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Xuanyu Wang (✉ wangxuanyu0419@gmail.com)

School of Psychological and Cognitive Sciences, Peking University <https://orcid.org/0000-0002-2458-8115>

Shunyu Shi

School of Psychological and Cognitive Sciences, Peking University

Yan Bao

Peking University

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Parallel processes of temporal control in the supplementary motor area and the frontoparietal circuit

Xuanyu Wang¹, Shunyu Shi¹ & Yan Bao^{1, 2, 3}

¹ School of Psychological and Cognitive Sciences, Peking University, Beijing, China

² Beijing Key Laboratory of Behavior and Mental Health, Peking University, Beijing, China

³ Institute of Medical Psychology, Ludwig Maximilian University Munich, Germany

1 **Abstract:**

2 Durations in the several seconds' range are cognitively accessible during active timing.
3 Functional neuroimaging studies suggest the engagement of basal ganglia (BG) and
4 supplementary motor area (SMA). However, their functional relevance and
5 arrangement remain unclear because non-timing cognitive processes temporally
6 coincide with the active timing. To examine the potential contamination by parallel
7 processes, we introduced a sensory control and a motor control to the duration
8 reproduction task. By comparing their hemodynamic functions, we decomposed the
9 neural activities in multiple brain loci linked to different cognitive processes. Our
10 results show a dissociation of two cortical neural circuits: the SMA for both active
11 timing and motor preparation, followed by a prefrontal-parietal circuit related to
12 duration working memory. We argue that these cortical processes represent duration
13 as the content but at different levels of abstraction, while the subcortical structures
14 including BG and thalamus provide the logistic basis of timing by coordinating
15 temporal framework across brain structures.

1 **Introduction:**

2 Timing is a crucial aspect of sensory processing and motor planning in the brain.

3 Durations in the range of seconds to minutes are relevant for cognitively controlled
4 behavior, requiring active mental engagement, usually referred to as *Interval Timing*.

5 With the help of functional imaging techniques, researchers have found
6 timing-associated activities across multiple brain regions including subcortical
7 structures in the basal ganglia (Rao et al., 2001; Ferrandez et al., 2003), cortical
8 structures such as the supplementary motor area (SMA; Teki et al., 2011; Kotz, Brown
9 & Schwartz, 2016; Protopapa et al., 2019), the pre-SMA (Rao et al., 2001; Coull et
10 al., 2008; Harrington et al., 2011), the insula (Wittmann et al., 2010; Kosillo & Smith,
11 2010) and the cerebellum (Rao et al., 2001; Pfeuty et al., 2015). However, the
12 functional role of these regions and their inter-regional organization during interval
13 timing remain unclear (Pöppel, 2004; Zhou et al, 2014). One difficulty of conducting
14 neuroimaging studies for interval timing tasks presumably comes from parallel
15 cognitive processes that are hard to be temporally disentangled.

16
17 The accumulation of blood-oxygen-level-dependent (BOLD) signal has been taken as
18 the neural substrate of temporal encoding in many studies (Wittmann et al., 2010;
19 Casini & Vidal, 2011), thus treating the encoding of duration as an evidence
20 accumulation process, similar to other decision-making tasks (Wittmann, 2013; Balci
21 & Simen, 2016). However, the link between ramping BOLD signal and timing is
22 under-specific: no physiological evidence on the neuronal or circuit level has been

1 established in support of the link between climbing hemodynamic signal and
2 accumulation of neural information. More importantly, it is unclear whether the
3 climbing signal is a result of persistent non-temporal processes or the dedicated
4 timing. Time acts as the context of all neural and cognitive processes. There is no
5 guarantee that all temporally evolving neural activities, even when decoding of time is
6 possible, are relevant for devoted timing.

7

8 In interval timing, time is at the same time the logistic, contextual framework, and the
9 content of the neurocognitive processes (Pöppel, 1997). Therefore, it is hard to tell
10 from the data whether the temporally evolving neural activity represents an active
11 involvement in measuring time or whether it is simply an artifact of persisting
12 non-timing parallel processes that lasts the same period being timed. Take the
13 example of the duration reproduction task (e.g., Shi et al., 2013; Maass, Schlichting &
14 van Rijn, 2019), in which the subjects are asked to firstly remember the duration of an
15 interval, i.e., ‘encode’ the interval duration, and ‘reproduce’ the duration by holding a
16 key or terminate an external display after a proper duration. During encoding, the
17 internal events actively engaged in sensory timing share identical time courses with
18 the external presentation of stimuli, thus temporally collide with sensory processing,
19 along with other task-general components like elevated attention. For reproduction,
20 the motor timing is similarly contaminated by sensory processing, attention, or motor
21 preparation.

22

1 One physiological model of interval timing is the basal ganglia (BG)–SMA circuit
2 (Wittmann, et al., 2010; Kotz, Brown & Schwartz, 2016). The basal ganglia,
3 especially the putamen, are considered as the subcortical clock governed by midbrain
4 dopaminergic inputs and synchronize the cortical processes across multiple regions
5 (Meck, 2005; Cheng et al., 2016). This is supported by pharmacological interference
6 of interval timing by dopamine antagonists and agonists (Parker, Ruggiero &
7 Narayanan, 2015; Fung, Sutlief & Shuler, 2021), as well as clinical evidence with
8 dopamine deficit patients (Jones et al., 2008; Högl et al., 2014). The BG-SMA theory
9 proposes that the basal ganglia generate relatively stable-paced pulses, which are
10 accumulated in dedicated cortical structures such as the SMA (Teki et al., 2011; Kotz,
11 Brown & Schwartz, 2016) into a cortical representation of passed time. Based on
12 these assumptions, hemodynamic changes in the BG structures and SMA during
13 timing tasks are often attributed to timing without closer inspection.

14
15 However, considering the more general role that the BG-SMA circuit plays in
16 goal-directed, task-context-sensitive behavior (Haber, 2003; Korb et al., 2017), it is
17 questionable whether the hemodynamic elevations in functional imaging studies are
18 relevant for active timing, or are simply artifacts of non-timing parallel processes (e.g.
19 attention and motor preparation). Since an explicit motor response is required in all
20 timing tasks, the preparation for the response is always concurrent with the active
21 timing, thus indistinguishable in the data. This possible confounding has not been
22 considered in previous studies.

1

2 One way to disentangle intermixed components is to perform subtraction with control
3 conditions containing only the non-timing elements. We therefore introduced two
4 controls to the duration reproduction task: a motor control requiring simple reaction
5 and a sensory control with only passive viewing. By comparing the time course of
6 BOLD signals in task epochs with identical sensory input and motor output, we were
7 able to decompose the neural activities in multiple brain loci linked to different
8 cognitive processes.

9

10 We confirmed that the SMA is bifunctional, participating in both motor planning and
11 timing, with an additive hemodynamic response when both components are present.
12 The fluctuation of hemodynamic signals in subcortical structures including putamen
13 and thalamus are less specific and more likely motion-related. In addition,
14 working-memory associated activities were observed in another group of loci
15 including the left dorsal lateral prefrontal cortex and the bilateral intraparietal sulcus.
16 Activity in the SMA leads the frontoparietal circuit during encoding of the temporal
17 duration, while the sequence is reversed during reproduction. Our results dissociate
18 the interval timing mechanism into an encoding stage in the SMA and a following
19 memory stage in the frontoparietal circuit.

20

21 **Results:**

22 *Behavior verification of duration reproduction task*

1 Duration reproduction task is popular in interval timing research partially because of
2 its complex cognitive spectrum. In a typical scenario, subjects are first presented with
3 an external event that lasts for a while, the duration of which is the sample to be
4 encoded and memorized. Following a delay, the subjects perform an anticipatory
5 timing task based on the reference memory of this sample duration (for a review, see
6 Mioni et al., 2014). To better disentangle the brain activities related to encoding,
7 working memory, and retrieval of interval duration, and for the sake of better
8 signal-to-noise ratio, a longer inter-stimuli interval (ISI) is required in functional
9 imaging. Considering the relatively long repetition time (TR) of fMRI scanning and
10 slow decay rate of the blood-oxygen-level-dependent (BOLD) signal, the ISI has to be
11 extended up to several seconds, which is much longer than what is usually
12 implemented.

13
14 A behavioral pilot experiment was conducted in search of an optimal length of ISI as
15 well as reaffirming the temporal reproduction accuracy of the 3-second sample
16 interval. The uniqueness of 2-3s interval presumably represents a borderline of the
17 logistic capacity of interval timing as it is observed in many cognitive processes (Bao
18 et al., 2015; Chen et al., 2020, Pöppel, 1997, 2009; Wang et al., 2016, Yu and Bao,
19 2020, Zhao et al, 2018). Since our focus is on the high-level semantic aspect of the
20 timing function, it is reasonable to keep the temporal framework of neural processing
21 in its optimal range to minimize the noise of low-level processing. The pilot task
22 design closely imitated the scanning experiment, except that the ISIs were randomly

1 chosen from either 4.5 or 9.0 seconds for each block, and the sample duration from 4
2 conditions (1.5, 3.0, 4.5, or 6.0 seconds), randomized within-block.
3
4 Trials were excluded from analysis if the reproduced durations exceeded 3 standard
5 deviations from the mean. $2(\text{ISI}) \times 4(\text{Sample Duration})$ repeated-measure ANOVA
6 found neither significant interaction effect ($p > .1$) nor significant main effect of ISI
7 ($p > .1$); only main effect of sample duration ($p < .001$, see *Fig. 2*). The result
8 indicated that the reproduction performance was not altered by a longer ISI (9s),
9 leading to the implementation of a similar ISI during scanning (8s). The reproduced
10 durations for each sample duration in the long ISI condition are highly consistent with
11 previous studies with a shorter ISI (e.g. Pöppel, 1972; Ulbrich et al., 2007).
12

13 *Duration reproduction and simple reaction time*

14 During scanning, participants were asked to reproduce a duration to match the sample
15 (See *Fig. 1* and *Methods*). Reproduced durations of all 15 participants in the scanner
16 were analyzed: subject means were in a range of 2.42 ~ 3.54s. Among the
17 participants, reproduced duration of 3 subjects were not significantly varied from
18 the sample ($p > .05$), another 2 tended to over-reproduce (i.e.,
19 reproduced duration $> 3\text{s}$, all with $p < .001$), while all the other 10 participants
20 showed a tendency to under-reproduce (all with $p < .005$). Even though identical
21 sample duration was implemented in all trials without explicitly indicated, most of the
22 participants reported variations in the perceived duration during a short

1 post-experiment interview. Group mean of reproduced duration = 2.775s (95% CI
2 [2.628, 2.921]); one-sample T-test revealed that the reproduced duration was
3 significantly smaller than the sample duration of 3 seconds ($p = .003$, one-tailed).
4 See *Table. 1*. Considering that the difference between reproduced duration and the
5 sample (Mean = 0.225s) was much smaller than the sampling rate of fMRI (TR =
6 2s), this did not alter the temporal envelope of BOLD signals remarkably (see
7 Supplementary *Fig. 1*). Therefore, all the following analyses were performed pooling
8 over all valid trials.

9
10 In the motor control phase of the task, participants were asked to make a simple
11 reaction to the offset of the visual stimulus (see *Methods*). The mean reaction time
12 (RT) of participants range from 0.253s to 0.515s; group mean = 0.346s (95% CI
13 [0.311, 0.381]). See *Table. 1*. Since the fluctuation of reaction time is also much
14 smaller than the TR, the following analyses were performed pooling over trials with
15 different reaction time.

16 17 *Comparisons between task phases*

18 Taking together the two additional control tasks, the behavior paradigm can be split
19 into four task phases: the Encoding Phase (EP) when subjects were presented with a 3
20 s visual stimuli; the Reproduction Phase (RP) when subjects were required to
21 terminate another stimulus when its duration subjectively matched the sample; the
22 Visual Control (VC) phase when the same 3s visual stimulus was just passively

1 viewed, and the Motor Control (MC) phase when subjects were required to press the
2 key (identical motor response as the RP) following the removal of visual stimuli.
3 Therefore, each trial can be evenly divided into four task epochs with identical lengths
4 (12s).

5

6 For the first part of fMRI data analysis, simple contrasts were performed with a
7 general linear model (GLM, see *Methods*) on the whole-brain activation maps for the
8 period of stimuli presentation across four phases (see *Methods* for the experimental
9 design). Since overlapping compositions of cognitive processes were present in four
10 task phases, active timing and time-irrelevant activities can be disentangled by
11 psychological subtraction: comparison between EP and VC reveals timing-only
12 activities free from contamination by motor components; while comparing RP with
13 VC reveals duration working memory, decision-making, and motion preparation
14 activities in addition to those specific for timing. Comparison between MC and VC
15 was also performed in search of motor-specific components.

16

17 Subtracting visual components from the encoding phase, i.e., $EP > VC$, resulted in
18 significantly activated clusters mainly in the SMA, together with a small proportion of
19 medial superior frontal gyrus (See *Table.1* for details; also see *Fig.3, upper left* for
20 rendered view on cortical surfaces and medial wall structures). Reverse comparison
21 $VC > EP$ found no significant result.

22

1 Comparison RP > VC revealed a similar cluster at SMA and medial superior frontal
2 gyrus, as well as additional clusters spreading across bilateral thalamus, putamen,
3 pallidum, precentral gyrus, insula, and operculum (*Fig.3, upper-middle*). An
4 important difference between reproduction and encoding was the additional
5 involvement of bilateral Inferior Parietal Lobule, including structures alongside the
6 postcentral sulcus and intraparietal sulcus. These reproduction-specific brain activities
7 can be attributed to the duration working memory: maintenance of duration
8 information (reference memory) and its utilization in anticipatory timing (executive
9 control). Reverse comparison VC > RP revealed no significant cluster.

10

11 To control for non-timing motor components, a comparison MC > VC was performed
12 (*Fig.3, lower left*). Significant clusters spread in a similar set of regions as in RP,
13 including subcortical structures in bilateral thalamus, putamen, pallidum, and caudate,
14 as well as cerebral activations in bilateral insula and SMA. Another cluster was in the
15 superior lobes of the left cerebellum. The operculum cortex, inferior frontal lobule,
16 and precentral gyrus were lateralized to the left hemisphere. Since no explicit timing
17 was required in this phase of the task, these activities should be caused by non-timing
18 motion preparation and motor initiation. Reverse comparison VC > MC revealed
19 significant clusters mainly in the occipital visual areas (*Supplemental Fig.2*).

20

21 To disentangle motor components from active timing which were intermingled during
22 reproduction, the comparison RP > MC was also performed, revealing higher

1 activation levels in the putamen, pallidum, insula, and precentral cortex, all lateralized
2 to the left. Operculum activation was found to be higher during reproduction in both
3 hemispheres. SMA also displayed elevated activity, indicating its participation in both
4 active timing and motor planning, thus its bifunctionality. The motor planning cortical
5 loci (SMA) may have an additional function in providing conscious access to the
6 duration of external and internal events, during both encoding and reproduction. The
7 basal ganglia structures (Caudate, Pallidum, and Putamen) were activated only in the
8 reproduction and motion control phase with a stronger activity during reproduction,
9 questioning its participation in sensory timing.

10

11 In addition to the SMA and the basal ganglia, significant clusters located in the right
12 middle frontal gyrus and bilateral structures alongside the intraparietal sulcus were
13 unique for duration reproduction; again, indicating their role in active and explicit
14 timing rather than motor planning. Reverse comparison MC > RP revealed clusters in
15 the cingulate cortex and left medial superior frontal gyrus (*Supplemental Fig.2*).

16

17 *Reference memory of duration*

18 To reproduce a duration in match of a previously given sample, information about the
19 sample duration must be kept in reference memory throughout the response delay. A
20 memory component was thus included in the GLM, starting right after the termination
21 of visual stimuli in ER and lasted 8s until the beginning of the RP phase. Group
22 analysis revealed significant clusters first in a leftward lateralized cluster composed of

1 SMA, Operculum, Precentral, and Insula, then in bilateral Inferior Parietal Lobule at
2 an approximately symmetric location, and in the left dorsal lateral prefrontal cortex
3 (dlPFC). (see *Fig.3 right*) This inter-stimulus sustained activity features the
4 engagement of these areas in maintaining the reference memory of sample duration.

5

6 *Hemodynamic function in regions of interest*

7 Since the GLM model provides a trend-line analysis between the observed signal and
8 the pre-hoc defined task design matrix, the reliability of the interpretation depends on
9 the neuropsychologic understanding of the task itself. However, in a timing task
10 where time itself is the information to be encoded, it is unknown what cognitive
11 progress is taking place at when. Therefore, the task design matrix of the GLM model
12 is based on hypothetical prior assumptions about the temporal profile of cognitive
13 processes. From a statistical perspective, the results cannot be more reliable than the
14 assumptions, neither can they justify these assumptions. A data-driven,
15 hypothesis-free approach is preferential in this case.

16

17 We then took a data-driven approach by comparing the temporal envelope of BOLD
18 signal across different loci. Our behavior task was designed in a way that the BOLD
19 signal sampling can be temporally aligned across all the trials. All four task epochs
20 were extended to 12s, corresponding to 6 sampling points. The whole trial added up to
21 48s or 24 sampling-point lengths of the BOLD envelope. Overlapping between the
22 BOLD signal of adjacent events is optimally balanced between each phase of the task.

1 The mean BOLD envelop is thus a reliable approximate of the task-evoked
2 hemodynamic functions (HDF) in each region-of-interest (ROI).
3
4 In bilateral SMA (*Fig. 4A*), the HDF showed three peaks following the encoding,
5 reproduction, and motor control phase. Interestingly, only in the right SMA, the last
6 peak of HDF during motor control came later than prediction and its left-hemisphere
7 counterpart (estimated with 6s offset, see Methods). Considering the delay by reaction
8 time and the left-hand response, the delayed activity of right SMA might be better
9 explained by the motor response. In addition, the peak amplitude following
10 reproduction was higher than both encoding and motor control phase (paired t-test, all
11 with $p < .001$). Confirming the simple contrast between RP > MC. This again
12 supports the bifunctionality of SMA, with additive BOLD signals when both
13 functionalities are called.

14
15 A similar time course of HDF was observed in the insula (*Fig. 4B*), another structure
16 previously suspected for time-encoding (e.g., Kosillo & Smith, 2010; Wittmann et al.,
17 2010). Signal was elevated in bilateral insula during encoding, reproduction, and
18 motor control. A delayed peak was observed in the right insula during motor control,
19 but not in the encoding and reproduction phases.

20
21 The HDF in the thalamus (*Fig. 4C*) suggests that its function might be more
22 motor-related, with peaks only in the two phases with a motor response, i.e.

1 reproduction and motor control. It is thus consistent with the results of simple
2 comparisons. The right thalamus ROI revealed more dramatic signal fluctuation
3 compared to the left side, in line with the left-handed motor response.
4

5 The BOLD signal changes during the timing task in basal ganglia structure putamen
6 (*Fig. 4D*), on the other hand, was smaller in size compared to other ROIs. Signal
7 remained high throughout the first two phases (encoding, reproduction compared to
8 visual control); as well as during motor control but was delayed and much steeper. It
9 might indicate a different hemodynamic response while participating in motion
10 generation as compared to explicit timing.
11

12 In the inferior parietal lobule (IPL, *Fig. 4E*), the HDF followed a similar pattern like
13 the SMA, with three peaks in encoding, reproduction, and motor control, and the
14 highest response was reached during reproduction. Interestingly, a plateau of activity
15 between encoding and reproduction was observed only in the left IPL (*Fig. 4E-left*),
16 probably related to the maintenance of duration reference memory. Although activities
17 in bilateral IPL were both significantly altered by the task, it seemed that the reference
18 memory of duration information was leftward lateralized as suggested by its activity
19 pattern.
20

21 A similar pattern as IPL was found in the middle frontal gyrus (MFG, *Fig. 4F*), with a
22 more prominent signal fluctuation in the right hemisphere and a plateau-like activity

1 in the left. Concerning results of simple contrasts that the left MFG was found
2 significant during the memory phase and the right MFG significantly activated during
3 reproduction, bilateral MFG might play a different role in duration reference memory
4 (left) and executive control (right).

5

6 In contrast, no such plateau-like activity was found in the left inferior frontal
7 operculum (*Supplemental Fig.3*), another significantly activated region in both the
8 reproduction and memory phase. It also illustrates that comparing the temporal
9 envelope of the BOLD signal can reveal more than the common hypothesis-driven
10 way.

11

12 *Inter-regional cross-correlation*

13 To further investigate the strength and direction of inter-regional interaction, a
14 cross-correlation analysis was performed on the HDF for each pair of ROIs within the
15 four task epochs. The peak of activity was estimated by fitting a quadratic function to
16 the more sparsely sampled data. This allows interpolation beyond the 2s sampling rate
17 of the fMRI (see *Methods* and *Fig.6A*). Dramatic changes in the direction of
18 inter-regional correlation were observed in the inter-regional time lag matrix (see
19 *Fig.6B*): during encoding, BOLD signals in the putamen and the thalamus lead the
20 SMA and the insula, which then lead the frontoparietal circuit. While during
21 reproduction and motor control this relation was partially reversed, that the SMA and
22 insula signals lead the putamen, which then leads the thalamus. The temporal

1 sequence suggests the direction of information flow through the hierarchy: duration
2 information is transferred in the bottom-up direction from subcortical regions in basal
3 ganglia and thalamus to cortical regions in SMA and insula; while the same pathway
4 is re-used but in a reversed direction down the hierarchy during motor output.

5

6 For higher associative cortical regions such as the middle frontal gyrus and the
7 inferior parietal lobe, the parietal ROIs slightly lead the frontal ROIs during encoding,
8 which was remarkably reversed during reproduction, with the left middle frontal
9 region leading the parietal ROIs. It should also be noted that during the visual control
10 phase when significant activity is missing in most subjects, the interpolation method
11 we used for inter-regional temporal lag estimation is not as reliable as the other three
12 phases.

13

1 **Discussion:**

2 Disentangling parallel cognitive processes is the core challenge in neurocognitive
3 research on timing. All physical events, including those that take place in the brain,
4 take a certain interval. The most common methodology in analyzing all types of
5 neurophysiological data (BOLD fMRI, electrical signals in intra-/extra-cellular
6 recording and EEG, etc.) is by correlating the observed temporal sequences with the
7 temporal profile of external or internal events. However, interpretation of this
8 temporal correlation becomes problematic when several events temporally coincide.
9 This problem is especially eminent when the duration of time itself is the input to the
10 neuronal system, as in interval timing research.

11
12 In previous imaging studies on interval timing, researchers either look for
13 accumulating signals that correlate with the passage of time or simply compare brain
14 activities between a timing task and a non-timing task in a block design. However,
15 both ways fail to address whether these observed activities are truly relevant for
16 dedicated timing in the brain. The same problem persists even when temporal
17 information can be post-hoc decoded from neural signals (e.g. Cueva et al., 2020;
18 Bruce et al., 2021): even if the observed neural processes are temporally organized,
19 there is no guarantee that the embedded time is utilized for perception or explicit
20 estimation of time. A distinction should be made between time as a *logistic function* of
21 the neural system that acts as the cognitive context, is usually intrinsic and does not
22 infer time (Pöppel, 2009); and as a *semantic function* that provides the duration as a

1 cognitive content, can be explicit and infers time.

2

3 One historical approach to disentangle different cognitive processes in intermixed
4 data is the psychological subtraction method invented by Donders (1969; Bao et al.,
5 2016). The subtraction method was first implemented on reaction time, following the
6 idea of sequential processing, but has been frequently revisited in modern
7 neuroscience with measurements far more advanced than the reaction time paradigm.

8 The underlying idea is the same: as long as the detected signal is systematically
9 modulated by each additional cognitive process, subtraction of the data can
10 presumably disclose the difference between cognitive compositions. The simple
11 contrast between whole-brain activity maps of different tasks is a typical example of
12 subtraction. It has the potential to differentiate activities even when they share the
13 same time course.

14

15 The duration reproduction paradigm is widely used in interval timing research
16 partially due to its rich cognitive composition. It consists of a near-complete
17 spectrogram of cognitive components: encoding, memory, and retrieval of duration
18 information, for both external sensory input and prospective motion planning.
19 However, its complexity also adds to the difficulty of interpreting the task-data
20 temporal correlation. Linking any activity that is temporally evolving with the timing
21 mechanism risks contamination from non-timing parallel components. In this study,
22 we tried to dissect the duration reproduction task by comparing the hemodynamic

1 function of the timing task with control tasks, in both hypothesis-driven and
2 data-driven ways.

3

4 The basal ganglia – supplementary motor area (BG-SMA) circuit has been repeatedly
5 reported in various timing tasks and has thus been suspected the neural substrate of
6 dedicated timing (Ferrandez et al., 2003; Casini & Vidal, 2011; Kotz, Brown &
7 Schwartze, 2016). However, considering the basal ganglia’s more general role in
8 goal-directed, task-context-sensitive behavior (Haber, 2003; Korb et al., 2017), it is
9 questionable whether their neurophysiological responses represent merely a logistic
10 function of time that coordinates activities across the cortex, or is relevant for the
11 semantic function that encodes duration of time into a readily accessible mental
12 representation.

13

14 Our result shows that the SMA is involved in both timing and motor planning, with an
15 additive BOLD response when both cognitive components are present during
16 reproduction. Similar signatures of activity were observed in the insula but turned out
17 to be statistically insignificant during encoding, as shown in the simple contrasts.
18 Comparatively, the BOLD signal in part of the dorsal striatum, the putamen, was
19 subtle during encoding and reproduction but had a clear and sharp response during
20 motor control. However, given its elevated response throughout EP and RP compared
21 to VC, putamen may also be bifunctional, only less specific during timing than its
22 well-known function in motion initiation (Turner & Desmurget, 2010). We also found

1 in temporal cross-correlation that the direction of connectivity went from BG to SMA
2 during encoding but from SMA to BG and thalamus during reproduction, suggesting
3 some information might have been passed from BG to SMA during encoding. We
4 propose that the additive hemodynamic response in the SMA may result from distinct
5 neural populations and independent microscopic organizations for the motor and
6 timing functions, while the relatively flat fluctuation in the BG may represent
7 overlapping and multifunctional neural populations. In that case, representation of
8 time is generated in the cortex by interpreting the subcortical inputs differently in a
9 goal-directed manner, while the temporal coordination function in the basal ganglia is
10 merely a logistic temporal function but not semantic by itself.

11

12 The most persuasive evidence on timing in the BG comes from clinical research (e.g.,
13 Dušek et al., 2012; Högl et al., 2014) and animal studies (Kononowicz & van Rijn,
14 2014; De Corte et al., 2019). The midbrain dopaminergic input to the striatum was
15 suspected to be relevant (Parker, Ruggiero & Narayanan, 2015; Soares, Atallah &
16 Paton, 2016). However, in these studies, the timing function is evaluated on the net
17 output of the whole system; it might be that the subcortical dopamine dynamic
18 influences the timing behavior via acting on the logistic temporal function (e.g.
19 coordinating the cortical activities; Bao et al., 2015) instead of the semantic function,
20 which is located at a higher hierarchy in the cortex.

21

22 In addition to the SMA, a working memory network was observed in a different group

1 of cortical regions including the left dorsal lateral prefrontal cortex (dlPFC) and
2 bilateral structures alongside the intraparietal sulcus (IPS). Noticeably, the left dlPFC
3 leads the parietal regions during reproduction, probably indicated the direction of
4 executive control. The dlPFC has been proved critical for working memory
5 manipulations and computations in lesion studies (see Barbey, Koenigs & Grafman,
6 2013 for a review) and imaging studies (Olesen, Westerberg & Klingber, 2004). The
7 IPS is known to be important for working memory of not only duration but also other
8 domains of magnitudes, together as so-called “general magnitude system (GMS)” (or
9 ‘approximate number system (ANS)’; Walsh, 2003; Bueti & Walsh, 2009). Evidence
10 supporting duration representation in the GMS comes from clinical observations of
11 the deficit timing function in Developmental Dyscalculia patients (Skargerlund &
12 Träff, 2014), imaging studies showing common activation of inferior parietal lobe by
13 number, spatial magnitudes, and duration (Bueti & Walsh, 2009; Sokolowski et al.,
14 2017), cross-modality transferring effects under training or brain stimulation
15 (Cappelletti et al., 2013; Lourenco, Ayzenberg & Lyu, 2016) as well as developmental
16 and non-human primate studies (Jacob, Vallentin & Nieder, 2012; Nieder, 2016). This
17 frontoparietal circuit might govern the higher-order cognitive processing of duration
18 information, which abstracts the duration of several seconds into a magnitude
19 representation which allows for comparison between memory items.

20

21 The two different cortical systems related to timing, along with the supporting
22 subcortical structures, may perform a different level of abstraction and thus compose

1 a hierarchy of functions for duration processing. In subcortical structures, time is not
2 explicitly encoded, but rather as a logistic function that temporally synchronizes
3 different neural subsystems in the brain. The same network and population of BG
4 neurons might broadcast to cortical downstream areas of all functions, only being
5 interpreted differently in a task-dependent manner by the receiver. In the first-order
6 cortical region for timing, i.e. SMA, these subcortical inputs are integrated in a way
7 that duration can be actively measured, thus the logistic time is translated into a form
8 of content, i.e. the semantic aspect of time. This first level of abstraction can be very
9 concrete, for example, via firing-rate modulation ('ramping' activities) in a
10 subpopulation of neurons (Cueva et al., 2020; Bruce et al., 2021). The increased
11 neuronal activity might in turn affect the energy consumption in the region and thus
12 leading to the observed climbing BOLD signal. Following this first-order
13 low-dimensional encoding, more abstract representation is created in the
14 frontoparietal circuit as a domain of magnitude, taking the form of populational
15 coding similar to the number senses (Tudusciuc & Nieder, 2007), which allows for
16 complicated cognitive manipulation as well as longer and more energy-friendly
17 memory storage. This implies that a limited number of neural subgroups codes the
18 duration in a specific manner without increasing their energy consumption with time,
19 which would explain why memory traces of duration evoke plateau BOLD signal
20 instead of climbing signal as in the SMA.

21

22 In conclusion, by comparing BOLD signals between different tasks in multiple brain

1 areas, we were able to disentangle different cognitive components of the duration
2 reproduction task. Based on differentiating the logistic function and the semantic
3 function of time, we attribute the devoted timing mechanism to the cortex. More
4 specifically, two distinct cortical circuits were discovered: the supplementary motor
5 area which displayed additive BOLD signal for both timing and motor planning,
6 probably result from involvement of independent subpopulations in different tasks;
7 and a working-memory related frontoparietal circuit. The plateau BOLD signal
8 observed in these working memory regions may suggest a different coding strategy
9 and thus different levels of abstraction for the semantic duration information.

10 Activities in the subcortical regions such as the putamen and thalamus are less
11 specific. This may be because of overlapping populations realizing different functions
12 or simply the lack of functional differentiation in these subcortical regions. Thus, we
13 propose the distinction between a subcortical logistic function of time and a cortical
14 semantic function of time.

15

16 However, although we succeeded in attributing different processing stages to different
17 brain loci, one should keep in mind that functional imaging catches only a summation
18 of underlying neurocognitive and neurophysiological processes. It remains unclear
19 what are the neural coding mechanisms underlying each level of this hierarchy. More
20 down-to-the-neuron observations are required to justify our hypothesis.

21

Online Methods:

Duration reproduction task:

The whole experiment was divided into 5 imaging sessions, each with 12 trials (60 trials for each subject). Each trial was made up of 4 sequential phases: Encoding Phase (EP), Reproducing Phase (RP), Visual Control (VC), and Motor Control (MC), as depicted in *Fig. 1*. At the beginning of each phase, a visual cue (Size: 0.8×0.8 deg visual angle) appeared for 1 second in the center over a dark background, followed by a square target (Size: 10×10 visual angle). In the first task phase (EP), the square lasted for exactly 3 seconds as the sample duration. The sample duration was selected based on previous research showing maximum accuracy of reproduction between 3.0 and 3.5 seconds (Pöppel, 1972).

In the next phase of task (RP), participants were asked to reproduce the sample duration by terminating a comparison stimulus with a keypress. In the third phase (VC), the same square was presented again for 3 seconds, only passive viewing was required. In the last phase (MC), the square was presented for the same duration as reproduced in RP. To control for timing-irrelevant brain activities, e.g., motion preparation and initiation, participants were asked to make a keypress following the disappearance of the stimulus as soon as possible. They were instructed not to deliberately time the stimuli in the MC phase but only react when the square was gone. In case participants failed to press a key in RP, the stimulus was presented for 11 seconds and then turned off; the missing trial would be excluded from the analysis.

1 All key presses were performed with the left index finger.

2

3 Each task phase was extended to exactly 12 seconds with a blank screen, allowing
4 hemodynamic response back to baseline. With identical lengths for each task phase, it
5 is possible to obtain trial-average hemodynamic curves for each region of interest
6 (ROI).

7 Trials were first screened by the reproduced duration during the RP phase to ensure
8 that participants were attending and following the instructions; further screening was
9 conducted on the reaction time in MC, ensuring no anticipation or active timing.

10 Outlier trials were both defined individually as beyond 2 standard deviations from the
11 mean. This post-hoc data screening supplements the verbal instructions to guarantee
12 that all trials analyzed were performed as instructed.

13

14 *Behavior verification of duration reproduction task:*

15 6 right-handed college students (all males; mean age: 21.5 years; age range: 21-23
16 years) participated in the pilot behavioral experiment, all with normal or
17 corrected-to-normal vision, and reported no neurological, psychiatric or medical issue.
18 The experiment was conducted in a soundproofing chamber equipped with a computer.
19 The visual parameters were identical to the fMRI study. Sample durations were
20 randomly chosen from 1.5, 3.0, 4.5, or 6.0 seconds as the within-block variable; each
21 of the four alternatives was repeated four times, resulting in 16 trials per block. The
22 interstimulus interval (ISI) following the reference stimuli was either 4.5 or 9.0

seconds, randomized between blocks; each ISI was repeated three times, composing 6 blocks. Participants were instructed to terminate the second visual object with a press on a 4-key reaction box (Sinorad Inc., China) when its duration matched the sample, and not to apply any timing strategy such as counting or tapping. Each trial was followed by a 7-second inter-trial interval with a blank screen.

6

All visual stimuli were displayed in the center of a 27-inch ViewSonic VX2268wm LCD monitor, 80 cm away from the participant. Stimuli display and response collection were performed with the help of Psychtoolbox extensions (Brainard, 1997) in MATLAB 2014b (MathWorks Inc., USA).

11

MRI Participants:

16 college students (8 females and 8 males) were money-rewarded for participation in the functional imaging study, with ages ranging from 19-28 ($M = 21.7$, $SD = 2.6$). All participants were right-handed and with normal or corrected to normal vision. No record of neurological, medical, visual, or memory issues was reported. Participants were given written consent and several practice trials to familiarize themselves with the task before the scanning session. They were asked to maintain a regular daily schedule and not to consume any psychostimulants, drugs, or alcohol within 3 days before the experiment. One Subject was excluded from data analysis due to bad signal spatial alignment due to excessive head movement (> 4 mm). The study was approved by the departmental ethical committee of Peking University.

1

2 *MRI acquisition parameters:*

3 MRI data were collected on a 3T MR750 General Electrical scanner with a
4 32-channel head coil. T1-weighted anatomical images were acquired in 188 slices (3D
5 MPRAGE; $1 \times 1 \times 1 \text{ mm}^3$ resolution; gap = 0 mm). Functional T2*-weighted
6 echoplanar images were acquired with 33 axial slices in interleaved order (3.5 mm
7 thickness, $3.5 \times 3.5 \text{ mm}$ in-plane pixel size, TE = 30 ms; TR = 2000 ms; FOV =
8 $224 \times 224 \text{ mm}^2$; matrix = 64×64 ; flip angle = 12° ; gap = 0.7 mm). The trial
9 presentation was synchronized to TR onset by scanner trigger pulses. Visual stimuli
10 were back-projected on a $25 \times 19 \text{ cm}$ translucent screen 90 cm away from the
11 participant. Cushions were placed around the head and neck to maximize comfort and
12 minimize motion. A complete imaging session took about an hour, depending on the
13 subject-determined length of inter-block breaks.

14

15 *fMRI preprocessing:*

16 Analysis was performed with the Statistical Parametric Mapping toolbox (SPM-12;
17 Penny et al., 2011) on MATLAB R2018a. During data preprocessing, images were
18 first corrected for slice acquisition delay and then spatially realigned to correct for
19 head movements. Co-registration was then performed in reference to the T1-weighted
20 structural image, followed by normalization to the T1 template of the Montreal
21 Neurological Institute (MNI), with parameters derived individually from nonlinear
22 normalization of grey-matter T1 images. All images were then smoothed with a

1 Gaussian kernel of FWHM = 8 mm.

2

3 *fMRI analysis:*

4 A general linear model including periods of visual stimuli presentation (i.e., 1s to 4s

5 after phase onset) in each of four different phases was established. To investigate the

6 reference memory component involved in the reproduction task, a memory

7 component was added to the GLM model, spanning the 8-second interval between

8 visual object offset in EP and the cue onset in RP. The subtraction method was applied

9 to disentangle each component. Invalid trials were excluded from the GLM model.

10 The analysis was performed first on the individual level, resulting in an individual

11 T-statistic map for each comparison of interest; group analysis was then performed for

12 each of these comparisons. Results were visualized with the help of the xjview

13 toolbox for MATLAB (<https://www.alivelearn.net/xjview>) based on Automated

14 Anatomical Labeling (AAL, <http://www.gin.cnrs.fr/AAL-339>) atlas.

15

16 *ROI analysis:*

17 To further investigate the temporal envelope of BOLD signal related to different

18 cognitive processes, region of interest (ROI) analysis was performed in a set of

19 regions derived from the group-level simple contrasts (*Table. 3*). Spherical masks

20 were applied for each ROI, centered at the peak voxel of the simple contrasts. The

21 radius of each sphere was determined by the cluster size. BOLD signals were

22 extracted with the help of the MarsBaR toolbox for MATLAB (Brett *et al.*, 2002). The

1 hemodynamic function (HRF) of each ROI was obtained first on the individual level,
2 and then averaged across subjects and plotted with the between-subject variance
3 (*Fig. 4*). All HRFs were baseline-corrected to the average BOLD signal during the
4 visual control phase (30-40 sec after trial onset). Predicted positions of the peaks were
5 indicated by vertical dash lines, with 6 seconds delay following the end of stimulus
6 display (10 seconds from phase onset).

8 *Temporal cross-correlation of regional HDF:*

9 Trial averaged HDFs for each subject were then fed into an interregional temporal
10 cross-correlation analysis to investigate the connectivity pattern. The HDFs were
11 divided into 4 segments, corresponding to the delayed hemodynamic response for 4
12 task phases (start at 6s, 18s, 30s, and 42s after trial onset, see *Fig. 5A*), resulting in a
13 cross-correlation function for each ROI pair. A quadratic function was fitted with the
14 highest 3 points around the peak in estimation for the inter-regional lag (*Fig. 5B*). A
15 heatmap was created to visualize the inter-regional lag between selected ROIs during
16 each of the task phases (*Fig. 5C*).

18 **Reference of the Methods:**

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1

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4

Table.1 | Group-mean and 95% confidence interval (CI) of reproduced duration in
Reproduction Phase, and simple reaction time in Motor Control phase.

	Mean	SD	CI
Reproduced duration (s)	2.775	0.265	[2.628, 2.921]
Simple reaction time (s)	0.346	0.069	[0.311, 0.381]

5

6

Table.2 | Clusters with familywise error (FWE) corrected significance in different
comparisons between task phases. 3D coordinates of the peak voxel and subregions of
each cluster are reported. Only subregions with voxel size > 30 were included.

Comparison	Peak coordinates			$p(\text{FWE}_{\text{cluster}})$	Sub-region
	x	y	z		
EP > VC	-10	-2	64	0.002	SMA L&R
					Medial Superior Frontal
					Gyrus L
RP > VC	-10	-14	4	0.000	Thalamus L&R
					Insula L&R

					Inferior Frontal Operculum
					L&R
					Putamen L&R
					Precentral L&R
					Rolandic Operculum L&R
					Caudate L
					Pallidum L
					Inferior Frontal Triangularis
					L&R
	50	-32	48	0.000	Inferior Parietal R
					Supramarginal Gyrus R
					Postcentral R
					Superior Parietal R
	-46	-42	48	0.000	Inferior Parietal Gyrus L
					Supramarginal L
					Postcentral L
	-8	-6	64	0.000	SMA L&R
					Mid-Cingulate Cortex L&R
					Medial Superior Frontal
					Gyrus L&R
					Superior Frontal Gyrus L&R
MC > VC	-34	-62	-28	0.010	Cerebellum L

	-8	-14	-2	0.000	Thalamus L&R
					Putamen L&R
					Caudate L&R
					Insula L&R
					Inferior Frontal Triangularis
					L
					Pallidum L&R
	-46	2	12	0.015	Rolandic Operculum L
					Inferior Frontal Operculum
					L
					Precentral L
					Insula L
	-8	0	62	0.000	SMA L&R
					Mid-Cingulate Cortex L&R
					Medial Superior Frontal
					Gyrus L
					Superior Frontal Gyrus L
					Anterior Cingulate L
	42	-22	50	0.013	Precentral R
					Postcentral R
RP > MC	-38	8	10	0.001	Insula L
					Putamen L

					Inferior Frontal Operculum
					L
					Pallidum L
	54	12	26	0.026	Inferior Frontal Operculum
					R
	-52	0	24	0.029	Precentral L
					Inferior Frontal Operculum
					L
	42	44	20	0.030	Middle Frontal Gyrus R
	-4	14	68	0.000	SMA L&R
					Medial Superior Frontal
					Gyrus L
	54	-30	54	0.000	Inferior Parietal R
					Supramarginal R
					Postcentral R
					Superior Parietal R
	-50	-42	62	0.042	Inferior Parietal L
Memory	-14	10	60	0.000	SMA L&R
					Inferior Frontal Operculum
					L
					Precentral L
					Superior Frontal Gyrus L

					Middle Frontal Gyrus L
					Insula L
-26	40	26	0.028		Middle Frontal Gyrus L
54	-36	50	0.005		Inferior Parietal Gyrus R
					Supramarginal R
-56	-38	48	0.007		Inferior Parietal Gyrus L

1

Table.3 | Spherical ROIs derived from significant clusters in whole-brain level comparisons. The center coordinate was defined by peak voxels within the clusters of interest. ‘*’ marks those ROIs derived from its contralateral analog by mirroring the location.

Location in the brain	Contrasts of identification	Coordinate of center			Radius (mm)
		X	Y	Z	
SMA L	EP > VC	-10	-2	64	4
SMA R	RP > MC	4	16	56	4
Thalamus L	RP > VC	-10	-14	4	6
Thalamus R	RP > VC	14	-18	10	6
Putamen L	RP > MC	-24	0	14	4
Putamen R	RP > MC*	24	0	14	4
Pallidum L	RP > MC	-18	-6	2	2
Pallidum R	RP > MC*	18	-6	2	2
Insula L	RP > MC*	-32	18	10	4

Insula R	RP > MC	32	18	10	4
Inferior Frontal Operculum L	RP > MC	-38	8	10	4
Inferior Frontal Operculum R	RP > MC	54	12	26	4
Inferior Parietal L	RP > MC	-48	-42	48	4
Inferior Parietal R	RP > MC	54	-30	54	4
Supramarginal L	RP > VC	-56	-24	24	4
Supramarginal R	RP > VC	50	-32	48	4
Middle Frontal L*	RP > MC*	-42	44	20	4
Middle Frontal L	Memory	-26	40	26	4
Middle Frontal R	RP > MC	42	44	20	4

1

2

3

Fig.1 | Schematic diagram of the duration reproduction paradigm during fMRI scanning. In each trial, four phases were in a continuous sequence with a fixed order, durations of all four phases were extended to 12 seconds. In each phase, a box appeared at the screen center following a visual cue of 1s. In the encoding and visual control, the visual stimuli persisted for 3s; while in the other two phases the duration was dependent on the subject-reproduced duration in that trial.

Fig.2 | Reproduced duration for each sample duration in two different ISI conditions. Error bar marks the range of 95% confidence interval. No significant difference in reproduction performance was observed between different inter-stimulus intervals. Reproduction for the 3s sample duration was more accurate than the over-reproduced 4.5 and 6 seconds.

Fig.3 | Rendered view of results displaying contrasts of interest. The period with visual stimulus display in each of the four task phases was included in the design matrix together with a memory component in between the encoding and reproduction. The design matrix was then convolved with the hemodynamic function, resulting in a GML model. Voxel-wise comparisons between the regressors of interest lead to the activity-contrast map as depicted above. SMA activation was observed in both timing phases (EP>VC and RP>VC) as well as in the motor control and during the memory delay. Thalamus and basal ganglion structures (e.g. putamen) were activated only in the two phases containing a motor response (RP>VC and MC>VC) In addition, a frontoparietal circuit including the left dlPFC and bilateral intraparietal sulcus structures was specifically activated during the memory phase. The significant level was set at cluster-level $p(\text{FWE}) < 0.05$.

1

2

Fig.4 | Trial average hemodynamic functions of interval-timing-related brain regions. Baseline was defined as the average signal strength during visual control. Paired T-test was performed on the differences from baseline (red: significantly higher; green: significantly lower). Timing and motor-related activities were observed in the SMA (**A**), insula (**B**), thalamus (**C**), and the putamen (**D**). An activation plateau was observed in the middle frontal gyrus (dlPFC, **F**) and the inferior parietal lobe (**E**), both lateralized to the left hemisphere, probably related to the duration working memory.

Fig.5 | Inter-regional cross-correlation of hemodynamic function. **(A)** The trial average HDF of each ROI was first obtained for each individual and then segmented into 4 phases. Cross-correlation functions were calculated for each pair of ROIs and then averaged across subjects. The temporal lag between each pair of ROIs was estimated by fitting a quadratic function to the highest 3 data points of the cross-correlation function. **(B)** Inter-regional time lag matrix for each task phase. A negative value ($-n$) indicates that the region specified on the Y-axis leads the region on the X-axis by n seconds; while a positive value indicates the X-labeled region leading the Y-labeled region. In the encoding phase (EP), thalamus and putamen activities lead SMA and insula, while the relationship was partially reversed during reproduction (RP), in accordance with the direction of information flow.

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