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A dual-task paradigm for behavioral and neurobiological studies in nonhuman primates

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HIGHLIGHTS

- We introduce a novel dual-task paradigm for neurobiological experiments in monkeys.
- The present paradigm is analogous to that used in human studies.
- Monkeys exhibited dual-task interference effect on this paradigm.
- We describe the method to efficiently teach monkeys to learn the dual task.

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ABSTRACT

Background: The dual-task paradigm is a procedure in which subjects are asked to perform two behavioral tasks concurrently, each of which involves a distinct goal with a unique stimulus–response association. Due to the heavy demand on subject's cognitive abilities, human studies using this paradigm have provided detailed insights regarding how the components of cognitive systems are functionally organized and implemented. Although dual-task paradigms are widely used in human studies, they are seldom used in nonhuman animal studies.
New method: We propose a novel dual-task paradigm for monkeys that requires the simultaneous performance of two cognitively demanding component tasks, each of which uses an independent effector for behavioral responses (hand and eyes). We provide a detailed description of an optimal training protocol for this paradigm, which has been lacking in the existing literature.
Results: An analysis of behavioral performance showed that the proposed dual-task paradigm (1) was quickly learned by monkeys (less than 40 sessions) with step-by-step training protocols, (2) produced specific behavioral effects, known as dual-task interference in human studies, and (3) achieved rigid and independent control of the effectors for behavioral responses throughout the trial.
Comparison with existing methods: The proposed dual-task paradigm has a scalable task structure, in that each of the two component tasks can be easily replaced by other tasks, while preserving the overall structure of the paradigm.
Conclusions: This paradigm should be useful for investigating executive control that underlies dual-task performance at both the behavioral and neuronal levels.

1. Introduction

1.1. Dual-task paradigm in human and nonhuman animal studies

The study of human dual-task performance has received considerable interest in the fields of experimental psychology and cognitive neuroscience because it provides detailed insights into the functional architecture of human cognitive systems. The general principle of the dual-task paradigm is to present, either simultaneously or in rapid succession, two component tasks that

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involve their own distinct goals and stimulus–response associations. In its basic procedure, a trial of one component task intervenes in a trial of the other component task, such that, for example, a series of noun/verb judgments is inserted during the memory maintenance period of a verbal short-term memory (STM) task with word memoranda (Wager et al., 2014). Alternatively, the two component tasks can be initiated simultaneously by the presentation of two cue stimuli after an inter-trial interval (e.g., Kuo et al., 2008), or can be performed along an independent, continuous stream of cue presentation (e.g., D'Esposito et al., 1995). Despite the remarkable flexibility of cognitive abilities, human subjects often exhibit decreased performance in the component tasks under dual-task conditions (Pashler, 1994). Often, the insertion of a more cognitively demanding secondary task produces stronger disruption in the performance of the primary task. This effect, known as dual-task interference, has been extensively studied to examine the functional organization of hierarchical, multi-component working memory systems (Baddeley and Hitch, 1974; Just and Carpenter, 1992), and to make inferences about the dynamics of cognitive resource allocation (Kahneman, 1973; Wickens, 1980). Theories based on human dual-task performance emphasize the importance of executive control which coordinates the information-processing streams of multiple tasks (Meyer and Kieras, 1997; Sigman and Dehaene, 2006).

The dual-task paradigm has rarely been adopted in studies of nonhuman animals. In the existing literature, dual-task experiments in monkeys have typically used a delayed matching-to-sample (DMTS) paradigm as a primary task, with a variety of tasks inserted during the retention period of the DMTS task as a secondary task. These experiments have primarily relied on manual responses using response buttons attached to a screen (Moise, 1970), joystick (Washburn and Astur, 1998; Smith et al., 2013), or touch screen (Basile and Hampton, 2013). Most of these studies did not focus on the psychological mechanisms that are specifically related to the information processing required for dual-task performance. Rather, these studies used dual-task paradigms as a tool for evaluating the functional similarity of STM between humans and nonhuman animals, such as the involvement of active rehearsal in STM.

In human studies, neuroscientific approaches involving functional magnetic resonance imaging (fMRI) have identified the key brain regions, including the lateral and medial prefrontal cortices, in the information-processing required for dual-task performance (D'Esposito et al., 1995; Klingberg, 1998). However, the precise functional role and mechanisms of these prefrontal regions remain largely unknown due to the lack of appropriate dual-task paradigms that are directly amenable to various invasive neurobiological techniques, including single-neuron recording, histology and lesion/inactivation approaches. Thus, the development of appropriate tasks for studies in nonhuman primates would be highly desirable for better understanding the mechanisms underlying dual-task processing.

1.2. Oculomotor- and hand-movement-based dual-task paradigm

While the dual-task paradigms in previous behavioral studies are suitable for assessing the behavioral performance of monkeys, they are not directly applicable to neurobiological investigations, primarily due to the lack of adequate control of the effectors for behavioral responses throughout the task phases. For example, while pressing a button (Moise, 1970) or touching a screen (Basile and Hampton, 2013) are intuitive behaviors for monkeys to learn, unconstrained movement of the effector prior to the response period (i.e., during the delay period) would make it difficult for the researcher to interpret neural activities during that time period. To achieve a long-term goal of elucidating the neural mechanisms that underlie dual-task performance and the interference effect, we developed a novel dual-task paradigm by combining two cognitive tasks that are frequently used in neurophysiological experiments, i.e., the visuospatial working memory task (Funahashi et al., 1989; Constantinidis et al., 2001) and the visuospatial attention task (Chelazzi et al., 1993; Buschman and Miller, 2007). The visuospatial working memory task was performed using memory-guided saccadic eye movements to the location where a visual cue had been presented. The monkeys were required to keep gazing at the fixation spot presented at the center of a screen before the response period. In the response period, a behavioral report of memory content was expressed by making a memory-guided saccade toward a correct target. The visuospatial attention task was performed using simple manual responses. The monkeys were required to hold down a lever placed in front of them while they attended to a location where a small circle was presented on the monitor. They were then required to perform a quick lever-release when they detected a change in the color of that circle. The combination of these two tasks is particularly useful because each component task is performed using a quick, standardized behavioral response of an independent effector. This would eliminate spontaneous and inappropriate behavior of the animals and warrant the adequate, independent control of task-related effectors throughout a trial both before and during the response period, which is critical in experiments involving neurophysiological techniques. The use of independent effectors would also enable independent analyses of dual-task effects on recorded neuronal activities throughout the trial (i.e., from cue presentation to response execution) for each of the two component tasks, by minimizing the confounding of response-preparatory and response-executant activities related to the performance of the other component task.

The present paradigm offers several potential advantages for exploring the neural mechanism of dual-task performance. First, the two component tasks in this paradigm, the visuospatial working memory and visuospatial attention tasks, have been extensively studied in neuroscience. The neural mechanisms that underlie the performance of these tasks are well characterized in humans and nonhuman animals. Both tasks are known to require intact function of the lateral prefrontal cortex (LPFC) and recruit the activation of many LPFC neurons. In particular, spatially selective neuronal activities in the LPFC are known to play a key role in the performance of these tasks, such as the deployment of covert spatial attention in the attention task, and the encoding and maintenance of mnemonic contents in the memory task. Second, as we will discuss later, the present paradigm has a highly scalable task structure, in that each of the two component tasks can be replaced by other tasks, while preserving the overall structure of the paradigm and the amenability to various neurobiological approaches.

In the following sections, we show that the present dual-task paradigm (1) was efficiently learned by monkeys with a step-by-step training regimen; (2) produced a significant dual-task interference effect; and (3) successfully minimized the influence of the effect of behavioral responses in the other component task and achieved a clear separation of processes dedicated to response preparation for the two concurrent tasks. We emphasize the training method of dual-task paradigms in monkeys because it is often presumed that dual-task performance requires sustained, complex cognitive processing and that nonhuman animals are not suitable for performing such complex tasks (Wager et al., 2014). Apart from a brief description of the training regimen by Moise (1970), previous reports on animal studies have lacked detailed descriptions of the training protocols for a dual-task. Therefore, in this report we hope to promote the use of the dual-task methodology in nonhuman animals by presenting a step-by-step training protocol for