



# Distinct representation of absolute and relative auditory time

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## Introduction

• **Timing network**: Cerebellum, basal ganglia, pre-SMA/SMA, pre-motor and prefrontal cortex.

• <u>Cerebellum</u>: Perception of absolute duration of discrete time intervals. (*Grube et al., 2010*)

• <u>Basal ganglia</u>: Perception of beat-based, metrical rhythmic sequences. (*Grahn*, 2009)

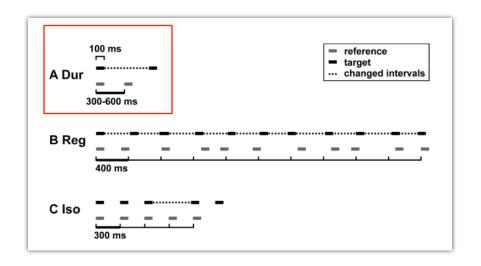
#### Aim:

Test for dissociation between the timing functions of cerebellum and basal ganglia



# Absolute, duration-based timing

 Patients with Spino Cerebellar Ataxia type 6: impaired in absolute timing of single intervals but not in relative timing of rhythmic sequences with a regular beat. (Grube et al., 2010: PNAS)



 Normal subjects with TMS over medial cerebellum: impaired on the same absolute timing task after stimulation

(Grube et al., 2010:

#### Frontiers)

> Absolute, duration-based timing:



# Relative, beat-based timing

A regular beat offers beneficial temporal cues in perceptual timing

 Parkinson's patients with decreased striatal dopamine release show deficits in perceptual timing tasks.

(Artieda et al. 1992, Harrington et al. 1998)

 Basal ganglia, pre-SMA/SMA, and pre-motor cortex implicated in perception of beat-based and metrical rhythmic sequences

(Grahn,

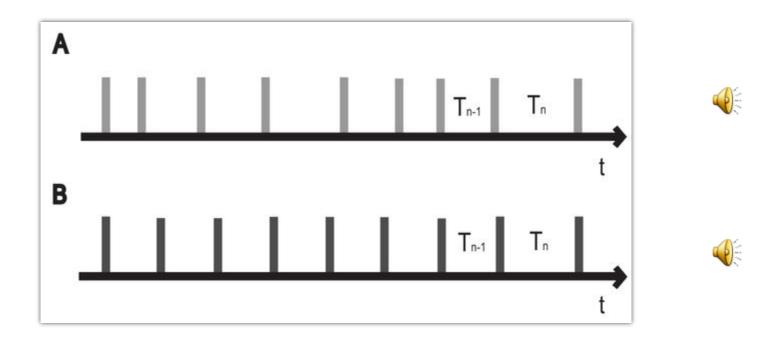
2009)

Relative, beat-based timing:

Perception of time intervals relative to a regular beat  $(\Delta T_i/T_{beat})$ 



## **Stimulus and Task**



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

**Sequence A:** Irregular sequence (15% mean jitter)

**Sequence B:** Regular sequence (isochronous)



# **Stimulus Design**

• Click duration: 0.5 ms

Inter-onset interval (ioi): 440 - 560 ms (roved in steps of 30 ms)

Total no. of intervals: 7 – 10

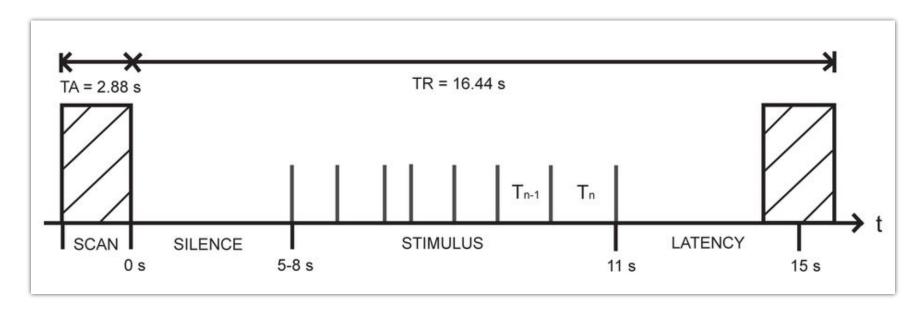
Max. Response time: 3 s

40 conditions/sequence: 5 ioi x 4 no. of intervals x 2 (shorter or longer)

- Time difference between final and penultimate interval:
  - 30% of ioi for irregular sequences
  - 15% of ioi for regular sequences



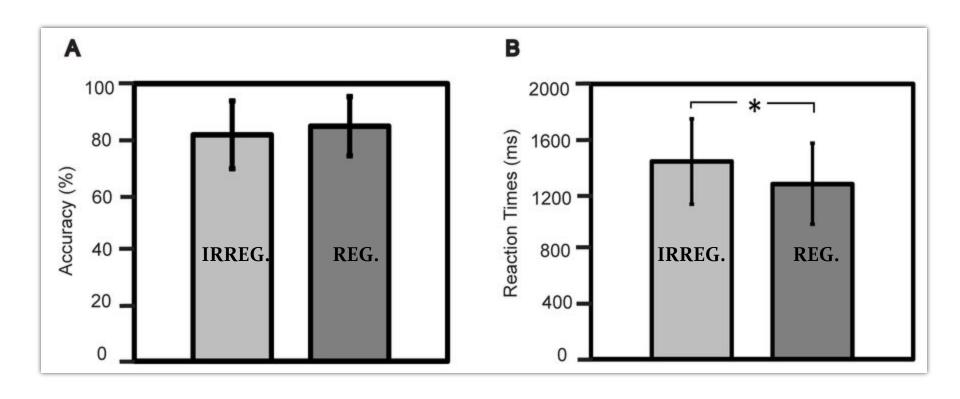
## Functional imaging paradigm



- Sparse temporal sampling; 3 Tesla Siemens Allegra MRI Scanner
- 48 contiguous slices per volume
- TR: 16.44 s; TA: 2.88 s; flip angle α: 90°
- Slice thickness: 2 mm
- In-plane resolution: 3.0 x 3.0 mm<sup>2</sup>
- Slices were tilted by 7° (T>C) to obtain full coverage from the cerebellum



## Behaviour in scanner (n=18)



> Relative timing more accurate and faster than absolute timing



# fMRI analysis

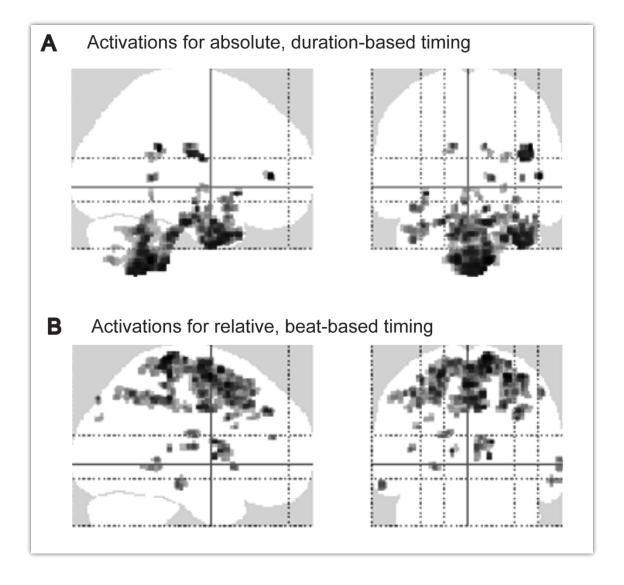
- A priori hypotheses for cerebellum and basal ganglia
- 18 subjects (normal hearing, no current musical training)
- Standard pre-processing with SPM8, normalization using DARTEL
- Whole brain analysis; random effects design

#### Key contrasts:

- (a) Irregular vs. Regular (measure of absolute timing)
- (b) Regular vs. Irregular (measure of relative timing)

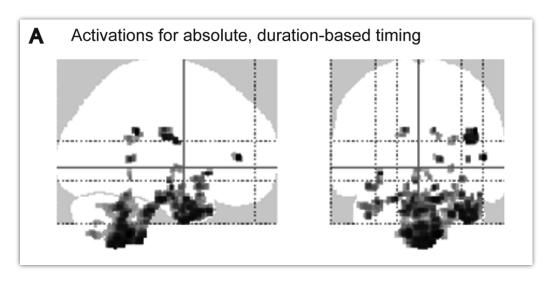


## **fMRI** Results





## I. Absolute Timing



**OLIVO-**

**CEREBELLAR NETWORK** 

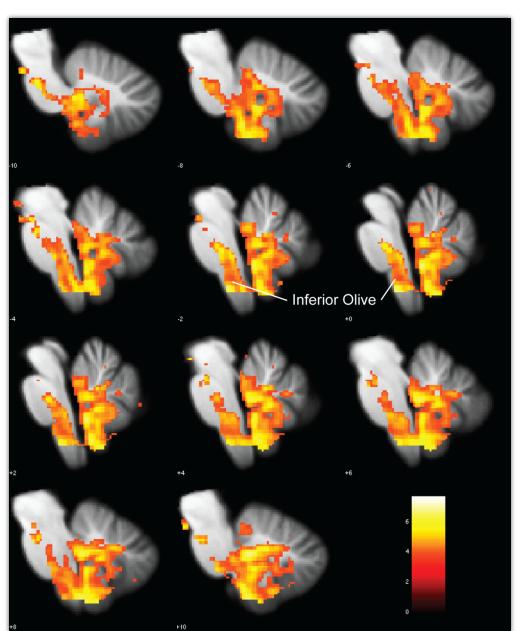
Inferior Olive

Vermis
Cerebellum
Dentate Nucleus
Cerebellar Lobules IX and X

Also: Superior Temporal Gyrus, Cochlear nucleus



## Olivocerebellar activations

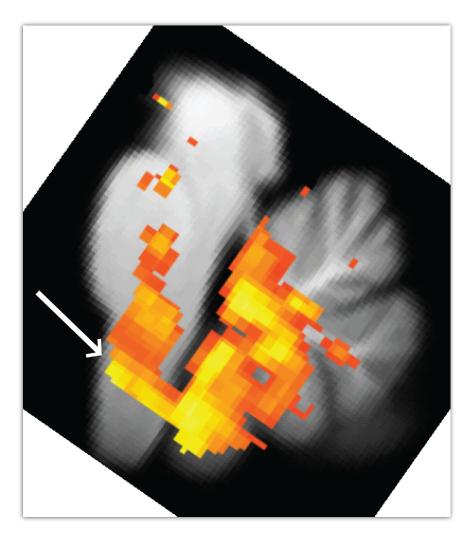


x = -10 to +10 mm

p < 0.001 (unc.)



## **Inferior Olive**



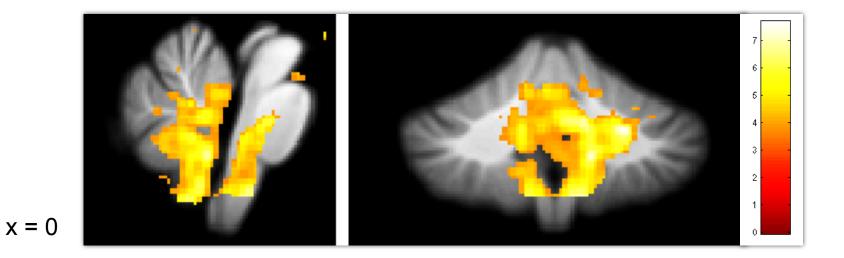
present study



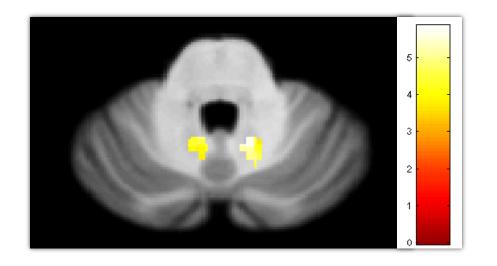
reproduced from Xu et al. (2006)



## Cerebellum

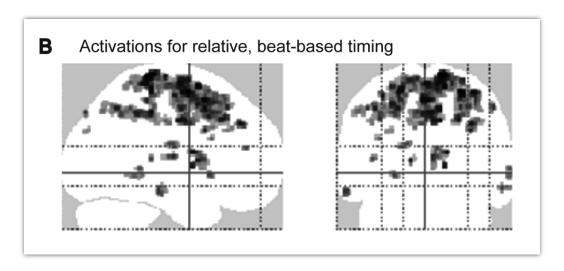


**Dentate nucleus** x = 9





## II. Relative Timing



STRIATO-NETWORK **THALAMO-**

**CORTICAL** 

Putamen
Caudate Nucleus
Internal Capsule

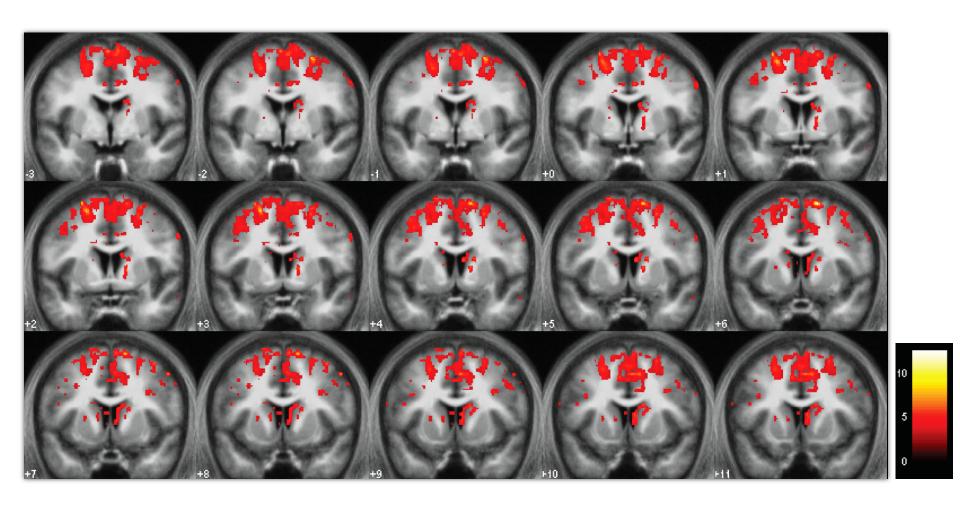
**Thalamus** 

Pre-SMA/SMA
Pre-motor cortex
Dorsolateral prefrontal

Also: Superior Temporal Gyrus



## Striatal, premotor & prefrontal activations



y = -3 mm to +11 mm



## Summary

- Results consistent with previous work:
  - Absolute, duration-based timing in the Cerebellum
  - Relative, beat-based timing in the Basal ganglia
- Distinct timing mechanisms and underlying subsystems:
  - Olivocerebellar network mediates absolute, duration-based timing
  - Striato-thalamo-cortical network mediates relative, beat-based timing
- First study to implicate inferior olive in auditory timing using fMRI



## **Inferior Olive and Timing**

- motor timing and timing error correction of ongoing movement
- adaptive timing in vestibulo-ocular reflex and eye-blink conditioning

(Ito and others)

- sole source of climbing fibre input to the Purkinje cells (PC)
- displays sub-threshold oscillations at ~5-15 Hz
- intrinsic oscillations are synchronized via electrical coupling
- electrical coupling regulated by deep cerebellar nuclei (inhibited by PC)
- organized into dynamic, functional subgroups

(Llinas, Yarom, de Zeeuw and others)

- receives visual, somatosensory and auditory inputs
- implicated in perceptual timing of visual sequences using fMRI

(Xu et al., 2006; Liu et al., 2008)

## Acknowledgments



**Manon Grube** 

**Sukhbinder Kumar** 

**Tim Griffiths** 

**Newcastle Auditory Group** 



**Radiology and Physics Group** 

**Wellcome Trust Centre for Neuroimaging** 

**University College London** 





