Action Imagery Combined With Action Observation Activates More Corticomotor Regions Than Action Observation Alone

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Background and Purpose: Both action observation (AO) and action imagery have been proposed as therapeutic options for stroke rehabilitation. Currently, it is not clear to what extent their underlying neuronal mechanisms differ from each other and whether one of these therapeutic options might be preferable for this purpose.

Methods: Twenty-six neurologically healthy subjects were investigated using functional magnetic resonance imaging during AO alone and during AO with additional action imagery of video clips showing simple, object-related hand actions.

Results: The blood oxygenation level dependent (BOLD) signal induced by AO increased in a bihemispheric, symmetrical network of areas including the occipital, superior, and inferior parietal cortex, dorsal and ventral premotor regions, and the prefrontal cortex. The addition of imagery to the AO elicited additional activation in both cerebellar hemispheres, caudate nucleus, ventral and dorsal premotor cortex, inferior parietal cortex, and the supplementary motor area.

Discussion and Conclusion: These data reveal more profound activations of the motor system during AO in conjunction with imagery than during AO alone. These results may have important implications for neurorehabilitation and motor learning.

Key words: *fMRI, mental training, mirror neuron system, neurorehabilitation, video training*

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INTRODUCTION

Mental practice is a widely accepted training method to improve performance in sports.[1,2] Recently, mental training has also become increasingly popular in stroke rehabilitation as suggested in several studies.[3-7] Remarkably, however, there are more reviews recommending the use of mental imagery in clinical practice than there are original works demonstrating its effectiveness.[8-14] A recent randomized controlled study did not confirm the effectiveness of mental training in stroke rehabilitation.[14] Mental practice covers different training methods such as observation, imitation, and imagery. The mechanisms underlying observational learning have been subject to intensive research,[15] and the neuroscientific community is also greatly interested in the neural mechanisms of imagery and their similarity to action execution.[16] Importantly, the distinction between these different mental processes in clinical settings is not precisely delineated, and potential advantages or disadvantages for their use in stroke rehabilitation have not yet been evaluated.

It is important to note that not all people are able to rehearse motor tasks continuously.[17] Consequently, persons such as athletes or musicians who are experienced in imagery may benefit more from imagery than inexperienced people.[2,18] This difference may be due, in part, to the greater activity in the mirror neuron system (MNS; neurons in the premotor and parietal cortices that are active when a person performs a behavior and also when the person observes others performing the same behavior) in experts than that in novices.[19] In general, the quality of mental imagery is difficult to evaluate and standardize. Questionnaires are available to attempt to quantify the vividness as well as the imaginative capacities of the volunteers.[20-22]

Studies of mental imagery in experimental settings point out the importance of the task *instruction.*[23,24] There are at least 2 different types of motor imagery: kinesthetic imagery from the first-person perspective and visual imagery from the third-person perspective.[25] Available evidence supposes that kinesthetic imagery facilitates the primary motor cortex (M1) to a greater extent than visual imagery does, and kinesthetic imagery is also reported to activate predominantly the inferior parietal and the motor association cortex.[26] During visual imagery, higher levels of activation are observed in the superior

parietal cortex and the occipital cortex.[27] Nevertheless, the impact of these findings on stroke rehabilitation is currently not clear.

Adding to the possible limitation in applying mental training in persons with stroke is the assumption that the movement to be imagined should be familiar to the person concerned,[28] making the use of mental training in clinical settings problematic. A less-complicated procedure, which might be easier to apply in clinical practice, is a form of training in which persons with stroke observe a video demonstrating a desired motor behavior.[29] In this case, action observation (AO) is suggested to promote motor memory formation.[30,31] However, it remains questionable whether AO alone can induce the cortical changes associated with motor learning. In elderly subjects, AO alone did not change the direction of thumb movements evoked by transcranial magnetic stimulation to a targeted cortical region; only the combination of AO and motor training led to changes in the direction of thumb movement.[32] Evidence indicates that activity within the MNS is not age dependent, and for this reason it has been suggested that training procedures relying on the MNS might be particularly suitable for elderly people, such as the majority of people with stroke.[33] The advantage is that AO activates or simulates the internal representation of motor behaviors, thereby facilitating the retrieval of motor engrams that might be suitable for improving on specific impairments.[34,35]

An example of simple clinical application of the concept of AO consists of asking persons with stroke to observe a video of an activity and to repeatedly execute the motor task for about 5 minutes while the video is continuously running.[29] As noted previously, the *instruction* for AO is of paramount importance for this approach to be successful, as there appear to be important differences in cortical activation depending on whether the *instruction* asks for passive observation or observation with the intention of imitating.[36] As another example, cortical processing is different when professional dancers are instructed to simply look at dancers during the repetition of movement figures or when they are asked to observe in order to decide whether the observed figures have been performed correctly.[37]

While various studies in subjects without disability have focused either on AO[4,5] or on action imagery (AI), there are only a few studies that have used a within-subjects design to assess differences in the mental processes associated with AO or AI during hand movements.[16,37-40] The aim of this study was to compare the neural correlates of AO with and without AI in subjects without disability in order to identify similarities and differences in activated functional networks that might have a potential for guiding neurorehabilitation. We predicted that AO alone would trigger low-level motor plans and facilitate the retrieval of motor engrams, while the addition of AI to AO would trigger an internal simulation of higher-level conceptual representations.[41,42] Therefore, we expected the activation associated with AO combined with AI to be higher than that associated with AO alone due to higher processing demands. Alternatively, different neural substrates may exist for AO and AI, in which case existing concepts would need to be rethought.

METHODS

Subjects

Twenty-six neurologically healthy volunteers (13 women; mean age: 44.6 years, SD: range 19.7, 19.7-79.1) were included in this study. All participants were right-hand dominant according to a modified Oldfield Handedness Questionnaire.[43] Participants were acquainted with the procedures of the study, and written informed consent was obtained. The study was approved by the local ethical committee of the University of Konstanz.

Experimental Conditions

The subjects were placed in the supine position in a magnetic resonance imaging scanner (Gyroscan NT; Philips Medical Systems, Hamburg, Germany) with a 1.5-T magnetic field. They viewed images projected via a video beamer onto a screen via a mirror mounted onto the head coil in the scanner. The experimental conditions were designed to match as closely as possible the video therapy sessions currently used with patients during rehabilitation. The subjects were presented with blocks of stationary pictures of goal transitive motor acts (behaviors wherein the hand interacts with an object, eg, a hand grasping a bottle), pictures of the same motor acts without objects (eg, hand grasping without the bottle), videos depicting transitive motor acts (eg, a hand grasping a bottle and pouring its content into a glass, lighting match sticks with a precision grip of the right hand, holding a spoon and stirring, using a brush, opening a bottle, and throwing a ball in the air and catching it), or videos showing movements of nonliving moving objects. Each of the blocks had a duration of 16 seconds, and the blocks were presented in alternation with periods of fixation in which only a fixation cross was presented on the screen (cross-fixation condition).

For the stationary pictures and for the videos showing moving objects and transitive motor acts, the subjects were instructed to simply observe the pictures or videos (AO condition). In addition, the pictures and videos of transitive motor acts were also presented with a prior instruction to both observe and imagine performing the displayed movement from a first-person perspective (AO + AI condition). This resulted in an experiment with a total of 6 different conditions as well as a fixation condition, all of equal duration (Figure 1). Before each block, apart from fixation, a short instruction for the task was presented for 3 seconds. The experimental design was intended to compare conditions with the same sensory content but with different instructions. The subjects saw the stimuli projected via a video beamer onto a screen via a mirror mounted onto the head coil in the scanner.

Data collection runs of functional magnetic resonance imaging data were acquired from each subject, with each run consisting of 18 pseudorandomly presented blocks of 16 seconds. Each run contained 1 to 2 catch trials in which the movement in the images stopped for a very short time while the magnetic resonance imaging data were acquired. The order of the runs was counterbalanced across subjects, and each of the experimental conditions was presented 3 times per run. Before undergoing the scanning, the subjects were familiarized with

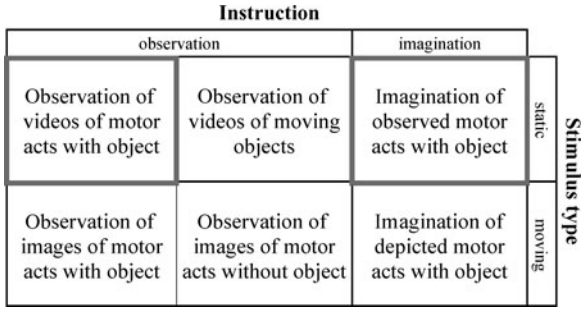

Figure 1. Study design illustrating 6 different pseudorandomly presented conditions in blocks of 16-s duration interleaved with cross-fixation condition of the same duration.

the stimulus and the instructions and performed a test trial with imagery of the movements from the first-person perspective. During the practice session, the subjects were instructed not to perform any movements while observing or imagining the actions. During the experiment, the subjects' hands and legs were closely monitored (via visual observation) to ensure that no movements were performed. After each run, the subjects were asked to report the vividness of the imagery, whether they had any problems with switching during the task, and whether they had noticed any unexpected events (catch trials). All subjects detected the catch trials and correctly reported their number.

Data Acquisition

Blood oxygenation level dependent contrast was measured via magnetic resonance imaging with a T2*-sensitive gradient-echo echo-planar imaging (32 axial slices of 3.1-mm thickness with 1-mm gap, field of view of 230 mm × 230 mm, 80 × 80 matrix, repetition time (TR) 2392 ms, echo time (TE) 40 ms, and flip angle 90°). A total of 280 volumes were acquired per session, wherein the first 4 volumes were discarded to allow for T1 equilibration effects resulting in a total of 276 volumes per session.

A fluid attenuated inversion recovery sequence (21 axial slices of 5-mm thickness with 1-mm gap, field of view of 250 mm × 250 mm, 512 × 512 matrix, TR 11000 ms, TE 140 ms, and flip angle 90°) and a T1-weighted volume (21 axial slices of 5-mm thickness with 1-mm gap, field of view of 250 mm × 250 mm, 512 × 512 matrix, TR 134.46 ms, TE 2.1 ms, and flip angle 80°) were acquired for each subject after the functional imaging experiment.

Data Analysis

The functional images were converted into the ANALYZE format and analyzed using the SPM5 software package (Wellcome Department of Imaging Neuroscience, London, the United Kingdom) implemented in Matlab 6.5 software (MathWorks, Natick, Massachusetts). All 1654 (6 × 276) volumes for each subject were realigned to the first image, normalized to the standard echo planar imaging template of the reference brain provided by the Montreal Neurological Institute, and smoothed using a Gaussian kernel of 8-mm full width at half maximum. The time series in each voxel was high-pass filtered at 1/128 Hz to remove low-frequency confounds. For each subject, condition-related activity was modeled with the stimulus onsets, convolved with a canonical hemodynamic response function within the context of the generalized linear model, as implemented in SPM5.[44] Confounding factors from head movement (realignment parameters) were also included in the model. After model estimation, main effects for each condition were calculated.

For assessing the task-specific activations, a second-level analysis was performed. Main effects and between-condition differences were determined in a mixed analysis of variance (flexible factorial design analysis in SPM5). The following contrasts were computed: Videos of motor acts with the instruction to observe versus fixation (AO contrast). A second contrast was videos of motor acts with the instruction to perform imagery versus fixation (AI contrast). Finally, videos of motor acts with the instruction to observe were contrasted versus the same videos but with the instruction to perform imagery (AO < AO + AI and AO > AO + AI). The significant threshold was $P < 0.001$ uncorrected with a minimum cluster size of 10 voxels. The values reported in Table 1 are corrected for cluster size and small volume (10-mm sphere).

RESULTS

Main Effects of Conditions

There were consistent and strong activations in visual areas of the occipital lobe (Brodmunn area [BA] 17-19), the inferior and superior parietal cortex, the dorsal premotor cortex, and the ventral premotor cortex (PMv), as well as in the ventrolateral prefrontal cortex (BA 47) during AO. There was no obvious or strong laterality, and activation on the cortical surface appeared to be symmetrical in both hemispheres. The fusiform gyrus as well as the extrastriate body area and visual area for perception of motion (V5/MT) were activated during both the conditions. Additional AI produced a similar pattern

Table 1. Significant Activation for the Contrast AI Compared to AO[a]

Region	Hemisphere	*P* Corrected	MNI Coordinates		
			x	*y*	*z*
Cerebellum	L	0.0001	−39	−57	−28
Cerebellum	R	0.0001	33	−57	−32
SMA		0.002	0	−3	64
Inferior frontal gyrus (pars orbitalis)	L	0.009	−39	27	−4
Inferior frontal gyrus (pars triangularis)	R	0.0001	42	18	4
Basal ganglia	L	0.006	−18	12	16
Basal ganglia	R	0.002	15	27	−4
Supra marginal gyrus	L	0.001	−54	−33	32
Middle frontal gyrus	R	0.002	30	48	12
Middle frontal gyrus	L	0.004	−33	51	32
Inferior frontal gyrus (pars opercularis)	L	0.001	−48	9	12

Abbreviations: AI, action imagery; AO, action observation; MNI, Montreal Neurological Institute; SMA, supplementary motor area.
[a]Coordinates represent the peak of activation.

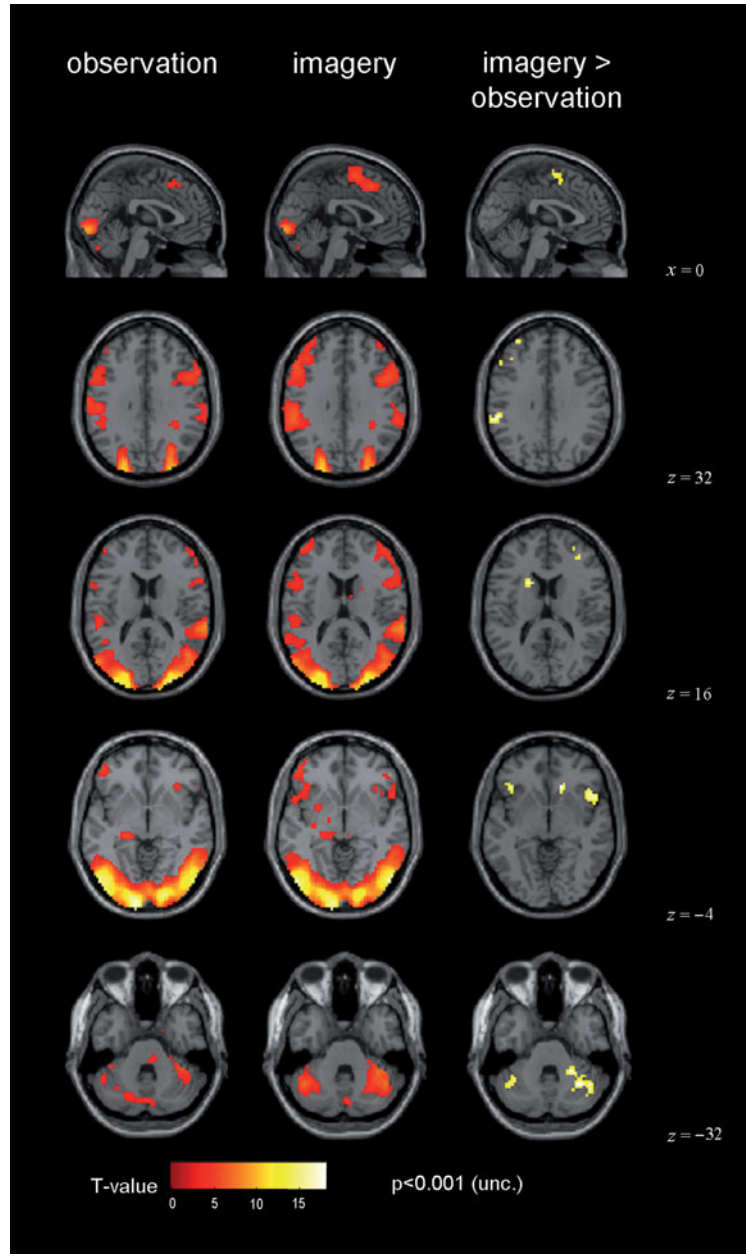

Figure 2. Activation during action observation (left column), action observation and action imagery (middle column), and contrast between action imagery and action observation (right column). Action observation was associated with additional activation in cerebellar hemispheres, basal ganglia, prefrontal cortex, ventral premotor cortex, inferior parietal cortex, and supplementary motor area.

of activation. Figure 2 displays the main effects of AO with and without AI and the differential contrast between both.

Differential Contrast Between Motor Imagery and Motor Observation

Compared with AO, additional imagery revealed additional activations in both cerebellar hemispheres, pars opercularis and pars triangularis of the inferior frontal gyrus, the inferior parietal cortex (IPL), the caudate nucleus, and the supplementary motor area (SMA) (Figure 2; Table 1). No significant activations were observed for the contrast AO versus AO + AI.

DISCUSSION

Both AO and AI are processed in a broad network of occipital, temporoparietal, and premotor-prefrontal areas including the MNS of the IPL and the PMv of both hemispheres. The fact that most functional imaging studies have revealed

more than the "classical mirror neurons" identified in primates during AO leads to the concept of an "expanded MNS" in humans.[45-47] The M1 was not activated in our study. There are controversial results concerning M1 activity during AI depending on the sensitivity of the method. Most researchers agree that M1 activity is typically smaller during AI than during motor execution (compare reviews[16] and Table 1 in Munzert et al[48]). In contrast to studies that investigated movement paradigms, activation during AI was less lateralized, which is in line with previous findings.[48,49] Imagery produced additional activation of the cerebellar hemispheres, pars opercularis and pars triangularis of the inferior frontal gyrus, IPL, caudate nucleus, and the SMA. The additional activation during the AO + AI condition may be due to a top-down generation of movement pattern. This interpretation suggests a common network for AI and AO. Activation increases with the addition of AI and, consequently, is presumed to reflect higher cognitive demand. Alternatively, AO may engage only a part of this network, and the activation during AI occurs in an additional network.

Areas of Activation

The following discussion will not repeat the extensive literature on motor imagery in general (the reader is referred to prior literature for comparison [16,48,50]). Instead, we briefly describe the neuroanatomical basis of AI compared with that of AO focusing on cerebellar hemispheres, the SMA, caudate nucleus, the IPL, and the PMv and discuss the potential as well as limitations of functional imaging studies with respect to physical therapy and neurorehabilitation strategies.

Cerebellar Hemispheres

A bilateral activation of the cerebellar hemispheres during AI has been previously described.[49,51] The motor cortex receives inputs from the cerebellum through the cerebellothalamocortical loop. This enables cerebellar signals to modulate the corticomotor activity, particularly during coordinated movements, sensorimotor integration, movement correction, and feedback processing. Cerebellar activity during motor execution presumably reflects somatosensory feedback of the movement to allow precise, coordinated spatial and temporal control of the movement. Activity in the anterior cerebellum is correlated with the accuracy of imagined pointing movements.[52] Importantly, in our study, the cerebellar activity was higher when the subjects were instructed to imagine the observed movement. Given the role of the cerebellum in motor planning and learning, as well as in the correction of inaccurate movements,[53] it can be speculated that AI might be favorable for improving motor control in persons with ataxia or with deficits or inaccuracies of motor execution. The implication for rehabilitation treatment is that additional imagery, in conjunction with movement training, could serve as a primer for the motor learning process during physical therapy.

Supplementary Motor Area

The SMA is known to be of major importance for AI[54] and is intimately related to simulation and preparation for movement. The SMA can be subdivided into 2 parts: an anterior part (pre-SMA) that is involved in planning and a posterior part (SMA proper) that is involved in movement execution.[55-57] The pre-SMA is probably responsible for internal generation of motor programs[58] or working memory maintenance of planned movements.[59,60] An alternative role of the medial frontal gyrus has been suggested for the inhibition of motor execution to prevent imitative responses.[61,62] Zentgraf et al[63] compared the observations of dancers with either the intent to imagine and to imitate whole-body gymnastic movements or the intent to evaluate these movements as a judge. Observation with the goal to later imagine the observed gymnastic sequence involves the transformation of the perceived movement in the third-person perspective into a representation containing own body coordinates (first-person perspective). Such observation with the goal to later imagine is closer to movement execution than AO with the intent to evaluate the movement accuracy, which is rather a cognitive task and contains less-integrative transformation processes.[63] A stronger activation of the SMA proper was found during observation with the intent to imagine. In the pre-SMA, the activity was higher during observation with the intent to evaluate. This finding is well in line with our results: AI (Figure 1, right column) preferentially engaged the SMA proper, which is closely related to movement execution. The implication for physical therapy practice would be that AO combined with AI might promote movement execution more than AO alone by triggering additional processing in movement planning and control structures, such as the SMA proper and the pre-SMA.

Caudate Nucleus

The present data support the idea of involvement of the caudate nucleus in motor imagery. This has been described before and explained by the assumption that the caudate nucleus is engaged in a cognitive loop, in contrast to the putamen, which is engaged in sensorimotor networks.[64] As a major player in the extrapyramidal system that promotes motor learning, it is conceivable that neural activity in the caudate nucleus could be associated with higher precision and smoothness of executed movements.

Ventral Premotor Cortex

The inferior frontal cortex is part of the MNS. It is supposed to contain the "vocabulary of motor acts."[65] A segregation of the pars triangularis and pars opercularis was described for action imitation and observation.[50,66] There is some disagreement concerning precise extent of activation during imitation, execution, and observation, which may depend on issues such as whether movements are goal- and object-oriented or whether they are intransitive (ie, wherein the hand does not interact with an object).[67,68] Our results complement the extensive literature on the PMv and the MNS. However, it is notable that we found additional/higher activation in the PMv during AO + AI than during AO alone.

Inferior Parietal Cortex

The superior parietal cortex and the IPL have been extensively described in a meta-analysis concerning execution, simulation, and observation.[16] The IPL has been engaged during fine finger movements as complex manipulation of objects,[69] grasping movements,[70] and immediate copying of

finger movements.[71] Both structures, the PMv and the IPL, are the core structures of the MNS and by definition involved in AO. Both of them, however, are engaged to a higher extent with the addition of AI.

Clinical Implications

What can we learn about treatment of patients with stroke from a functional imaging study in neurologically healthy control subjects? Physical therapy neurorehabilitation interventions have been largely developed by trial and error, observations, and experience working with individual patients. Although attempts have been made to identify underlying physiological and scientific concepts for different physical therapy methods, most of these concepts have been incomplete or inconclusive. Functional imaging provides a new opportunity to study brain function, the effect of lesions, and spontaneous reorganization and its acceleration and improvement through therapies. Functional imaging can be a tool for understanding the involvement of different cerebral structures in different motor or cognitive tasks. The ultimate goal might be to improve rehabilitative strategies for individual patients and to offer an individually tailored and optimal rehabilitation.

The present data corroborate and aptly illustrate the extensive activation of the motor association cortices, corticobasal ganglia, and cerebello-thalamo-cortical loops during AO alone and AO combined with AI. The study demonstrates an alternative access to the motor system, which might be of particular value in cases wherein the pyramidal tract is impaired or the person has no access to the motor output. Action imagery with AO offers a pathway to the higher-order motor areas "rostral" to the pyramidal tract. The activation maps also make it clear that the system is bilaterally organized, which opens the opportunity to stimulate motor areas in the presence of a unilateral damage. While the executive motor system—mainly relying on the pyramidal tract and M1—is very much lateralized and sensitive to hemispheric lesions, AI with AO may be more resistant to unilateral lesions and still be functioning.

Despite the possible benefits, there may be limitations in using AI. In a recent study, for example, Liepert et al[72] confirmed that AI is impaired in persons with stroke who have sensory deficit. In another study, they investigated the effect of AI in persons with stroke who have a sensory deficit. Preliminary results may indicate that people with sensory impairment did not improve on their AI as defined by a chronometric test in contrast with people without sensory deficit (J. Liepert, personal oral communication, August 24, 2012). Future development will show whether AI with AO has true promise for improving outcomes of neurorehabilitation.

CONCLUSION

Our study confirmed activation of a large bilateral, symmetrical network of the motor association cortices during AO alone and AO with AI. This offers an alternative or additional access to the motor system, especially to the higher-order motor areas. The bilateral organization suggests that the network might be effective even after unilateral damage, such as that occurring with stroke. Several studies suggest effectiveness of AI in stroke rehabilitation, while there are fewer randomized controlled studies to indicate effectiveness of AO. A comparison of effect sizes of AI and AO after stroke has not yet been performed. Whether AI or AO is more advantageous in stroke rehabilitation is also not known. It appears that the challenge for the coming years is to identify the right patients at the right time in the right context to integrate AO and AI into existing procedures in stroke rehabilitation.

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