Functional neuroimaging of duration discrimination on two different time scales

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Abstract

Analyses of neural mechanisms of duration processing are essential for the understanding of psychological phenomena which evolve in time. Different mechanisms are presumably responsible for the processing of shorter (below 500 ms) and longer (above 500 ms) events but have not yet been a subject of an investigation with functional magnetic resonance imaging (fMRI). In the present study, we show a greater involvement of several brain regions – including right-hemispheric midline structures and left-hemispheric lateral regions – in the processing of visual stimuli of shorter as compared to longer duration. We propose a greater involvement of lower-level cognitive mechanisms in the processing of shorter events as opposed to higher-level mechanisms of cognitive control involved in longer events.

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The experience of time can be classified in numerous ways, but two kinds of time perception can clearly be discerned. Whereas *succession* refers to the perceived succession and temporal order of events, *duration* refers to the perceived time interval between events or to the persistence of an event over time. When comparing neural models of temporal mechanisms it becomes clear that several independent hypotheses exist on how subjective time could be implemented in the neurobiological machinery [2,12,19,23]. However, no consensus exists on which areas of the brain and what kind of processes account for the perception of time in humans [40]. Multiple brain regions are usually participating in time perception tasks which suggests that different neuro-cognitive mechanisms such as attention, interval encoding, short-term memory, and decision making are involved [18,26,30].

Several studies on the neural basis of duration processing suggest the involvement of the right frontal lobes, basal ganglia and the cerebellum. Patients who suffered right-hemispheric brain injury [13] or focal frontal lesions [22] show impairments in the processing of duration. Patients with damage to basal ganglia and cerebellar structures exhibit deficits in time perception and motor timing of temporal intervals [6]. Functional neuroimaging studies with healthy volunteers show that the processing of duration is associated with activations in the right prefrontal cortex and the striatum [4,10,16,26]. Other brain regions, however, also seem to play a decisive role. For example, increased insula activation has been observed repeatedly in neuroimaging studies of time estimation (e.g., [15,18]), though its functional role is rarely discussed (but see Craig [5] and Wittmann [40]). Depending on the experimental paradigm, sensory modality and time scale used, additional structures have shown to be involved (e.g., anterior cingulate cortex, supplementary motor area, posterior parietal cortex).

Regarding neurotransmitter systems, studies indicate that both dopaminergic agonists and antagonists influence the estimation of time intervals by increasing and decreasing the speed of a hypothesized internal clock, respectively [1,3]. Moreover, patients with dysfunctions of the dopaminergic system such as with schizophrenia [6] or with Parkinson’s disease [8], as well as individuals with chronic use of cocaine and methamphetamine [41] are impaired in the processing of duration.

The duration of the temporal interval is a critical variable in time perception studies. There is accumulating evidence that
different time perception mechanisms operate on different time scales [25]. For example, it has been repeatedly shown that intervals up to 2–3s are differently processed than intervals exceeding this time range [32,34,39]. Different timing systems are also assumed for events in the seconds vs. the milliseconds range for perception [9,17] and for timing control mechanisms in sensorimotor coordination [21,31]. The processing of longer intervals around 1s has shown to be cognitively mediated as performance in temporal discrimination is impaired when a cognitive secondary task has to be performed at the same time. The processing of brief durations with a base duration of 50 ms, however, was not affected by a simultaneous cognitive task [29]. Moreover, pharmacologic agents affecting short-term memory impaired only the ability to discriminate durations around 1s, while duration processing around 50 ms was not affected [28].

Although it has been proposed that temporal integration mechanisms exist that would distinguish between the processing of shorter and longer intervals [37,42] neuronal evidence is scarce. In this study, we wanted to investigate whether the processing of temporal intervals with different durations necessitates the involvement of different areas of the brain or whether time processing is independent of the selected time intervals of shorter (below 500 ms) and longer (above 500 ms) duration. We expected to find (1) overlapping areas of the brain activated in both conditions (e.g. basal ganglia) and (2) separate brain areas preferentially activated in the longer (e.g. dorsolateral prefrontal cortex) or the shorter (e.g. sensorimotor cortex, cerebellum) duration condition.

Thirteen right-handed (Edinburgh Handedness Inventory) healthy adults (male: female = 7:6, mean ± S.D. age = 29.2 ± 6.2 years, range 20–39) with no history of neurological or psychiatric illness, head trauma or psychoactive substance abuse participated in the study. The subjects were interviewed concerning common contraindications for MRI (e.g., pacemaker implant, pregnancy); all had normal or corrected to normal vision and were tested for red-green dichromacy with the Ishihara color-vision test. Written informed consent to participate was collected prior to the study, and subjects were informed of their right to discontinue participation at any time. The study was carried out in accordance with the Declaration of Helsinki principles and was approved by the ethics committee of the Medical Faculty of the LMU Munich. Subjects received payment for their participation. The data of one female subject had to be excluded from the analysis because of technical recording problems during the experiment.

Tasks consisted of a sequence of four elements: 1st stimulus, inter-stimulus interval (ISI); 2nd stimulus, response period (Fig. 1). Stimuli were colored squares (red or green) with a side length of about 5° visual angle, presented in the center of the visual field on a black background. In the perception of duration task subjects were required to report by pressing a corresponding button what the color of the longer stimulus was (right key = “red”, left key = “green”). Each stimulus was presented for 100 or 250 ms in test sessions (runs) with shorter durations; or for 1000 or 1300 ms in runs with longer durations. Stimuli were separated by an inter-stimulus interval of 600 ms. A fixation cross on a black background was presented during the response period that lasted 4000 ms. The experiment was conducted in six runs: three for shorter (S) and three for longer (L) stimulus durations, arranged in S–L–S–L–S–L order.

Each run consisted of the experimental task described above and two control tasks: (1) perception of succession – subjects were required to report what the color of the 2nd stimulus was (right key = “red”, left key = “green”); (2) color judgment – whether colors of the two stimuli differed or were the same (right key = “the colors are identical”, left key = “the colors are different”). The two control tasks, which are standard paradigms in neuroimaging studies of time perception, aimed to control for general task-unspecific effects of visual perception, attention, working memory, and motor response. A classic block-design was utilized as experimental procedure: during each run three conditions (perception of duration, perception of succession and color judgment) were presented twice in a counterbalanced order as blocks consisting of 6 similar tasks. The experimental instruction was presented prior to each block; the color and duration of stimuli presentation within blocks were pseudo-randomized. A fixation cross on the black background was presented for 30 s between blocks.

Stimuli were presented under computer control (Presentation, Neurobehavorial Systems, Albany, USA) through a commercially available video projector onto a translucent screen that subjects viewed inside the scanner via a head coil-compatible mirror system. Timing of the stimulus presentation was triggered by a pulse produced by the scanner at the start of each run. Choice-responses and reaction times for index and middle fingers of the right hand were recorded. No feedback on performance was given to the subject. Due to technical recording problems, 1 out of 216 values was missing in 2 subjects, 11 values were missing in 1 subject and 36 values in 2 further subjects.

Experiments were conducted in a 1.5-T whole body system (Magnetom VISION, Siemens, Erlangen, Germany), equipped with a standard head coil, at the University Hospital LMU Munich, Grosshadern. The subject’s head was securely but comfortably fastened by foam cushions in order to minimize head movements. For blood oxygen level dependent (BOLD) functional imaging, an T2*-weighted Echo-Planar Imaging (EPI) sequence was used with the following parameters: repetition time (TR) = 3680 ms, echo time (TE) = 60 ms, flip angle (FA) = 90°, number of slices = 28, slice thickness = 4 mm, inter-slice gap = 1 mm, interleaved acquisition, field of view (FOV) = 240 × 240 mm, matrix = 64 × 64, in-plane resolution = 3.75 × 3.75 mm. Functional images were acquired in axial orientation, covering the whole cerebrum. To provide an anatomical reference and rule out structural abnormalities, a sagittal high-resolution 3D T1-weighted Magnetization Prepared Rapid Gradient Echo (MPRAGE) sequence was performed: TR = 11.4 ms, TE = 4.4 ms, FA = 8°, number of slices = 144, FOV = 270 mm, matrix = 224 × 256, rect. FOV = 7/8, effective thickness = 1.25 mm). A run lasted for approximately 7 min, the functional measurement session lasted approximately 42 min in total.

All MRI data were archived in the institution’s picture archiving and communicating system (PACS) and analyzed off line on a personal computer. For preprocessing and statistical analysis BrainVoyager® QX 1.8.6 (BrainInnovations BV, Maastricht, The Netherlands) was used. The first five functional volumes of each run were discarded due to T1 saturation effects. The remain-
The experimental conditions were modeled with boxcar regressors convolved with the hemodynamic response function (two-gamma HRF) and the general linear model was applied to the time series, using standard BrainVoyager parameters. BOLD signal time course was normalized by the percent transformation. Data were then subject to a random-effects analysis of variance (ANOVA), with experimental conditions as within-subject factor and gender as between-subjects factor. Statistical maps for specific contrasts were calculated as post $t$-statistic on a voxel-wise basis. A cluster analysis was performed on the results of the contrasts using a $p$ value of 0.01, corrected for false discovery rate, and with a spatial extent of minimally 135 $\mu$m. Anatomical labeling of the identified clusters was done using the Talairach Daemon (www.talairach.org; [14]) and the Talairach and Tournoux atlas [36]. Analyses of behavioral responses were performed using the statistical software package SPSS (version 12.0). Since the data was normally distributed (Kolmogorov–Smirnov test), parametric tests were applied for testing differences (2-tailed $t$-test).

First we analyzed the behavioral performance in the different tasks. In the perception of duration task the mean percentage of correct responses was better for shorter (mean = $\pm S.E.: 96.74 \pm 1.45\%$) than longer (83.88 $\pm 4.24\%$) stimuli ($t(11) = 3.16; p < 0.01$). The reaction times did not differ significantly (783 $\pm 218$ ms for shorter stimuli, 807 $\pm 290$ ms for longer stimuli, $t(11) = -0.563; p < 0.585$).

For the perception of succession and perception of color control tasks the success rate was $97.82 \pm 6.28\%$ and $98.30 \pm 4.35\%$, correspondingly.

Then we assessed hemodynamic characteristics of the brain activity. A significant main effect of experimental conditions was observed, but no significant main effect of gender. To define localization of neuronal networks generally involved in subserving duration judgments irrespective of the time scale, data for shorter and longer stimuli were pooled together and the perception of duration task was compared to both control tasks (for figures and activation foci see Supplementary data): (1) In the comparison to the perception of succession, significant increase of the BOLD signal was observed in voxels matching cortical midline structures: bilateral activations in the medial prefrontal cortex (MPFC) and anterior cingulate cortex (ACC), left supplementary motor area (SMA); lateral cortical structures: left dorsolateral prefrontal cortex (DLPFC), bilateral superior frontal gyrus and anterior temporal cortex (superior and middle temporal gyrus); right thalamus; as well as the right cerebellum (anterior lobe). (2) In the comparison to the perception of color, cortical midline structures (bilateral MPFC, left ACC) as well as left anterior temporal cortex (superior and middle temporal gyrus) showed increased activation.

Finally, we compared perception of duration on different time scales by contrasting the corresponding conditions with shorter and longer stimuli. The results are shown in Fig. 2 and Table 1. Parameter estimates for the hemodynamic response function were significantly increased for judging the duration of shorter stimuli in cortical midline structures: right anterior and posterior cingulate gyrus (ACC and PCC), precuneus and cuneus; in lateral cortical structures: left DLPFC and anterior temporal cortex, right posterior inferior temporal area (posterior inferior temporal and lateral}
fusiform gyri); and in the left thalamus. No increase of the HRF parameter estimates for longer stimuli were observed.

The contrasts between the duration discrimination task and the two respective control tasks (temporal order, color discrimination) have shown common brain regions usually activated in time perception tasks: the supplementary motor area (SMA), anterior cingulate (ACC), the striatum, thalamus, dorsolateral prefrontal cortex as well as the insula [15,21]. These distributed areas of the brain could represent different processing stages of a complex timing system. However it is still an open question whether there is an actual clock-type mechanism in the brain and in which region of the brain it may be located [40].

The main goal in this study was concerned with assessing whether different areas of activation can be discerned depending on the duration of the stimuli (below 500 ms vs. above 500 ms). In contrast to our expectations, we found significantly stronger activity for the shorter duration condition only. As compared to the longer stimulus condition, right-hemispheric medial areas (anterior and posterior cingulate as well as precuneus and cuneus) and left-hemispheric lateral areas (dorsolateral prefrontal cortex, temporal cortex) of the brain show an increased BOLD signal. One could argue the rapid tempo of information processing could lead to the obtained results: although the shorter duration condition seems to be the easier task (fewer mistakes made in detecting the temporal difference) it may nevertheless recruited additional brain areas in order to cope with the time constraints (speed of stimulus presentation). This might have led to stronger activation in regions of the brain typically involved in time perception (anterior cingulate, dorsolateral prefrontal cortex) [15] but also in other regions of the brain that serve complementary functions such as monitoring sensory events and in generating responses (anterior and posterior cingulate cortices) [20,38].

On the other hand, it has been suggested that a time interval of about 500 ms could represent the lower border of the temporal window for conscious processing [17,24,33]. Accordingly, events below about 500 ms duration would rely more on lower-level neuro-cognitive mechanisms; and events above about 500 ms have greater reliance upon higher-level cognitive control. In a recent study on intuitive and explicit judgments, the midline structures (anterior and posterior cingulate cortices, pre-SMA) as well as the dorsolateral prefrontal cortex were active for intuitive processes not under explicit cognitive control. The authors stress the effortlessness of fulfilling task demands in the intuitive condition, which was defined as a fast and automatic process that did not require extended cognitive evaluation [11].

Moreover, a greater participation of the anterior and posterior cingulate cortex (belonging to the extended limbic system) indicates an involvement of the so-called default network [27] in the processing of shorter durations. The default network, e.g. predominantly the midline structures of the brain, is characteristic for the “resting” state and is usually deactivated during tasks under explicit cognitive control. One could argue that during the longer stimulus condition the midline structures (the cingulate cortex constituting the default network) are deactivated in relation to the shorter stimulus condition. The additional cognitive demand during the processing of the longer stimuli, as reflected by the decreased success rate, may lead to stronger relative deactivation of the default network.

Since this is the first fMRI study to employ stimuli with both these durations more studies with different paradigms (varying durations, task difficulty) and methods (e.g. using event-related designs) have to be conducted. Although arguments for timing mechanisms independent of stimulus modality exist [7], data on modality-specific time processing were also reported (e.g. [35]). Hence assessing temporal mechanism of duration processing in other sensory modalities is desirable.

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Appendix A. Supplementary data


References