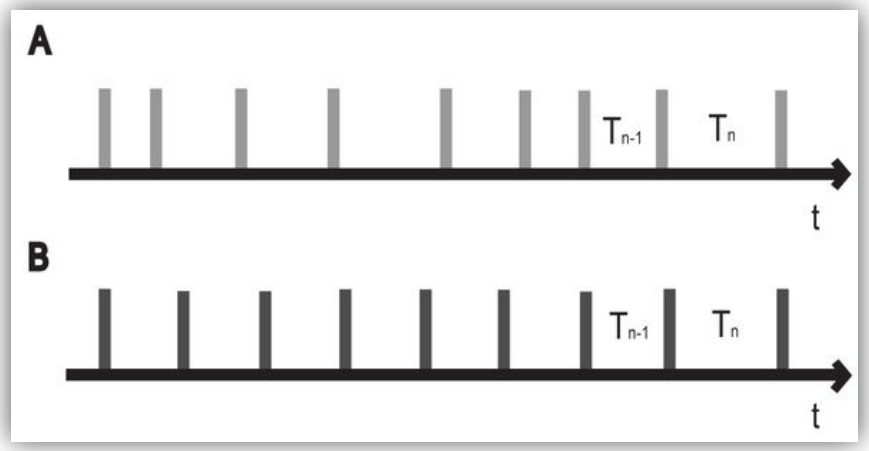
- Striatum to superior temporal lobe **(Yeterian & Pandya, 1998)**
- Cerebellum and auditory function **(Huang & Liu, 1985; Petachhi et al., 2005)**

Unified model

IV. Function:

Serial processing: beat-based timing with error-correction by duration-based clock

A. Isolated context:



B. Regular context:

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

C. Irregular context:

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

Is striatum the default clock?

Is there a strict functional dissociation in timing functions of BG and CB?

- CB lesions do not affect relative timing (Grube) or emergent timing (Ivry)

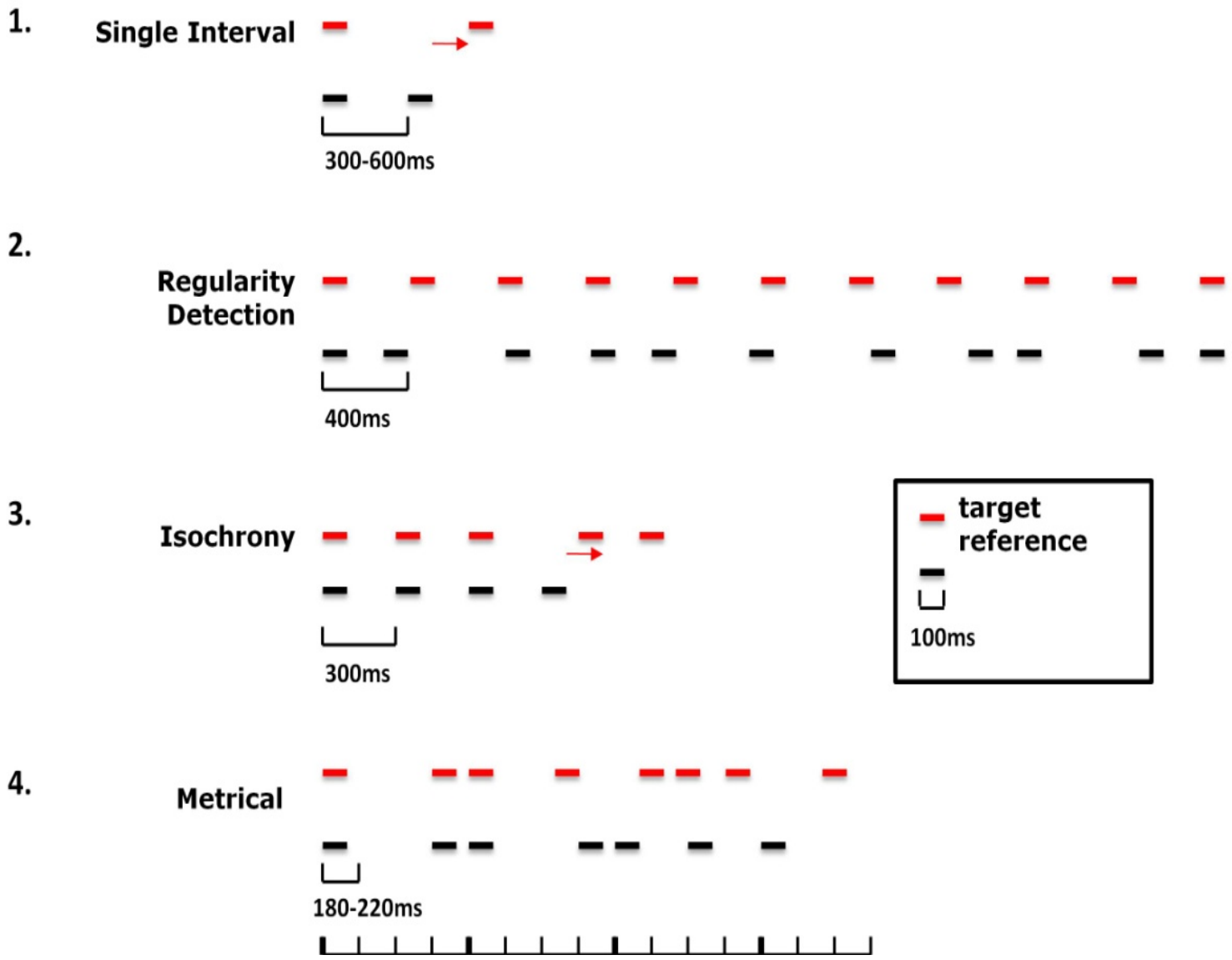
But...

- Striatal lesions affects both relative and absolute timing. New evidence from:

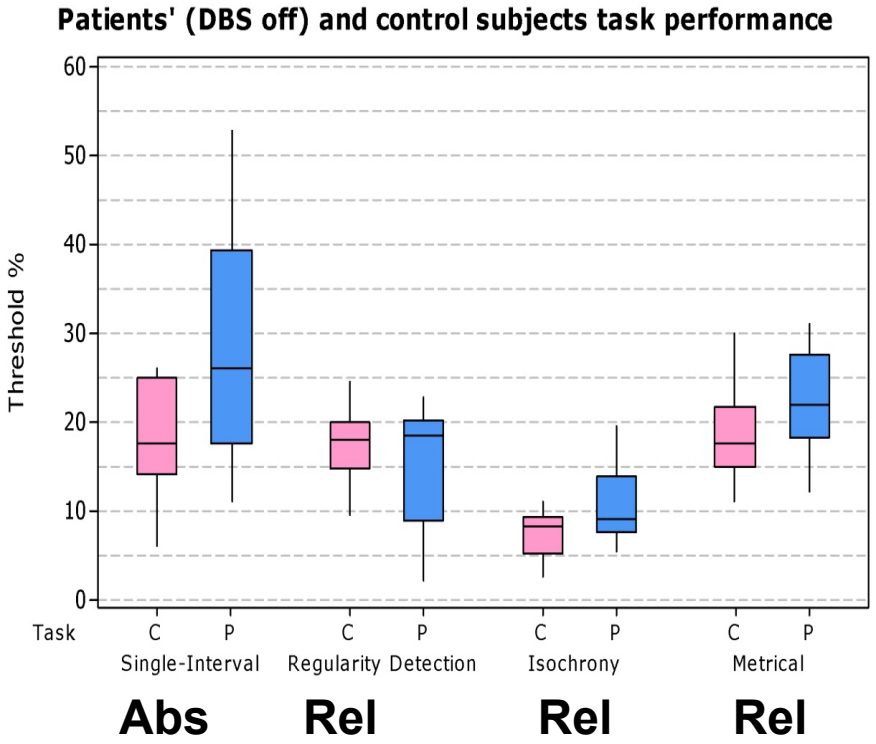
    1) Parkinson's disease

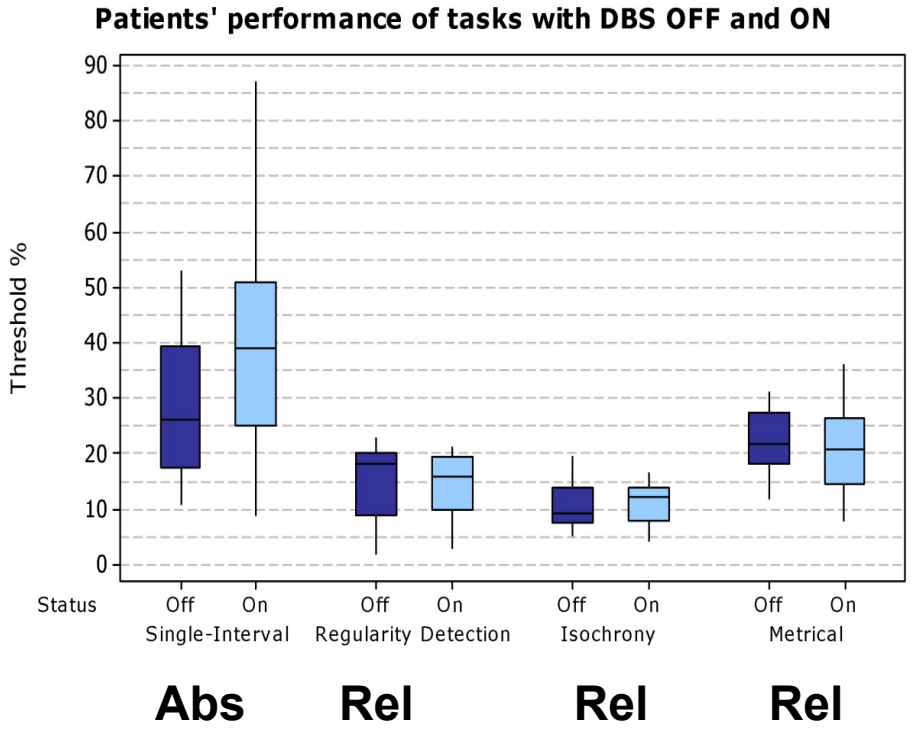
    2) Huntington's disease and Multiple Systems Atrophy

I. PD patients



I. PD patients



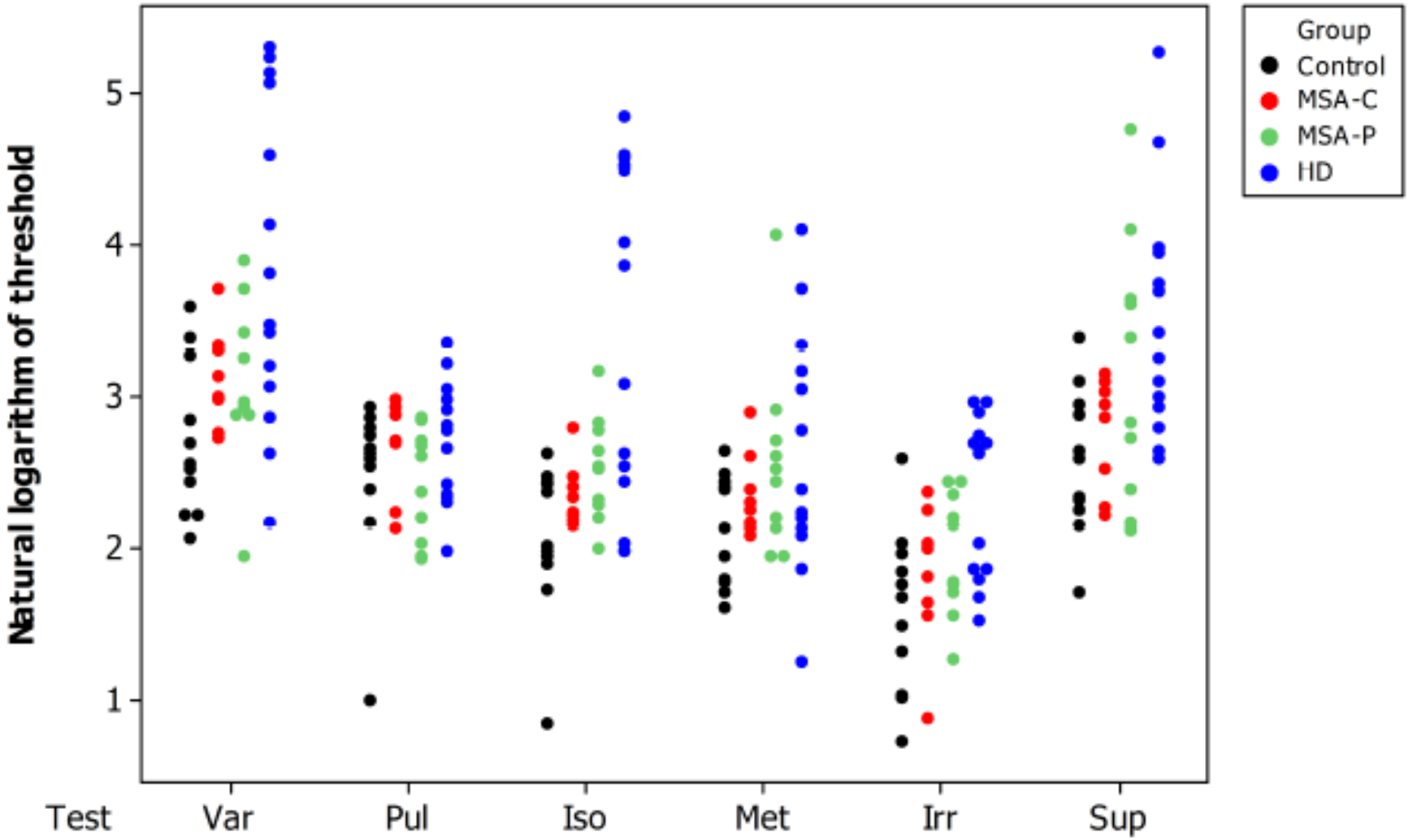


- PD (DBS OFF) worse than controls on single-interval discrimination (abs task)
- PD (DBS ON) worse than PD (DBS OFF) on same absolute timing task

➢ **PD patients also impaired on absolute timing tasks**

Mandal et al., (in prep.)

II. HD/MSA patients



Timing: **Abs** **Rel** **Rel** **Rel** **Abs** **Abs**

II. HD/MSA patients

Figure 2: Mean thresholds by group and task

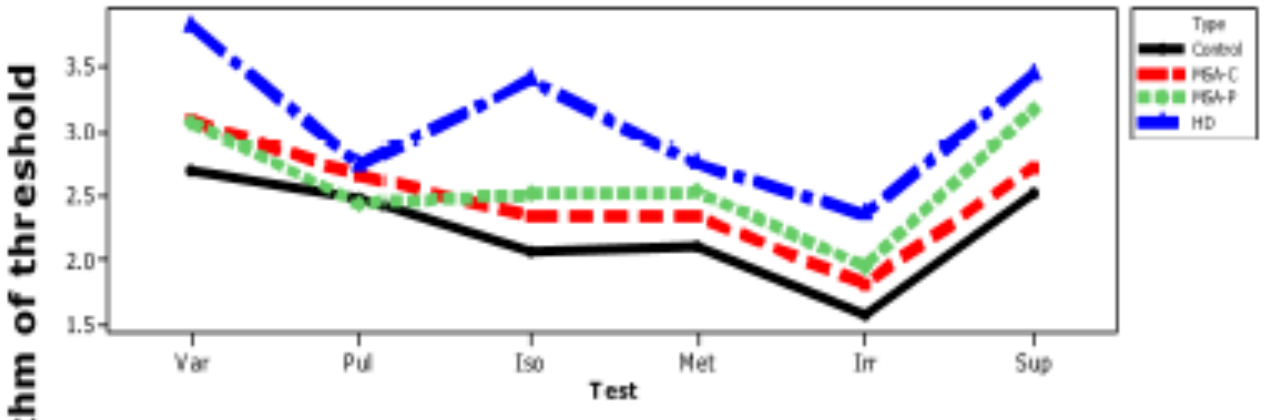
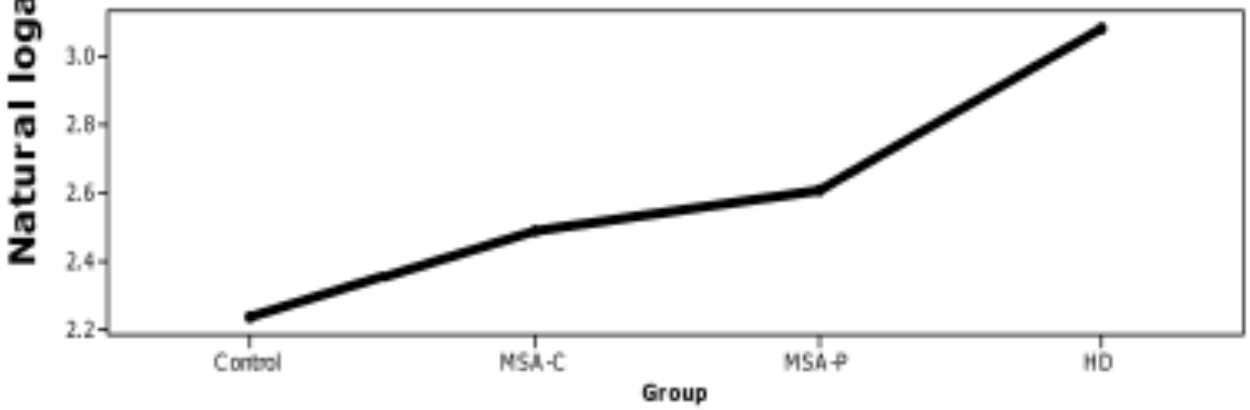


Figure 3: Mean threshold main effects by group



- **HD & MSA-P patients are significantly worse than controls on absolute and relative timing tasks**

Cope et al., (in prep.)

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.

- Analysis of time by motor circuits maybe achieved by parallel processing in striatum and cerebellum.

- Patients with striatal lesions (PD, HD, MSA-P) impaired on both absolute and relative timing tasks.

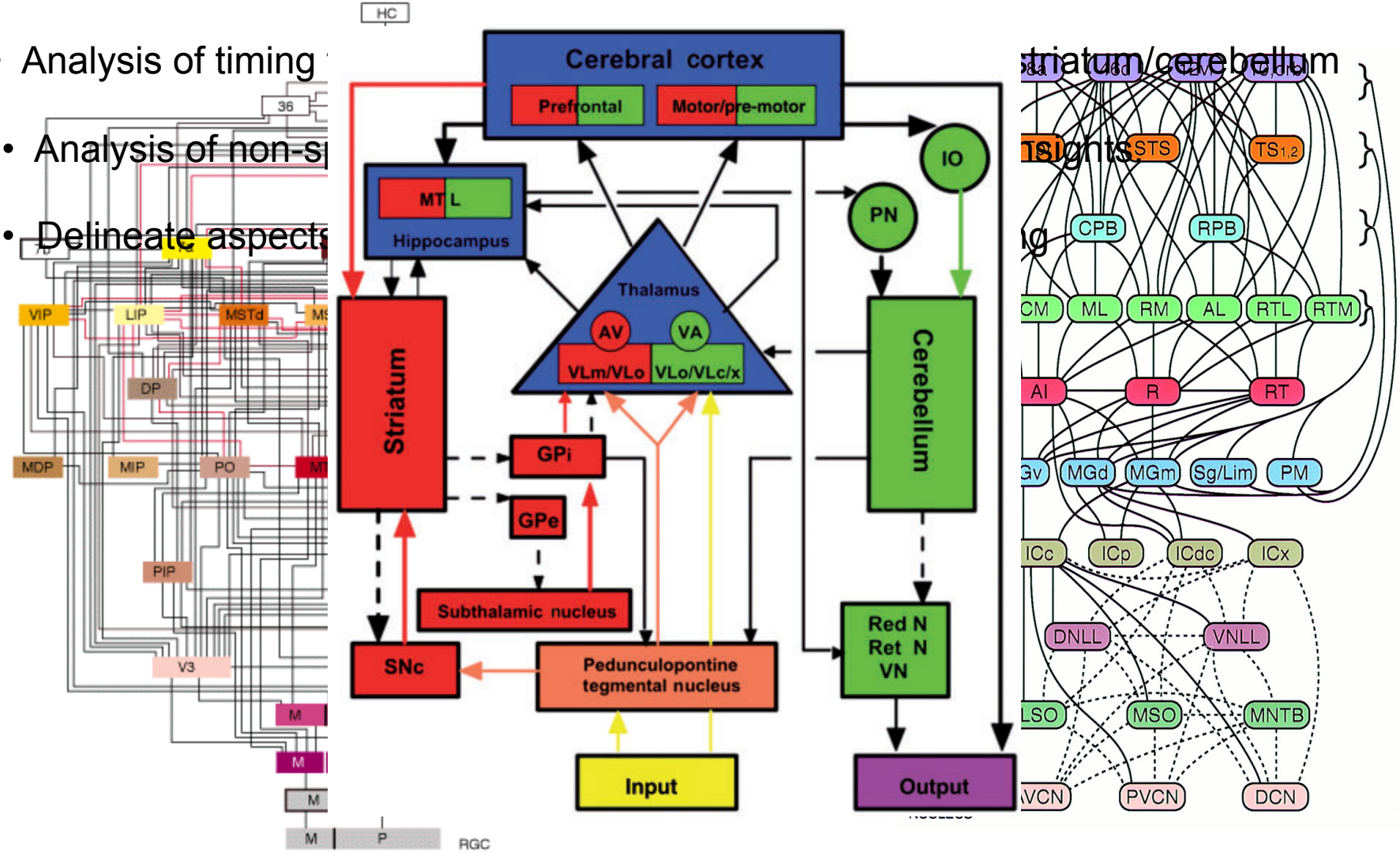
V. Discussion

- Analysis of timing circuits and network models like in vision and audition
- Analysis of timing
- Analysis of non-s
- Delineate aspects

striatum/cerebellum

sights.

g



Van Essen et al., 1992

Kaas & Hackett, 2000

Acknowledgments

Manon Grube (NCL)

Sukhbinder Kumar (NCL/UCL)

Tim Griffiths (NCL/UCL)

wellcome trust