Brain oxygenation patterns during the execution of tool use demonstration, tool use pantomime, and body-part-as-object tool use

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Abstract

Divergent findings exist whether left and right hemispheric pre- and postcentral cortices contribute to the production of tool use related hand movements. In order to clarify the neural substrates of tool use demonstrations with tool in hand, tool use pantomimes without tool in hand, and body-part-as-object presentations of tool use (BPO) in a naturalistic mode of execution, we applied functional Near InfraRed Spectroscopy (fNIRS) in twenty-three right-handed participants. Functional NIRS techniques allow for the investigation of brain oxygenation during the execution of complex hand movements with an unlimited movement range. Brain oxygenation patterns were retrieved from 16 channels of measurement above pre- and postcentral cortices of each hemisphere. The results showed that tool use demonstration with tool in hand leads to increased oxygenation as compared to tool use pantomimes in the left hemispheric somatosensory gyrus. Left hand executions of the demonstration of tool use, pantomime of tool use, and BPO of tool use led to increased oxygenation in the premotor and somatosensory cortex of the left hemisphere as compared to right hand executions of either condition. The results indicate that premotor and somatosensory cortices of the left hemisphere constitute relevant brain structures for tool related hand movement production when using the left hand, whereas the somatosensory cortex of the left hemisphere seems to provide specific mental representations when performing tool use demonstrations with the tool in hand.

Keywords:
Praxis, fNIRS, Tool Use Demonstration, Tool Use Pantomime, Tool Use BPO, Hemispheric Specialization

1. Introduction

Human activities of daily living are characterized by a variety of skillfully actions with tools and objects. Knowledge about underlying brain functions is mainly based on studies of apraxia, i.e., the inability to execute learned purposeful movements (Donkervoort et al., 2000; Gazzaniga et al., 1967; Goldenberg, 2003; Heilman et al., 1982; Heilman and Rothi, 2003; Kimura, 1977; Laimgruber et al., 2005; Lausberg et al., 2003; Liepmann, 1905, 1908; Liepmann and Maas, 1907; Osiurak, 2013; Poeck, 1983; Rothi and Heilman, 1997). The results from apraxia research suggest that the conceptualization and execution of tool related actions crucially depends on left hemispheric functions (De Renzi and Lucchelli, 1988; Lausberg et al., 2003; Lewis, 2006; Liepmann, 1905, 1908, 1920; Rothi and Heilman, 1997). However, only a few studies have, thus far, investigated the neural correlates of tool related hand movements during production tasks (Choi et al., 2001; Hermsdorfer et al., 2007; Imazu et al., 2007; Johnson-Frey et al., 2005; Moll et al., 2000; Ohgami et al., 2004). The present study therefore aims to investigate brain functions that underlie tool related performances during actual movement production tasks in a naturalistic mode of execution.

Due to the typical methodological constraints in neuroimaging studies (e.g., restricted movement range of the arms), tool use pantomime executions have often been used as a proxy for tool use actions (Lewis, 2006). By a pantomime execution, the gesturer pretends to perform a motor action, i.e., pretending to brush the teeth with an imaginary toothbrush. However, neuroimaging data (Hermsdorfer et al., 2007; Imazu et al., 2007) and kinematic analyses of different manual aperture formations during natural and pantomimic grasping (Goodale et al., 1994; Westwood et al., 2000) indicate that natural hand movements, i.e., tool use actions, would rely on different neural substrates than pantomimed tool use movements. In fact, it has been proposed that neural activity associated with tool use pantomimes may reflect some levels of abstraction that may or may not be present during actual tool use (Lausberg et al., 2003).

Several brain imaging studies addressed tool use related hand movement production in healthy participants (Choi et al., 2001; Hermsdorfer et al., 2007; Imazu et al., 2007; Johnson-Frey et al., 2005; Moll et al., 2000; Ohgami et al., 2004). However, only two studies compared tool use pantomimes with actual tool use with the tool in hand (Hermsdorfer et al., 2007; Imazu et al., 2007). The use of chopsticks, relative to a control task such as watching the right hand when it was placed into the starting position activated several regions within both hemispheres, i.e., prefrontal, temporal, parietal, and occipital cortices (Imazu et al., 2007). When tool use was compared to tool use pantomimes, greater levels of activation in the left hemispheric postcentraly gyrus, and in the right hemispheric inferior parietal lobule, and cerebellum were observed (Imazu et al., 2007). However, Imazu et al. (2007) investigated right hand performances only. Thus, left hemispheric activations due to tool use could not be differentiated from executions with the contralateral hand. In a study by Hermsdorfer et al. (2007), participants performed tool use demonstration and tool use pantomime tasks using either the left or the right hand. The authors found that tool use demonstrations with tool in hand compared to tool use pantomimes lead to activations in temporal, parietal, and frontal sites. Within prefrontal and premotor cortices, Hermsdorfer et al. (2007) observed a strong bias towards the right hemisphere during tool use executions as compared to tool use pantomimes. However, a lateralization to the right hemisphere during tool use actions contradicts previous reports of a left hemispheric lateralization for processing objects or tools (Grafton et al., 1997). Furthermore, Hermsdorfer et al. (2007) showed that tool use tasks additionally activated sensory and motor areas when compared to tool use pantomime executions. However, due to the nature of their design, the authors could not differentiate whether these sensory-motor activations were driven by cognitive differences between tool use demonstrations and tool use pantomimes or merely represented the additional sensory stimulation elicited by holding the tool in hand during tool use demonstrations. In order to unambiguously detect whether the production of tool use demonstrations and tool use pantomimes relies on distinct cognitive representations in sensory-motor areas, the present study will control for sensory differences between conditions by introducing an additional 'hold' condition (see study design).

Goldenberg et al. (2007) emphasized that tool use pantomimes rely in particular on precentral cortices when performances are conducted in a naturalistic way of execution. However, naturalistic performances are not the case in fMRI studies in which participants are lying in a scanner with a restricted way of execution and no visual feedback from someone's own manual actions. Functional Near InfraRed Spectroscopy (fNIRS) techniques allow for the investigation of brain oxygenation during the execution of complex hand movements (Chang et al., 2014; Holper et al., 2009; Mehagnoul-Schipper et al., 2002; Wriessnegger et al., 2008) allowing less restricted movement ranges (Wolf et al., 2007), the participant's direct view on the acting hand(s), and the maintenance of the normal upright body position (Yoshino et al., 2013). Thus, fNIRS is particularly suitable for the investigation of naturalistic and complex tool use related hand movement production and has been therefore chosen for the present study. Since tool use demonstrations showed increased activation patterns in sensory cortices when compared to tool use pantomimes (Hermsdorfer et al., 2007; Imazu et al., 2007), we hypothesize that when demonstrating tool use with tools in hand but not when performing tool use performances with imaginary tools, i.e., during tool use pantomimes will lead to increased brain oxygenation within the postcentral cortex of the left hemisphere.

Furthermore, tool use pantomimes can differ whether they are performed by holding an imaginary object in hand or whether the imaginary object is integrated into the own body, i.e., a body-part-as-object (BPO) demonstration. For example, tool use pantomimes of hammering would usually be performed by forming the hand around an imaginary hammer whereas when demonstrating the use of a scissor the gesturer would normally integrate the imaginary scissor into the own body by using the index and middle finger to demonstrate the tool. In fact, patients with apraxia showed BPO executions as an error pattern of tool use pantomimes more often than healthy adults (Haaland and Flaherty, 1984; Lausberg et al., 2003; Ochipa et al., 1997; Poole et al., 1997). As the right hemisphere showed to particularly subserve BPO but not tool use or tool use pantomimes (Lausberg et al., 2003; Ohgami et al., 2004), we secondly hypothesize that tool use demonstrations and tool use pantomimes but not BPO presentations of tool use lead to increased oxygenation within left hemispheric cortices.

Thus, by using fNIRS to investigate neuronal correlates of tool related hand movement production the present study addresses whether the production of tool use demonstration, tool use pantomime, and tool use BPO demonstrations relies on distinct cognitive representations in sensory-motor areas when performed in a more a naturalistic way of execution. We control for sensory differences between conditions by introducing an additional ‘hold’ condition. We hypothesize that the left hemisphere, in particular premotor and sensory cortices subserve tool related hand movement production overall, however, only tool use demonstrations will show increased activation patterns in sensory cortices when compared to tool use pantomimes.

2. Materials and methods

2.1 Participants

Twenty-three participants (10 females, 13 males; age 29 ± 6 years [mean, SD]) took part in the study after written informed consent was obtained. All participants had normal or corrected to normal vision and no known history of any neurological or psychiatric disorder. The local Ethics Committee of the German Sports University Cologne approved the study. Handedness was established with two questionnaires, the Edinburgh Inventory (Oldfield,

1971) and a questionnaire currently used at the Montreal Neurological Institute (Crovitz and Zener, 1962). All participants were right-handed.

2.2 Training of the participants

To familiarize participants with the experimental setting (see below), participants practiced the task before the actual scanning session. An assistant named each tool and demonstrated its specific use and each gestural type of the three experimental conditions. During the training, most errors occurred during the BPO and pantomime conditions. Immediately, the participant received feed-back about his/her error. Thereby, the display of errors during the actual experiment were substantially reduced. If however, during the experiment an error occurred, this was noted by the experimenter and the trial was excluded from further analysis. To control for re-exposure effects during the experiment (van Turennout et al., 2000), each tool was presented at least twice in the training session.

2.3 Experimental setting and design

During the experiment, the participant was sitting in a dimmed room in a comfortable chair with armrests. Sixteen common tools were presented to the participant to elicit tool use actions: scissors, hammer, screw driver, box cutter, pencil, rattle, key, pizza knife, sponge, fork, spoon, knife, syringe, rake, stamp, and rubber.

Each tool was presented once in each of the three experimental conditions "*tool use demonstration*", "*tool use pantomime*" and "*tool use BPO*". Each condition was executed with the right and with the left hand. In addition, an "*Execution*" and a "*Hold*" condition was implemented to account for the sensory stimulation during the tool use demonstration with tool in hand which is not present during BPO and pantomimes. By this, we could subtract out the sensory activation when holding an object in the hand ("*Execution*" condition minus "*Hold*" condition) in order to compare the three performance conditions. Together, this led to 12 different movement conditions. Figure 1 shows all twelve movement variations for one exemplary tool (here: the scissor tool). Each movement condition comprised 2 randomized blocks, each of which included 8 trials (8 tools), resulting in a total of 16 trials per condition. Thus, the 16 tools were presented once in each condition. The blocks and trials were presented in a pseudo-random order with the following constraints: (i) no repetition of a tool / trial within a block, (ii) no repetition of a trial sequence within the experiment, (iii) no immediate repetition of the same condition, and (iv) no repetition of a condition sequence. Moreover, block sequences between subjects were also randomized.

[INSERT Figure 1 NEAR HERE; Figure 1: Example of the twelve movement conditions for the scissors tool.]

The experiment was designed as follows (Figure 2): After the baseline (10 s), in which the subjects were asked to rest the hands on the pad and to fixate the screen, an instruction cue was given (10 s), e.g. “Pantomime execution right hand”. After instruction, the block consisting of eight trials (eight tools) each lasting 13 s followed. Each trial started with a “beep” sound, which indicated to the assistant to place the tool on the table (2 s). The following acoustical signal “go” indicated to the participant to start the performance. In the conditions "tool use demonstration", the subject grasped the tool and demonstrated the use of the tool with the tool in the left or right hand, either executing or holding the object. In the tool use pantomime and BPO conditions, the tools remained on the table and the subject pantomimed the use or executed the BPO condition with the left or right hand (without tool in hand). After five seconds, the signal “stop” indicated to the subject to stop the performance, and in the condition "tool use demonstration", to also put the tool back on the table. The trial ended with a “beep” sound that indicated to the assistant to remove the tool from the table. The entire duration of the experiment was 42 minutes. The stimulus presentation was triggered using the experimental control software Presentation (Neurobehavioral Systems Inc, Albany, CA). The participants were instructed to not move any other parts of their body other than their right or left hands. During the experiment, the investigator verified that the participants did not move other parts of the body. If a participant moved another part of the body during a trial, the trial was excluded from the evaluation.

[INSERT Figure 2 NEAR HERE; Figure 2: Illustration of the block design.]

2.4 fNIRS acquisition and analysis

Cerebral oxygenation changes were recorded using a near-infrared optical tomographic imaging device (DYNOT Imaging System, NIRx, Wavelengths 760nm, 830nm, Sampling rate 1.81 Hz). Methodology and underlying physiology are explained in detail elsewhere (Cope et al., 1988; Obrig and Villringer, 2003). A total of 20 optodes were placed in two 2x5 grids above each hemisphere resulting in 16 channels of measurement (Figure 3). Optodes were placed with an interoptode distance of 2.5 cm around C3 and C4 according to the 10-20-system (Jasper, 1958) symmetrically above each hemisphere. Coordinates of optode positions were collected for spatial registration of NIRS channels into the standard brain from the Montreal Neurological Institute (MNI space) according to Singh et al. (2005) using a 3-D digitizing system (Zebris 3D Measuring Systems, Zebris Medical GmbH). Coordinates of MNI and equivalent brodmann areas of each channel were exported using the NIRS-SPM toolbox (Jang et al., 2009; Ye et al., 2009). Optodes covered identical regions above both hemispheres including the Primary Motor Cortex, Premotor Cortex, Supplementary Motor Cortex, Primary Somatosensory Cortex, Subcentral Area, and the Supramarginal Gyrus (Figure 3). Optodes were mounted with a customized plastic hard shell system on the participant's head to gain placement stability and to avoid movement artifacts.

[INSERT Figure 3 NEAR HERE; Figure 3: Channel positions.]

Data were analyzed using the Matlab-based Homer2 software package from the Optics Division, Athinoula A. Martinos Center for Biomedical Imaging (Huppert et al., 2009). 16 channels (ch) were converted to hemoglobin concentration changes according to Cope et al. (Cope et al., 1988). As fNIRS data can be affected by movement artifacts, for each participant each individual channel was visually inspected and movement artifacts were corrected using the artifact correction algorithm by Scholkmann et al. (Scholkmann et al., 2010). The raw intensity data was normalized to provide a relative (percent) change by dividing by the mean of the data. High-frequency components, mainly caused by the heartbeat, were attenuated by a low-pass filter at 0.2 Hz. To correct drifts and slow fluctuations, an additional high-pass filter at 0.03 Hz was applied. To obtain an average response to stimulation the data were block averaged from 2 seconds before stimulus onset to 13 seconds after onset (Figure 4). Statistical analyses focused on the increases in oxygenated hemoglobin [HbO_2], as these appear to reflect task-related cortical activation more robustly than do decreases in deoxygenated hemoglobin [HHb], as evidenced by the stronger correlation between the former and the blood oxygenation level dependent signal measured by fMRI (Strangman et al., 2002) and by the results of animal studies (Hoshi et al., 2001). In order to compare conditions with or without tool in hand, we controlled for the influence of tactile stimulation, which is present only in the tool use demonstration condition. Thus, we subtracted the block averages during the *hold* performance from the *execution* performance within the same condition, e.g. *tool use demonstration execution right hand* minus *tool use demonstration hold right hand*. Statistical significance of the condition differences (i.e., execute – hold) of HbO_2 was then analyzed using a repeated measures ANOVA for each of the 16 channels. Each ANOVA used two within-subject factors; i.e., the factors *condition* (tool use demonstration, tool use pantomime and tool use BPO) and *hand* (right vs. left hand). Multiple post-hoc pairwise comparisons were corrected using Bonferroni corrections.

3. Results

The results section focuses on two channels for which significant effects of *condition* and/or *hand* were found. These are Channel 16 (MNI coordinates: -66 -9 32, left postcentral gyrus (percentage of overlap 0.96) and Channel 14 (MNI coordinates: -46 4 57, left premotor cortex (percentage of overlap: 0.97). A more detailed analysis using the AAL atlas (Tzourio-Mazoyer et al., 2002) as well as the SPM Anatomy toolbox (Eickhoff et al., 2005) suggests that the anatomical locations of these two channels are best described as left premotor cortex (Channel 14) and left primary somatosensory cortex (S1, Channel 16).

[INSERT Figure 4 NEAR HERE; Figure 4: Representative hemodynamic response from channel 16 over the left hemisphere of one participant during tool related performances with the right and left hand.]

A significant effect of *condition* was observed in Channel 16 (ΔHbO_2, $F(2, 44) = 3.3$, $p < 0.05$), indicating the type of hand movement production tasks significantly modulated blood oxygenation of the left primary somatosensory cortex. Post-hoc pairwise comparisons revealed greater changes of oxygenation for tool use demonstrations ($M= .116$, $SD = .04$) when compared to tool use pantomimes ($M = .031$; $SD = .033$; $p < 0.05$). The comparisons of tool use demonstrations vs. BPO ($M=.042$; $SD = .048$) and tool use pantomimes vs. tool use BPO were not significant.

[INSERT Figure 5 NEAR HERE; Figure 5: Relative changes of concentration of ΔHbO_2 in channel 16 covering the left hemispheric somatosensory cortex in the three conditions.]

A significant effect of *hand* was observed in Channels 14 and 16, which covered the left premotor (channel 14, ΔHbO_2, $F(1, 20) = 4.556$, $p < 0.05$;) and primary somatosensory cortices, respectively (channel 16, ΔHbO_2, $F(1, 22) = 5.627$, $p < 0.05$). This main effect of *hand* indicated that for both channels, the execution of *left hand* movements (Channel 14: $M = .082$, $SE = .038$; Channel 16: $M = .092$, $SD = .03$) lead to significantly greater changes of oxygenation than *right hand executions* (Channel 14: M = 0.14, SD = .04; Channel 16: M = .033, SD = .03). Thus, left premotor and primary somatosensory cortices responded stronger to ipsilateral (left-handed) than contralateral (right-handed) hand movements. No other effects were significant.

4. Discussion

The present study investigated the role of pre- and postcentral cortices of both hemispheres in tool use related hand movement production with the right and the left hands. Using functional NIRS cerebral activation patterns associated with the demonstration of tool use, pantomime of tool use, and body-part-as-object presentations of tool use were examined during the execution in a naturalistic manner. To compare tool use actions with and without tool in hand, we included a *hold* condition to subtract out the tactile stimulation and the grasping component during the conditions with tool in hand.

In line with our original hypotheses, our data showed distinct cerebral activation patterns for each condition, i.e., tool use demonstration, pantomime of tool use, and BPO presentations of tool use. In the channel covering the left postcentral gyrus (primary somatosensory cortex), tool use demonstrations showed significantly greater changes of oxygenation when compared to tool use pantomimes. This effect was independent of hand laterality. Previous studies that compared tool use with tool use pantomimes provided similar results showing that actual tool use displays distinct processing routes to those for pantomime executions (Hermsdorfer et al., 2007; Imazu et al., 2007). During tool use demonstration, Hermsdorfer et al. (2007) observed stronger activations in sensory and motor areas when compared to tool use pantomimes. Imazu et al. (2007) contrasted actual tool use executions with tool use pantomimes, and observed stronger levels of activation in the left postcentral gyrus. However, both studies did not control for sensory differences between tool use demonstration and tool use pantomime executions, which raises the possibility that some of these differences were due to the additional tactile input when actually holding the object or tool in hand. In contrast, our results show that when subtracting out tactile stimulation during tool use demonstrations by means of the *hold* condition of the same tool use performance, there is still a detectable change of brain oxygenation in the left postcentral gyrus. Thus, the left postcentral gyrus seems to contribute in particular to hand movements with tool in hand which cannot solely be explained by additional sensory stimulation. This suggests that the physical presence of an object triggers mental representations of tool use actions within sensory cortices of the left hemisphere. Randerath et al. (2011) showed improved hand movement performance in patients with left cerebro-vascular accidents when patients use a tool as compared to when the same patients perform tool use pantomimes. Tool use demonstration tasks involve the integration of an objects' intrinsic spatial properties and its related concepts of action. Thus, objects and tools might trigger a corresponding activation by the physical demands of the object that are not present during tool use pantomimes. It has been previously suggested that 'the human ability to identify different objects may depend on the activation of stored information about sensory- and motor-based attributes that define an object and distinguish it from other members of the same category' (Martin et al., 2000). Furthermore, postcentral areas seem to play a fundamental role in computing object properties (Culham et al., 2003). Producing tool use demonstration with tool in hand therefore might trigger an access of these representations within the postcentral gyrus of the left hemisphere. These representations might rely on previous sensory experiences with tools. Thus, we suggest that the greater brain oxygenation for tool use demonstrations relative to tool use pantomimes within the somatosensory cortex of the left hemisphere reflects the access of object-specific sensory representations.

Independently of the factor movement condition, two channels above premotor and somatosensory cortices of the left hemisphere showed significantly increased oxygenation changes during left hand executions as compared to right hand executions. Thus far, ipsilateral activation patterns have been observed in particularly during left hand movements (Chen et al., 1997; Cramer et al., 1999; Kawashima et al., 1997; Kim et al., 1993; Kobayashi et al., 2003; Li et al., 1996; Nirkko et al., 2001; van den Berg et al., 2011). Verstynen et al. (2005) showed strong ipsilateral activation patterns during sequence and chord movements, which was especially pronounced in the left hemisphere and left hand movements. The authors hypothesized that when a very complex movement pattern is performed and the contralateral hemisphere is not well trained in its' production, the ipsilateral hemisphere might shape the appropriate pattern through excitatory and inhibitory connections (Verstynen et al., 2005). The constant activation for all three movement conditions when using the left hand supports the important role of left hemisphere in tool related hand movement production (Geschwind, 1965a, b; Goldenberg et al., 2007; Haaland et al., 2000; Lewis, 2006). Ohgami et al. (2004) found similar activation patterns for pantomime and BPO demonstrations with the left hand. Heilman et al. (2000) demonstrated that limb-kinetic apraxia of the ipsilateral left hand is more likely to result from left hemisphere than right hemisphere dysfunction. Furthermore, damage to the left hemispheric premotor cortex has shown to evoke ideomotor limb apraxia more commonly than other areas (Haaland et al., 2000). In fact, patients often fail when they have to perform tool use pantomimes with the left hand (Buxbaum et al., 2000; Clark et al., 1994; Goldenberg and Hagmann, 1998; Goldenberg et al., 2004; Hermsdorfer et al., 2006; Laimgruber et al., 2005; Lausberg et al., 2003). Apraxia, however, was also shown for hand movements with tool in hand (De Renzi et al., 1982; Goldenberg and Hagmann, 1998; Goodale et al., 1991; Motomura and Yamadori, 1994) and BPO demonstrations (Manuel et al., 2013). The present findings indicate that the three variations of tool related hand movement production are subserved by similar left hemispheric premotor and somatosensory structures in particular when using the left hand.

Demonstration of tool use, pantomime of tool use, and body-part-as-object have in common that all three rely on knowledge about the correct use and how to execute a specific action with the tool. It has been suggested that the premotor cortex constitutes a repository of a vocabulary about motor actions (Binkofski et al., 2000; Rizzolatti and Luppino, 2001), in particular for the understanding of object semantics (Grafton et al., 1997). This cognitive feature might be relevant for all three movement conditions. Premotor activation showed to be left lateralized for the planning and the execution of left hand pantomimes (Bohlhalter et al., 2009; Wheaton et al., 2008). Left hemispheric somatosensory cortex was observed by Hermsdorfer et al. (2007) and Imazu et al. (2007) during the execution of tool use executions. However, the present data augments the view by an advanced study design that in particular tool use performances with the left hand rely on the somatosensory cortex of the left hemisphere. Thus, these brain activation patterns might reflect previous sensory experiences with tools. In fact, already Liepmann (1920) postulated that lesions to the sensory motor cortex may induce apraxia. It has been hypothesized that movement formulas or so-called “praxicons” are stored in the parietal cortex (Heilman and Rothi, 2003). Indeed, Moll et al. (2000) showed using functional imaging that regardless of which hand was used, the left hemisphere was more active than the right during tool use pantomime tasks when compared to a sequence of nonsymbolic complex movements of forearm, hand, and fingers. Activations clustered in the left intraparietal cortex and posterior dorsolateral frontal cortex (Moll et al., 2000). Moll et al. (2000) concluded that the left intraparietal cortex may store the representations of tool-use formulae, whereas the dorsolateral frontal cortex activation may reflect the switching between innervatory motor programs. Thus, we suggest that increased brain oxygenation within the premotor and somatosensory cortex of the left hemisphere during tool use related hand movements with the left hand might reflect the access of tool use specific movement representations that are necessary for tool related movement production with the left hand. The present findings show that this accounts solely for the left hemisphere when using the left hand.

Although the presented findings solely show minor differences between conditions, which is in line with previous findings (Hermsdorfer et al., 2007), they fit well with the suggestion that the 'left hemisphere must contain movement formulas that control purposeful skilled movements' (Liepmann and Maas, 1907). However, the data also call for further research regarding the involvement of other brain cortices on tool related hand movements. Several studies pointed out that the use of tools and objects depends on the integrity of further regions within the left hemisphere, i.e., the temporal, parietal, and frontal brain cortices (Choi et al., 2001; Frey, 2007; Goldenberg and Spatt, 2009; Haaland et al., 2000; Hermsdorfer et al., 2001; Hermsdorfer et al., 2007; Higuchi et al., 2007; Imazu et al., 2007; Inoue et al., 2001; Johnson-Frey et al., 2003; Johnson-Frey et al., 2005; Kroliczak and Frey, 2009; Lewis, 2006; Moll et al., 2000; Ohgami et al., 2004; Rumiati et al., 2004; Weiss-Blankenhorn and Fink, 2008). Goodale et al. (1994) argued that pantomimed grasping was driven by stored perceptual information about the object while real grasping of the object relies on visuo-motor online control system that directed actions in real time. It was proposed that pantomimed actions were mediated by the ventral visual stream, while real grasping depended on the dorsal stream (Milner and Goodale, 1995). A recent hypothesis maintains that the left parietal lobe provides information regarding external objects that is necessary for motor planning, but does not contain motor representation specifying particular grips or movements (Goldenberg and Spatt, 2009). Thus, the present findings provide details how tool related hand movements are subserved by pre- and postcentral cortices, but cannot answer the contribution of all relevant brain cortices that might conduce to tool use related performances. Upcoming research must therefore address the investigation of further brain areas and their interaction with each other during tool related hand movement production tasks.

In summary, the present study reports, for the first time, changes of brain oxygenation during a naturalistic paradigm of tool related hand movement production. The left hemispheric somatosensory cortex showed to provide specific information when performing tool use demonstrations with tool in hand as compared to tool use pantomimes. Thus, the present study provides evidence that tool use demonstration and tool use pantomime rely on different neural substrates. However, ipsilateral left hand performances of any type showed to activate left hemispheric premotor and somatosensory cortices indicating that the left hemisphere promotes tool related movement production in particular when using the left hand. We therefore conclude that the premotor and the somatosensory cortex of the left hemisphere constitute relevant brain structures for tool related hand movement production overall, whereas the somatosensory cortex of the left hemisphere provides specific mental representations when performing tool use demonstrations with the tool in hand.

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6. References

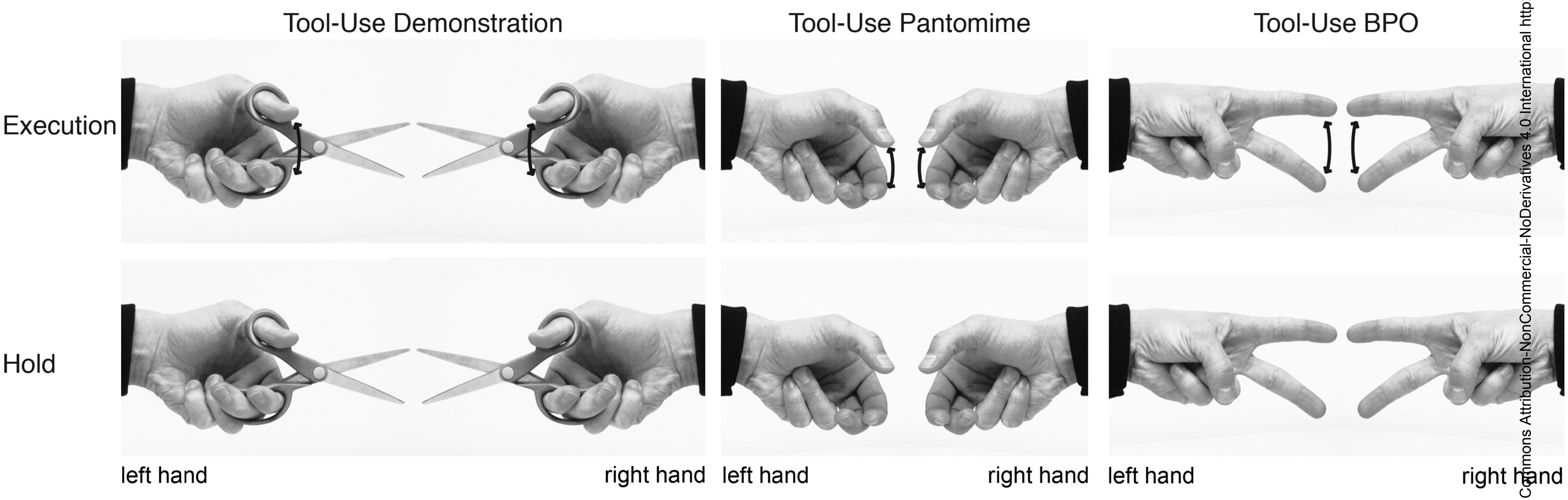
Binkofski, F., Amunts, K., Stephan, K.M., Posse, S., Schormann, T., Freund, H.J., Zilles, K., Seitz, R.J., 2000. Broca's region subserves imagery of motion: a combined cytoarchitectonic and fMRI study. Hum Brain Mapp 11, 273-285.
Bohlhalter, S., Hattori, N., Wheaton, L., Fridman, E., Shamim, E.A., Garraux, G., Hallett, M., 2009. Gesture subtype-dependent left lateralization of praxis planning: an event-related fMRI study. Cereb Cortex 19, 1256-1262.
Buxbaum, L., Giovannetti, T., Libon, D., 2000. The role of the dynamic body schema in praxis: evidence from primary progressive apraxia. Brain Cogn 44, 166-191.
Chang, P.-H., Lee, S.-H., Koo, K.-M., Lee, S.-H., Jin, S.-H., Yeo, S., Seo, J., Jang, S., 2014. The cortical activation pattern by a rehabilitation robotic hand : A functional NIRS study. Frontiers in Human Neuroscience 8.
Chen, R., Gerloff, C., Hallett, M., Cohen, L.G., 1997. Involvement of the ipsilateral motor cortex in finger movements of different complexities. Ann Neurol 41, 247-254.
Choi, S.H., Na, D.L., Kang, E., Lee, K.M., Lee, S.W., Na, D.G., 2001. Functional magnetic resonance imaging during pantomiming tool-use gestures. Exp Brain Res 139, 311-317.
Clark, M.A., Merians, A.S., Kothari, A., Poizner, H., Macauley, B., Gonzalez Rothi, L.J., Heilman, K.M., 1994. Spatial planning deficits in limb apraxia. Brain 117 (Pt 5), 1093-1106.
Cope, M., Delpy, D.T., Reynolds, E.O., Wray, S., Wyatt, J., van der Zee, P., 1988. Methods of quantitating cerebral near infrared spectroscopy data. Adv Exp Med Biol 222, 183-189.
Cramer, S.C., Finklestein, S.P., Schaechter, J.D., Bush, G., Rosen, B.R., 1999. Activation of distinct motor cortex regions during ipsilateral and contralateral finger movements. J Neurophysiol 81, 383-387.
Crovitz, H.F., Zener, K., 1962. A group-test for assessing hand- and eye-dominance. Am J Psychol 75, 271-276.
Culham, J.C., Danckert, S.L., DeSouza, J.F., Gati, J.S., Menon, R.S., Goodale, M.A., 2003. Visually guided grasping produces fMRI activation in dorsal but not ventral stream brain areas. Exp Brain Res 153, 180-189.
De Renzi, E., Faglioni, P., Sorgato, P., 1982. Modality-specific and supramodal mechanisms of apraxia. Brain 105, 301-312.
De Renzi, E., Lucchelli, F., 1988. Ideational apraxia. Brain 111 (Pt 5), 1173-1185.
Donkervoort, M., Dekker, J., van den Ende, E., Stehmann-Saris, J.C., Deelman, B.G., 2000. Prevalence of apraxia among patients with a first left hemisphere stroke in rehabilitation centres and nursing homes. Clin Rehabil 14, 130-136.
Eickhoff, S.B., Stephan, K.E., Mohlberg, H., Grefkes, C., Fink, G.R., Amunts, K., Zilles, K., 2005. A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. Neuroimage 25, 1325-1335.
Frey, S.H., 2007. What puts the how in where? Tool use and the divided visual streams hypothesis. Cortex 43, 368-375.
Gazzaniga, M.S., Bogen, J.E., Sperry, R.W., 1967. Dyspraxia following division of the cerebral commissures. Arch Neurol 16, 606-612.
Geschwind, N., 1965a. Disconnexion syndromes in animals and man. I. Brain 88, 237-294.
Geschwind, N., 1965b. Disconnexion syndromes in animals and man. II. Brain 88, 585-644.
Goldenberg, G., 2003. Apraxia and beyond: life and work of Hugo Liepmann. Cortex 39, 509-524.
Goldenberg, G., Hagmann, S., 1998. Tool use and mechanical problem solving in apraxia. Neuropsychologia 36, 581-589.

Goldenberg, G., Hentze, S., Hermsdorfer, J., 2004. The effect of tactile feedback on pantomime of tool use in apraxia. Neurology 63, 1863-1867.
Goldenberg, G., Hermsdorfer, J., Glindemann, R., Rorden, C., Karnath, H.O., 2007. Pantomime of tool use depends on integrity of left inferior frontal cortex. Cereb Cortex 17, 2769-2776.
Goldenberg, G., Spatt, J., 2009. The neural basis of tool use. Brain 132, 1645-1655.
Goodale, M.A., Jakobson, L.S., Keillor, J.M., 1994. Differences in the visual control of pantomimed and natural grasping movements. Neuropsychologia 32, 1159-1178.
Goodale, M.A., Milner, A.D., Jakobson, L.S., Carey, D.P., 1991. A neurological dissociation between perceiving objects and grasping them. Nature 349, 154-156.
Grafton, S.T., Fadiga, L., Arbib, M.A., Rizzolatti, G., 1997. Premotor cortex activation during observation and naming of familiar tools. Neuroimage 6, 231-236.
Haaland, K.Y., Flaherty, D., 1984. The different types of limb apraxia errors made by patients with left vs. right hemisphere damage. Brain Cogn 3, 370-384.
Haaland, K.Y., Harrington, D.L., Knight, R.T., 2000. Neural representations of skilled movement. Brain 123 (Pt 11), 2306-2313.
Heilman, K.M., Meador, K.J., Loring, D.W., 2000. Hemispheric asymmetries of limb-kinetic apraxia: a loss of deftness. Neurology 55, 523-526.
Heilman, K.M., Rothi, L.J., Valenstein, E., 1982. Two forms of ideomotor apraxia. Neurology 32, 342-346.
Heilman, K.M., Rothi, L.J.G., 2003. Apraxia, in: Heilman, K.M., Valenstein, E. (Eds.), Clinical neuropsychology, 4th ed. Oxford University Press, Oxford, pp. 215-235.
Hermsdorfer, J., Goldenberg, G., Wachsmuth, C., Conrad, B., Ceballos-Baumann, A.O., Bartenstein, P., Schwaiger, M., Boecker, H., 2001. Cortical correlates of gesture processing: clues to the cerebral mechanisms underlying apraxia during the imitation of meaningless gestures. Neuroimage 14, 149-161.
Hermsdorfer, J., Hentze, S., Goldenberg, G., 2006. Spatial and kinematic features of apraxic movement depend on the mode of execution. Neuropsychologia 44, 1642-1652.
Hermsdorfer, J., Terlinden, G., Muhlau, M., Goldenberg, G., Wohlschlager, A.M., 2007. Neural representations of pantomimed and actual tool use: evidence from an event-related fMRI study. Neuroimage 36 Suppl 2, T109-118.
Higuchi, S., Imamizu, H., Kawato, M., 2007. Cerebellar activity evoked by common tool-use execution and imagery tasks: an fMRI study. Cortex 43, 350-358.
Holper, L., Biallas, M., Wolf, M., 2009. Task complexity relates to activation of cortical motor areas during uni- and bimanual performance: a functional NIRS study. Neuroimage 46, 1105-1113.
Hoshi, Y., Kobayashi, N., Tamura, M., 2001. Interpretation of near-infrared spectroscopy signals: a study with a newly developed perfused rat brain model. J Appl Physiol (1985) 90, 1657-1662.
Huppert, T.J., Diamond, S.G., Franceschini, M.A., Boas, D.A., 2009. HomER: a review of time-series analysis methods for near-infrared spectroscopy of the brain. Appl Opt 48, D280-298.
Imazu, S., Sugio, T., Tanaka, S., Inui, T., 2007. Differences between actual and imagined usage of chopsticks: an fMRI study. Cortex 43, 301-307.
Inoue, K., Kawashima, R., Sugiura, M., Ogawa, A., Schormann, T., Zilles, K., Fukuda, H., 2001. Activation in the ipsilateral posterior parietal cortex during tool use: a PET study. Neuroimage 14, 1469-1475.
Jang, K.E., Tak, S., Jung, J., Jang, J., Jeong, Y., Ye, J.C., 2009. Wavelet minimum description length detrending for near-infrared spectroscopy. J Biomed Opt 14, 034004.

Jasper, H.H., 1958. Report to the committee on methods and clinical examination in electroencephalography. Electroencephalography and Clinical Neurophysiology 10, 371-375.
Johnson-Frey, S.H., Maloof, F.R., Newman-Norlund, R., Farrer, C., Inati, S., Grafton, S.T., 2003. Actions or hand-object interactions? Human inferior frontal cortex and action observation. Neuron 39, 1053-1058.
Johnson-Frey, S.H., Newman-Norlund, R., Grafton, S.T., 2005. A distributed left hemisphere network active during planning of everyday tool use skills. Cereb Cortex 15, 681-695.
Kawashima, R., Inoue, K., Sato, K., Fukuda, H., 1997. Functional asymmetry of cortical motor control in left-handed subjects. Neuroreport 8, 1729-1732.
Kim, S.G., Ashe, J., Hendrich, K., Ellermann, J.M., Merkle, H., Ugurbil, K., Georgopoulos, A.P., 1993. Functional magnetic resonance imaging of motor cortex: hemispheric asymmetry and handedness. Science 261, 615-617.
Kimura, D., 1977. Acquisition of a motor skill after left-hemisphere damage. Brain 100, 527-542.
Kobayashi, M., Hutchinson, S., Schlaug, G., Pascual-Leone, A., 2003. Ipsilateral motor cortex activation on functional magnetic resonance imaging during unilateral hand movements is related to interhemispheric interactions. Neuroimage 20, 2259-2270.
Kroliczak, G., Frey, S.H., 2009. A common network in the left cerebral hemisphere represents planning of tool use pantomimes and familiar intransitive gestures at the hand-independent level. Cereb Cortex 19, 2396-2410.
Laimgruber, K., Goldenberg, G., Hermsdorfer, J., 2005. Manual and hemispheric asymmetries in the execution of actual and pantomimed prehension. Neuropsychologia 43, 682-692.
Lausberg, H., Cruz, R.F., Kita, S., Zaidel, E., Ptito, A., 2003. Pantomime to visual presentation of objects: left hand dyspraxia in patients with complete callosotomy. Brain 126, 343-360.
Lewis, J.W., 2006. Cortical networks related to human use of tools. Neuroscientist 12, 211-231.
Li, A., Yetkin, F.Z., Cox, R., Haughton, V.M., 1996. Ipsilateral hemisphere activation during motor and sensory tasks. AJNR Am J Neuroradiol 17, 651-655.
Liepmann, H., 1905. Die linke Hemisphäre und das Handeln. Münchner Medizinische Wochenzeitschrift 49, 2322-2326.
Liepmann, H., 1908. Drei Aufsätze aus dem Apraxiegebiet. Karger, Berlin.
Liepmann, H., 1920. Apraxia. Ergebn. Ges. Med. 1, 516-543.
Liepmann, H., Maas, O., 1907. Fall von linksseitiger Agraphie und Apraxie bei rechtsseitiger Laehmung. . Journal für Neurologie and Psychologie, 214–227.
Manuel, A.L., Radman, N., Mesot, D., Chouiter, L., Clarke, S., Annoni, J.M., Spierer, L., 2013. Inter- and Intrahemispheric Dissociations in Ideomotor Apraxia: A Large-Scale Lesion-Symptom Mapping Study in Subacute Brain-Damaged Patients. Cereb Cortex.
Martin, A., Ungerleider, L.G., Haxby, J.V., 2000. Category-specificity and the brain: The sensory-motor model of semantic representations of objects., in: Gazzaniga, M.S. (Ed.), The Cognitive Neurosciences MIT Press, Cambridge, MA., pp. 1023–1036. .
Mehagnoul-Schipper, D.J., van der Kallen, B.F., Colier, W.N., van der Sluijs, M.C., van Erning, L.J., Thijssen, H.O., Oeseburg, B., Hoefnagels, W.H., Jansen, R.W., 2002. Simultaneous measurements of cerebral oxygenation changes during brain activation by near-infrared spectroscopy and functional magnetic resonance imaging in healthy young and elderly subjects. Hum Brain Mapp 16, 14-23.

Moll, J., de Oliveira-Souza, R., Passman, L.J., Cunha, F.C., Souza-Lima, F., Andreiuolo, P.A., 2000. Functional MRI correlates of real and imagined tool-use pantomimes. Neurology 54, 1331-1336.
Motomura, N., Yamadori, A., 1994. A case of ideational apraxia with impairment of object use and preservation of object pantomime. Cortex 30, 167-170.
Nirkko, A.C., Ozdoba, C., Redmond, S.M., Burki, M., Schroth, G., Hess, C.W., Wiesendanger, M., 2001. Different ipsilateral representations for distal and proximal movements in the sensorimotor cortex: activation and deactivation patterns. Neuroimage 13, 825-835.
Obrig, H., Villringer, A., 2003. Beyond the visible--imaging the human brain with light. J Cereb Blood Flow Metab 23, 1-18.
Ochipa, C., Rapcsak, S.Z., Maher, L.M., Rothi, L.J., Bowers, D., Heilman, K.M., 1997. Selective deficit of praxis imagery in ideomotor apraxia. Neurology 49, 474-480.
Ohgami, Y., Matsuo, K., Uchida, N., Nakai, T., 2004. An fMRI study of tool-use gestures: body part as object and pantomime. Neuroreport 15, 1903-1906.
Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9, 97-113.
Osiurak, F., 2013. Apraxia of tool use is not a matter of affordances. Front Hum Neurosci 7, 890.
Poeck, K., 1983. Ideational apraxia. J Neurol 230, 1-5.
Poole, J.L., Gallagher, J., Janosky, J., Qualls, C., 1997. The mechanisms for adult-onset apraxia and developmental dyspraxia: an examination and comparison of error patterns. Am J Occup Ther 51, 339-346.
Randerath, J., Goldenberg, G., Spijkers, W., Li, Y., Hermsdorfer, J., 2011. From pantomime to actual use: how affordances can facilitate actual tool-use. Neuropsychologia 49, 2410-2416.
Rizzolatti, G., Luppino, G., 2001. The cortical motor system. Neuron 31, 889-901.
Rothi, L.J.G., Heilman, K.M., 1997. Apraxia: the neuropsychology of action. Psychology Press, Hove, UK.
Rumiati, R.I., Weiss, P.H., Shallice, T., Ottoboni, G., Noth, J., Zilles, K., Fink, G.R., 2004. Neural basis of pantomiming the use of visually presented objects. Neuroimage 21, 1224-1231.
Scholkmann, F., Spichtig, S., Muehlemann, T., Wolf, M., 2010. How to detect and reduce movement artifacts in near-infrared imaging using moving standard deviation and spline interpolation. Physiol Meas 31, 649-662.
Strangman, G., Culver, J.P., Thompson, J.H., Boas, D.A., 2002. A quantitative comparison of simultaneous BOLD fMRI and NIRS recordings during functional brain activation. Neuroimage 17, 719-731.
Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage 15, 273-289.
van den Berg, F.E., Swinnen, S.P., Wenderoth, N., 2011. Excitability of the motor cortex ipsilateral to the moving body side depends on spatio-temporal task complexity and hemispheric specialization. PLoS One 6, e17742.
van Turennout, M., Ellmore, T., Martin, A., 2000. Long-lasting cortical plasticity in the object naming system. Nat Neurosci 3, 1329-1334.
Verstynen, T., Diedrichsen, J., Albert, N., Aparicio, P., Ivry, R.B., 2005. Ipsilateral motor cortex activity during unimanual hand movements relates to task complexity. J Neurophysiol 93, 1209-1222.

Weiss-Blankenhorn, P.H., Fink, G.R., 2008. [Functional imaging insights into the pathophysiology of apraxia]. Fortschr Neurol Psychiatr 76, 402-412.
Westwood, D.A., Chapman, C.D., Roy, E.A., 2000. Pantomimed actions may be controlled by the ventral visual stream. Exp Brain Res 130, 545-548.
Wheaton, L.A., Bohlhalter, S., Nolte, G., Shibasaki, H., Hattori, N., Fridman, E., Vorbach, S., Grafman, J., Hallett, M., 2008. Cortico-cortical networks in patients with ideomotor apraxia as revealed by EEG coherence analysis. Neurosci Lett 433, 87-92.
Wolf, M., Ferrari, M., Quaresima, V., 2007. Progress of near-infrared spectroscopy and topography for brain and muscle clinical applications. J Biomed Opt 12, 062104.
Wriessnegger, S.C., Kurzmann, J., Neuper, C., 2008. Spatio-temporal differences in brain oxygenation between movement execution and imagery: a multichannel near-infrared spectroscopy study. Int J Psychophysiol 67, 54-63.
Ye, J.C., Tak, S., Jang, K.E., Jung, J., Jang, J., 2009. NIRS-SPM: statistical parametric mapping for near-infrared spectroscopy. Neuroimage 44, 428-447.
Yoshino, K., Oka, N., Yamamoto, K., Takahashi, H., Kato, T., 2013. Functional brain imaging using near-infrared spectroscopy during actual driving on an expressway. Front Hum Neurosci 7, 882.


Tool-Use Demonstration
Tool-Use Pantomime
Tool-Use BPO
Execution
Hold
left hand
right hand
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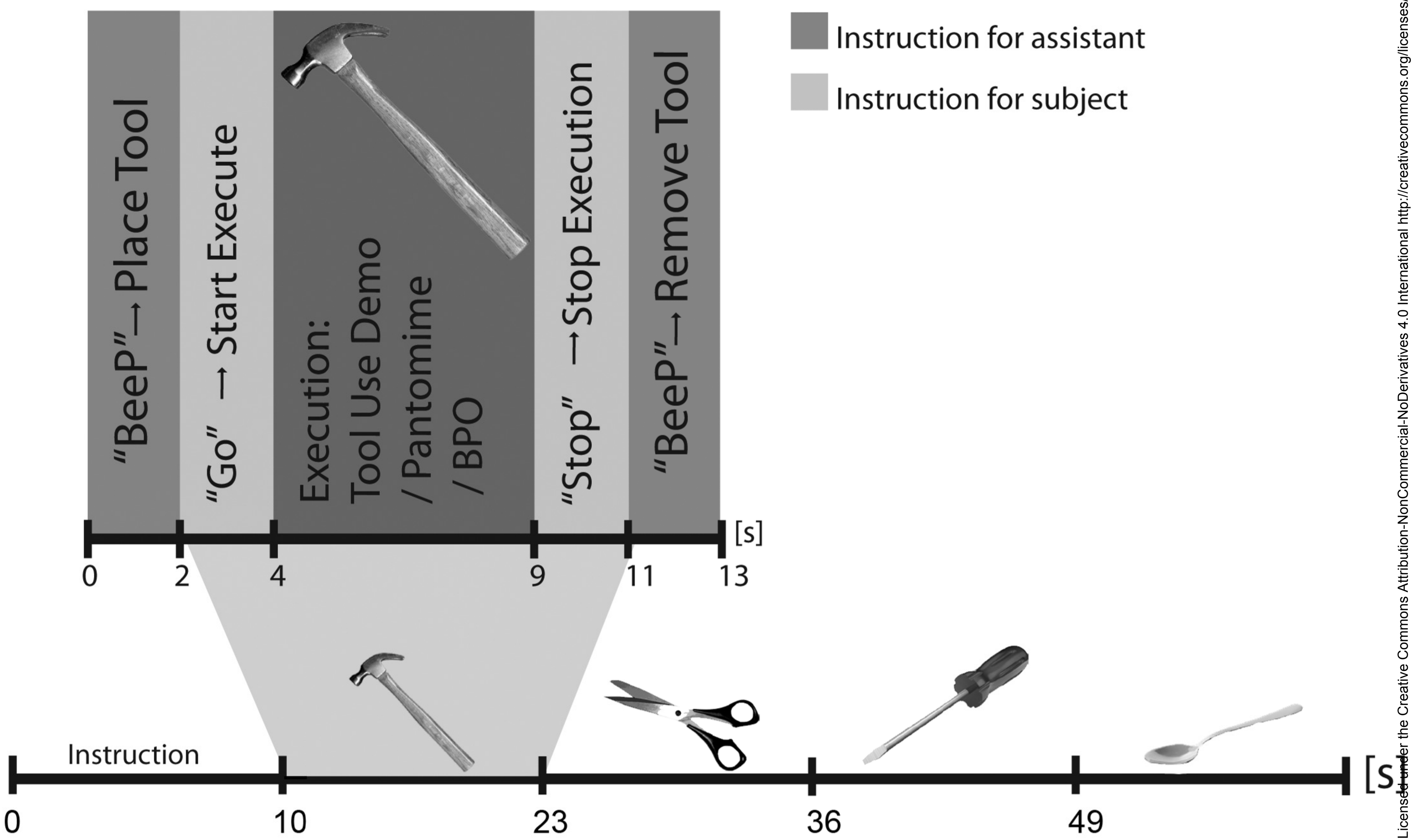
right hand


"BeeP"→ Place Tool
"Go" → Start Execute
Execution:
Tool Use Demo
/ Pantomime
/ BPO
"Stop" →Stop Execution
"BeeP"→ Remove Tool
Instruction for assistant
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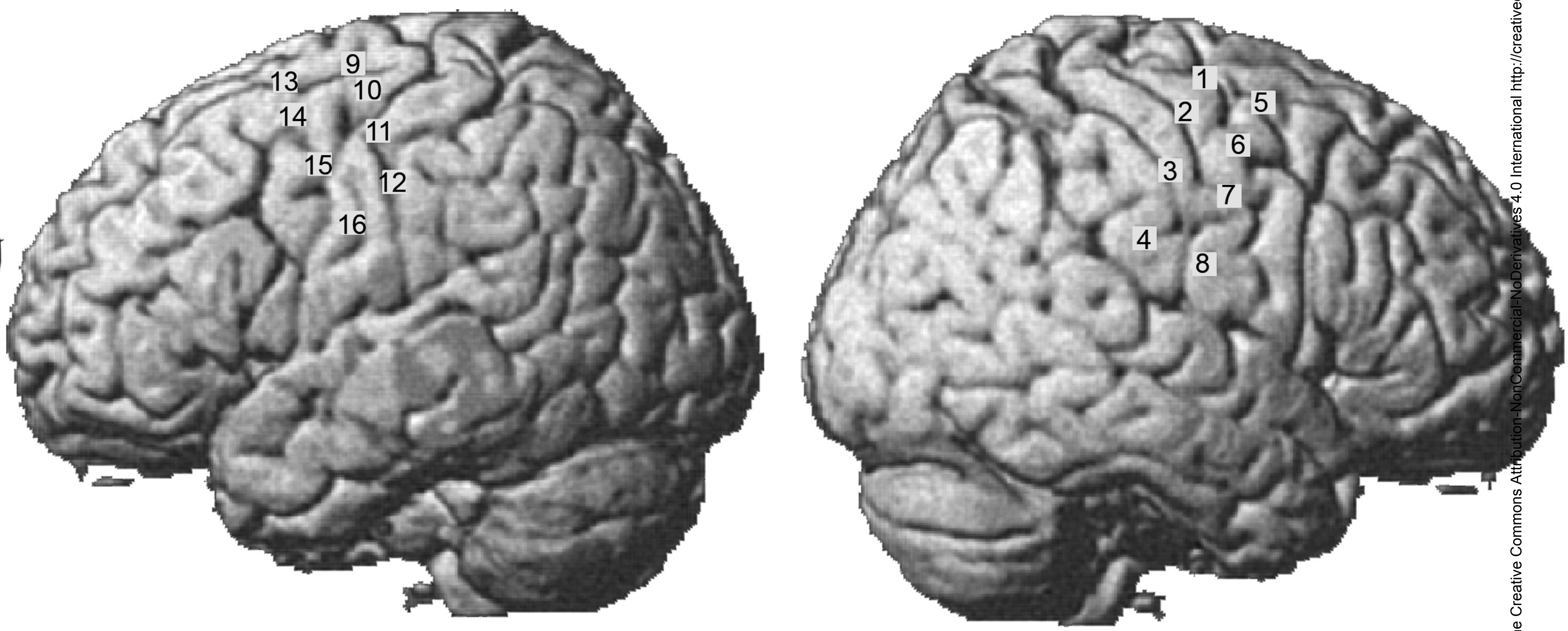
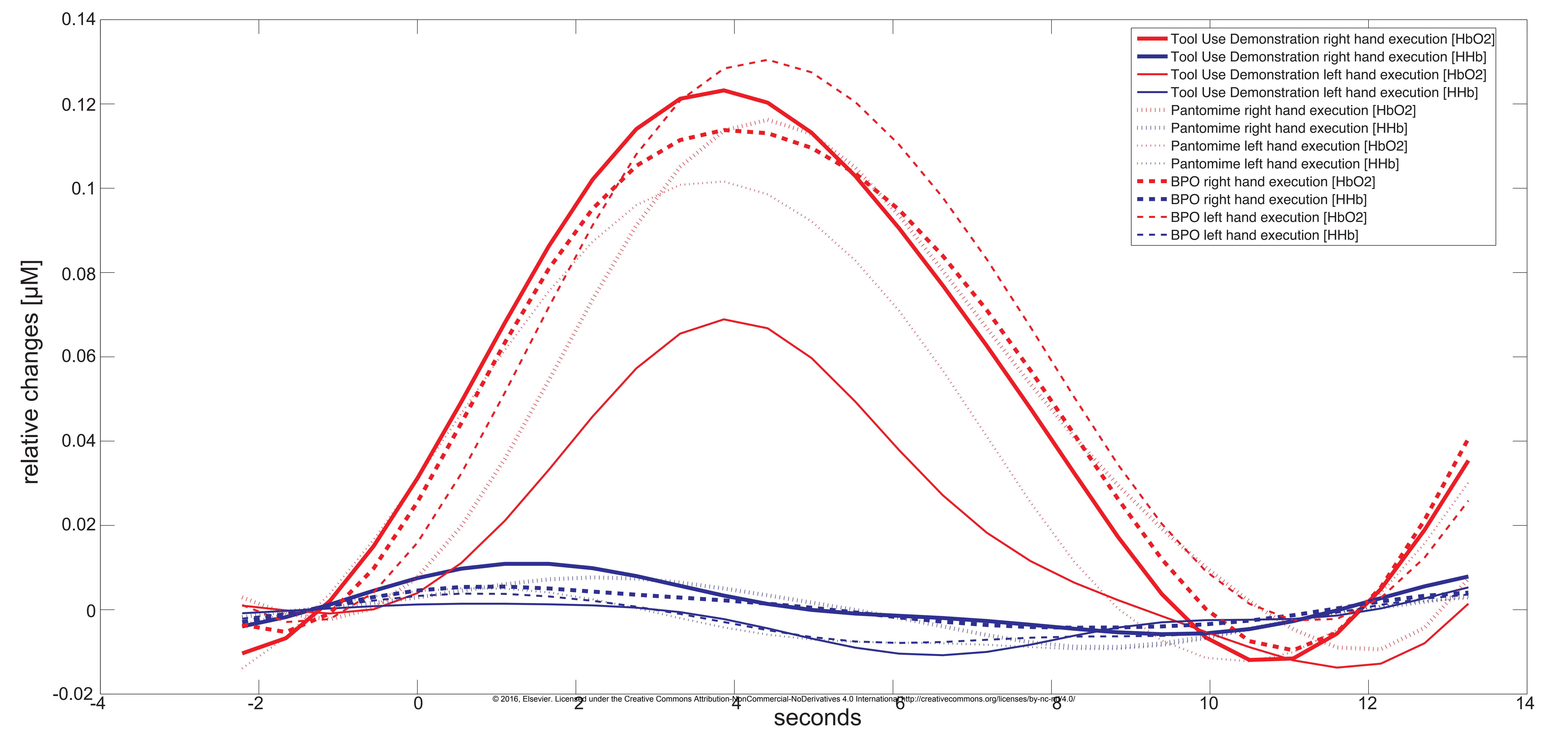


left hemisphere   right hemisphere


relative changes [µM]
seconds
Tool Use Demonstration right hand execution [HbO2]
Tool Use Demonstration right hand execution [HHb]
Tool Use Demonstration left hand execution [HbO2]
Tool Use Demonstration left hand execution [HHb]
Pantomime right hand execution [HbO2]
Pantomime right hand execution [HHb]
Pantomime left hand execution [HbO2]
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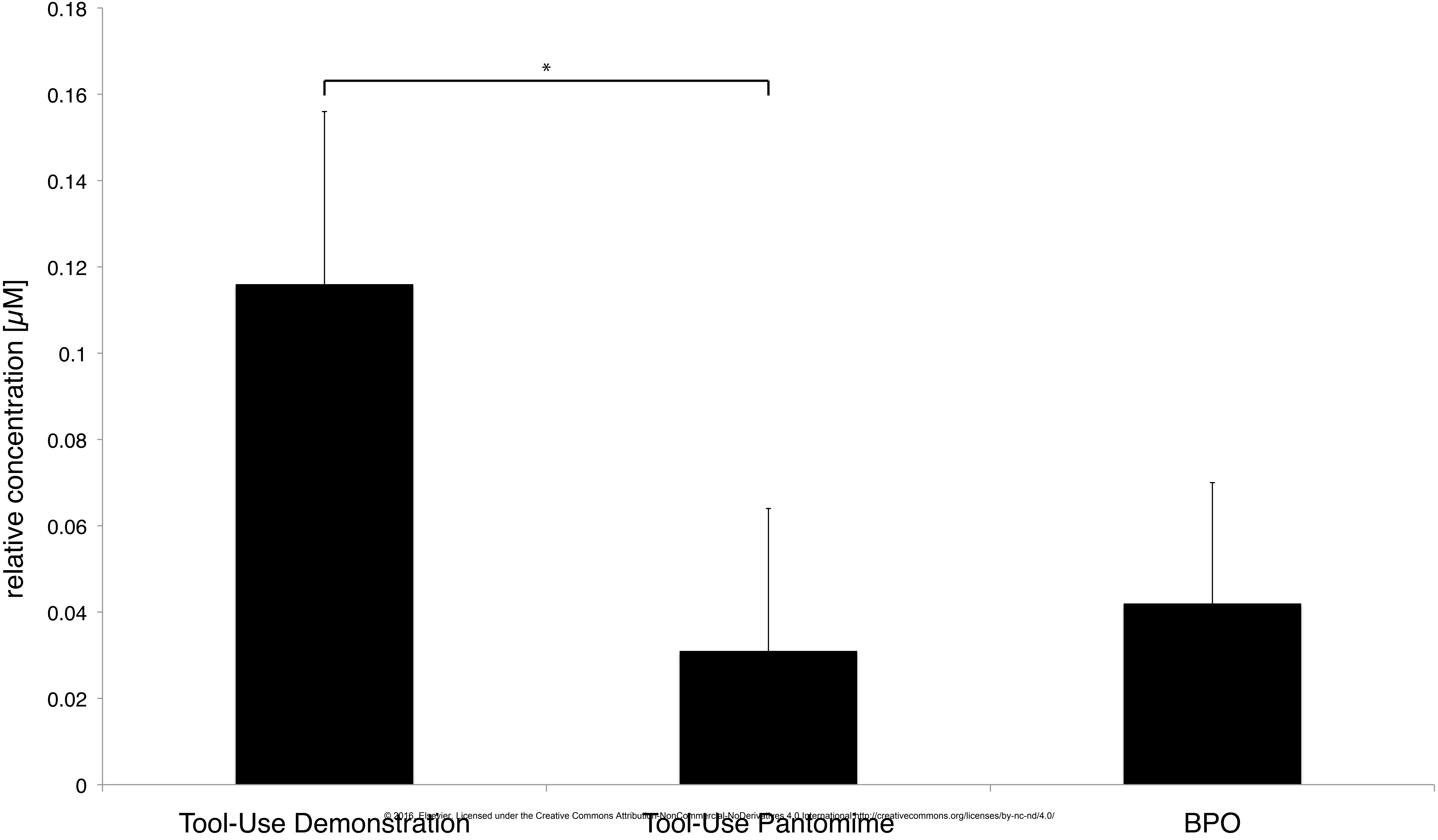
0.18
0.16
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relative concentration [μM]
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Tool-Use Demonstration
Tool-Use Pantomime
BPO