Video Article

A Cognitive Paradigm to Investigate Interference in Working Memory by Distractions and Interruptions

Jacki Janowich[1], Jyoti Mishra[2], Adam Gazzaley[2,3,4]

[1]Department of Psychology, University of New Mexico

[2]Department of Neurology, University of California, San Francisco

[3]Department of Physiology, Center for Integrative Neuroscience, University of California, San Francisco

[4]Department of Psychiatry, University of California, San Francisco

Correspondence to: Jacki Janowich at jackijanowich@gmail.com

URL: http://www.jove.com/video/52226
DOI: doi:10.3791/52226

Keywords: Behavior, Issue 101, Attention, interference, distraction, interruption, working memory, aging, multi-tasking, top-down attention, EEG, fMRI

Date Published: 7/16/2015

Citation: Janowich, J., Mishra, J., Gazzaley, A. A Cognitive Paradigm to Investigate Interference in Working Memory by Distractions and Interruptions. *J. Vis. Exp.* (101), e52226, doi:10.3791/52226 (2015).

Abstract

Goal-directed behavior is often impaired by interference from the external environment, either in the form of distraction by irrelevant information that one attempts to ignore, or by interrupting information that demands attention as part of another (secondary) task goal. Both forms of external interference have been shown to detrimentally impact the ability to maintain information in working memory (WM). Emerging evidence suggests that these different types of external interference exert different effects on behavior and may be mediated by distinct neural mechanisms. Better characterizing the distinct neuro-behavioral impact of irrelevant distractions versus attended interruptions is essential for advancing an understanding of top-down attention, resolution of external interference, and how these abilities become degraded in healthy aging and in neuropsychiatric conditions. This manuscript describes a novel cognitive paradigm developed the Gazzaley lab that has now been modified into several distinct versions used to elucidate behavioral and neural correlates of interference, by to-be-ignored *distractors* versus to-be-attended *interruptors*. Details are provided on variants of this paradigm for investigating interference in visual and auditory modalities, at multiple levels of stimulus complexity, and with experimental timing optimized for electroencephalography (EEG) or functional magnetic resonance imaging (fMRI) studies. In addition, data from younger and older adult participants obtained using this paradigm is reviewed and discussed in the context of its relationship with the broader literatures on external interference and age-related neuro-behavioral changes in resolving interference in working memory.

Video Link

The video component of this article can be found at http://www.jove.com/video/52226/

Introduction

An extensive literature has demonstrated a detriment to the maintenance of information in working memory (WM) by interference from the external environment [1-9]. External interference can be classified into two general types; interference by irrelevant information one intends to ignore: distraction, and interfering information which demands attention as part of another (secondary) task goal: interruption. Studies comparing these types of external interference using a within-participant design enable assessment of the neuro-behavioral impact of goal-focused top-down attention in the processing and resolution of external interference.

Recently, the Gazzaley lab designed a paradigm that facilitates comparison of 'to-be-attended' interruptions and 'to-be-ignored' distractions that occur in the setting of a working memory task. Emerging evidence from this paradigm suggests that these different types of external interference exert distinct effects on behavior and have distinct underlying neural mechanisms [2-5,10,11]. This paradigm has revealed differences in external interference processing in normal aging [2,3,4,10,11]; though aging deficits in the context of interference are not always found [5]; it has also distinguished mechanisms of interference by distractors versus interruptors using high-level visual stimulation of faces and scenes [2,3,4,12], low-level visual motion of dot kinematograms [5,10,11], and low-level auditory motion of frequency sweeps [5].

External Interference and Aging

External interference induces a detrimental impact on working memory throughout the lifespan, although older adults exhibit a more negative impact than younger adults [2,3,13-18]. Older adults also exhibit different patterns of neural activity compared to younger adults when attempting to resolve this interference [3,4,17,21]. However, some studies do not find evidence for such age-related behavioral [5,19,20] or neural [5] differences with interference.

Interestingly, the impact of aging on resolving interference seems to differ by sensory modality, although this issue remains unresolved at present. Visual intrasensory interference has been widely shown to exhibit age-related decline (summarized in an extensive review [22]). In contrast, many experiments suggest no age-related deficits during intra-sensory auditory interference [19,22-25], while other studies demonstrate significant age-related increases in auditory distractibility [19,22,26-32]. In addition, the salience of interfering stimuli (congruent or incongruent between the cue and probe stimuli) [2], and stimulus complexity (high or low processing load) [5] may interact with interference processing and its differences across task goals and age.

The paradigm described here supplements the aging interference literature by probing the mechanisms of top-down attention (in the form of task goals) and resolution of external interfering stimuli. Evidence from the visual face & scene version of this paradigm indicates an interaction between aging and interference type, with older adults demonstrating even greater vulnerability to attended interruptors relative to ignored distractors [3,4]. Characterizing the behavioral and neural differences between these types of interference are important to understand how cognitive control abilities change with aging.

Why do older adults show exacerbated deficits in resolving to-be-attended interruptors? Are older adults impaired by excessive processing of interruptors when they are presented, or by an inability to re-activate representations of the primary goal-relevant stimuli after interruptions, or by prolonged processing of interruptors after they are no longer present or relevant [33]? To address these questions, the current paradigm's design allows for comparison of neural activity at time-points before, during, and after different types of interference. For instance, by comparing neural activity elicited by ignored distraction versus activity during attended interruptions, one can ascertain the specific impact of top-down attention on resolution of interference in working memory.

Several studies have implemented multiple variants of this interference paradigm to understand the neural correlates of the different types of external interference both at high spatial and temporal resolution using functional magnetic resonance imaging (fMRI) and electroencephalography (EEG), respectively. This paradigm has also been used to clarify important distinctions between interference in the visual and auditory domains, as well as the impact of stimulus complexity and congruence on interference. Here, the paradigm variants are described in detail.

Protocol

The steps below enumerate how to execute this novel cognitive paradigm designed to elucidate the neuro-behavioral aspects of external interference on delayed recognition working memory, with variations optimized for pairing with EEG or fMRI. Prior to beginning data collection, complete all necessary human-participants research approvals through the appropriate Institutional Review Board and/or human participants review committee.

1. Preparation

1. Download and install experiment presentation software such as E-Prime, Presentation, or PsychoPy, as per manufacturer's instructions, onto a dedicated stimulus presentation computer.
2. Prepare an appropriate keypad for experimental responses. Add "YES" and "NO" labels to two adjacent keys (**Figure 1**).
   NOTE: For versions of this experiment utilizing MRI, use an MR-compatible keypad.
3. For auditory versions of this paradigm, prepare headphones appropriate for testing modality (ie: EEG or MR-compatible, if necessary), as per manufacturer's instructions, and adjust sound level for presentation at 65 decibels (dB) sound pressure level (SPL), which is a comfortable level for normal hearing individuals.
4. For experiments with older adults, conduct preliminary neuropsychological and sensory screenings such as vision and hearing to select an appropriately screened study population.
   1. Neuropscyhological screening
      1. Create a neuropsychological assessment battery to screen for cognitive impairment in older adults. Administer tests by paper-and-pencil, or adapt a battery for testing on a computer.
         NOTE: Tests may include the Mini Mental Status Exam (MMSE) [35], Global Deterioration Score (GDS) [36], California Verbal Learning Test (CLVT) [37], Digit Span [38,39], Symbol Span [40], Letter-Number Sequencing [41], Delis-Kaplan Executive Function System (D-KEFS) – Trail Making Test [42], Controlled Word Association Test (COWAT) [43, 44].
      2. Administer this battery to all prospective adult participants. Score all tests per their respective scoring guidelines.
      3. If recruiting for healthy older adults, exclude prospective participants with scores greater than two standard deviations below the population mean, or per custom exclusion criterion.
   2. Vision screening
      1. For visual experiments, screen for normal or corrected-to-normal vision using a preliminary questionnaire asking whether participants have normal or corrected-to-normal vision.
      2. To follow up, conduct a Snellen chart vision test, and exclude participants without normal or corrected-to-normal (20/20 or greater) vision.
   3. For auditory experiments, screen for normal hearing:
      1. In a preliminary questionnaire, ask whether participants have normal or corrected-to-normal hearing, and exclude those who do not.
      2. To follow up, obtain an objective measurement of hearing sensitivity. Conduct an in-lab audiometric assessment with one of several methods:
         1. Utilize a hearing loss screening test application such as 'uHear'. Using this application's auto-calculated results, exclude subjects with hearing sensitivity outside of the 'normal hearing' range.

2. Assess audiometric thresholds in the 250 - 6,000 Hz frequency range in both ears by the method of ascending and descending limits. Individuals with mean audiometric thresholds greater than 50 dB at any test frequency in either ear, signifying moderate hearing loss, should be excluded

2. Experimental Design

1. Administer a delayed recognition working memory task under three distinct interference conditions (and a fourth baseline condition for neural experiments) in a block design (see also **Figure 2 and Table 1**). Repeat each condition twice, in counterbalanced order (a balanced Latin square design is recommended). Note that experimental timing and number of trials vary between paradigm variants; utilize the parameters detailed in **Table 1**.
2. Ignore Distracting Stimulus Condition (DS):
    1. Display a prompt instructing participant to remember the cue stimulus and ignore the distracting stimulus while continuing to maintain a representation of the cue stimulus. Instruct the participant to respond “YES” if the probe stimulus matches the cue stimulus or “NO” if the probe does not match the stimulus.
    2. Present the cue stimulus, immediately followed by a short delay (Delay 1).
    3. Display an interfering ‘distractor’ stimulus, immediately followed by a second short delay (Delay 2).
    NOTE: The participant does not need to (and should not) interact with the distractor stimulus.
    4. Present a probe stimulus and collect responses.

3. Attend to Interrupting Stimulus (Secondary Task) Condition (IS):
    1. Display a prompt instructing participant to remember the cue stimulus and complete a secondary task using the interfering stimulus that appears thereafter. Display instructions to complete the secondary task as follows, “press a button only if the interrupting stimulus matches a set of discrimination criteria”. Instruct the participant to respond “YES” if the probe stimulus matches the cue stimulus or “NO” if the probe does not match the stimulus.
    NOTE: The discrimination criteria are distinct for each paradigm variant and described in the next section.
    2. Present the cue stimulus, immediately followed by a short delay (Delay 1).) Present an interfering ‘interruptor’ stimulus and collect responses for the secondary (discrimination) task. Following, present a second short delay (Delay 2).
    NOTE: Completing the secondary task requires attention to the ‘interruptor’.
    3. Present a probe stimulus and collect responses.
    NOTE: Ten percent of trials are catch trials in which the interruptor matches the discrimination criteria; add additional trials (10%) to this block to compensate for the discarded trials. Exclude all catch trials from neural analysis due to the confounding motor response.

4. No Interfering Stimulus Condition (NI):
    1. Display a prompt instructing the participant to remember the cue stimulus and keep it in mind. Instruct the participant to respond “YES” if the probe stimulus matches the cue stimulus or “NO” if the probe does not match the stimulus.
    2. Present the cue stimulus, immediately followed by a delay. Display a central fixation cross on a blank screen during the delay.
    3. Present a probe stimulus and collect responses.

5. Baseline/Passive View (or Listen) Condition (only for neural experiments) (PV/PL)
    1. Include a passive-view/listen condition during neuroimaging tasks to enable calculation of ‘enhancement’ and ‘suppression’ of neural activity during IS/DS conditions relative to baseline activity when participants passively view (/listen to) the working memory and interfering stimuli, free from task goals. (See **Table 2**.)
    2. Display a prompt instructing participant to passively view (/listen to) all visual (/auditory) task stimuli. Display instructions to complete the simple discrimination task.
        1. For visual tasks, instruct the participant to press a button corresponding to the direction of a displayed arrow (left or right).
        2. For auditory tasks, instruct the participant to press a button corresponding to the frequency range of an easily discriminable high (2 kHz) or low (0.5 kHz) frequency sound sweep (high or low).

    3. Sequentially present or display the cue stimulus, Delay 1, interfering stimulus, and Delay 2.
    4. Present an arrow (visual) or sound sweep (auditory) in place of the probe stimulus and collect responses as the participant completes the simple discrimination task (described above).

3. Stimuli

1. General Preparation of Stimuli

1. Select a set of stimuli from the categories described below (see also **Figure 2 and Table 1**).
2. Carefully decide whether to pair primary working memory task stimuli with thematically congruent or incongruent interfering stimuli (see NOTE below).
3. Ensure that all images are sized or re-sized to 225 pixels wide and 300 pixels tall (14 x 18 cm).
4. Present images foveally, subtending 3 degrees of visual angle from fixation.
NOTE: For fMRI experiments, use interference stimuli incongruent with the primary working memory task stimuli, for example, face interference during scene working memory or vice versa. To precisely localize face and scene specific sensory cortical regions, apply a fMRI localizer task prior to the working memory experiment. Then, during the interference paradigm, use these scene and face selective cortical

regions to simultaneously parse neural activity dynamics to the working memory cue stimuli (*e.g.,* scenes) and to the incongruent interference stimuli. (*e.g.,* faces)

2. High-level Visual Stimuli

1. For face stimuli, prepare several hundred Cue/Probe Face stimuli from gray-scale photos of male and female faces, with neutral expression, across a large adult age range. Remove hair and ears digitally, and apply a blur across the contours of the face.
2. For scene stimuli, prepare several hundred Cue/Probe Scene stimuli from gray-scale photos of natural scenes.
3. After Delay 1, present a interfering stimulus consisting of a scene or face. On 90% of trials, present a face that is not 'male AND aged over 40 years old'; on the other 10% of trials, present a face that is male and aged over 40 years old.
4. For "Attend to Interruption" condition, instruct participants to complete the following secondary task using the interfering stimulus (presented between the cue and the probe). Ask the participant to respond "YES" if interrupting face is male and aged over 40 years old.

3. Low-level Visual Motion Stimuli

1. Create Cue/Probe stimuli of a circular aperture containing 290 spatially-random grey scale dots (0.08 degrees x 0.08 degrees each) that subtend 8 degrees of visual angle at a 75 cm viewing distance, centered at the fovea.
2. Display moving dots with 100% motion coherence at an oblique angle of 10 degrees per sec, at one of 12 different directions of motion (3 in each sector).
3. Use an adaptive staircase thresholding procedure (2 degree increments) to establish a visual discrimination value yielding just under 100% accuracy, such that the discrimination threshold is reached upon the first error trial.
4. After Delay 1, present an interfering stimulus consisting of dots in counter-clockwise circular motion. Render this motion at a 'normal' speed (10 degrees per sec) on 90% of trials, and fast on the other 10% of trials.
5. In the Attend to Interruption condition, instruct participants to complete the following secondary task: respond "YES" if interrupting swirl is fast.

4. Low-level Auditory Motion Stimuli

1. Create Cue/Probe Stimuli of sound motion sweeps across a frequency range with mid-frequencies randomly chosen between 900 and 1,100 Hz. Construct the sound motion sweep frequencies to start at ± 0.5 octaves from the mid-frequency and end at ± 0.5 octaves from the mid-frequency.
2. Present an equal portion of 'up' (starting at -0.5 and ending at +0.5 octaves) and 'down' (starting at +0.5 and ending at -0.5 octaves) motion sweep stimuli.
3. Adjust the volume to comfortable hearing level of 65 dB SPL.
4. Thresholding: use an adaptive Zest procedure to establish auditory discrimination accuracy at 85% correct performance.
5. After Delay 1, present an interfering stimulus consisting of a single tone. Play a tone of frequency 2 kHz on 90% of trials, and a tone of 2.3 kHz on the other 10% of trials.
6. In the Attend to Interruption condition, instruct participants to complete the following secondary task: respond if interrupting tone is a higher frequency cue (2.3 kHz).

5. Probe Stimuli

1. For all WM tasks, ensure that 50% of probe stimuli match the cue.
2. In the low-level motion tasks with thresholded discrimination levels 5,10,11, set 50% of the probe stimuli, which do not match the cue, to differ from the cue by the absolute value of the participant's thresholded stimulus discrimination level.
   NOTE: For instance, if thresholding establishes a participant's visual discrimination level to be 10 degrees, pair a visual motion cue moving at 45 degrees with a probe moving at either 45 degrees (match on 50% trials) or 45 ± 10 degrees (35 or 55 degrees; each non-matches on 50% trials).

4. Comparing Interference Conditions

1. Use statistical software, such as SPSS, to compare behavioral performance and neural activity at important time-points before, during, and after different types of interference.
   NOTE: Several manuals online provide step-by-step instructions and screenshots describing how to use and run simple statistical analyses in SPSS.
   1. Calculate the impact of distractions versus interruptions on behavioral performance by contrasting working memory accuracies and response times during the interference conditions relative to the performance during the no interference condition (**Figure 4**). For instance, paired t-tests can be used to compare accuracy or RT between any two interference (or baseline) conditions.
      NOTE: Prior to t-test comparisons between two specific task conditions, a repeated measures ANOVA is recommended to compare across all working memory conditions in the paradigm .
   2. For neuro-imaging studies, pre-process and process the data according to the appropriate pipline for the modality and measures of interest.
      1. For EEG studies, process EEG data with EEGLAB or the software package of choice, using software's instructions and recommended processing stream.
      2. For fMRI studies, process fMRI data with the software package of choice (such as AFNI, SPM, FSL, etc.), using software's instructions and recommended processing stream.

   3. To assess neural activity modulations as a consequence of interference during working memory, statistically contrast neural data in these conditions to neural activity during passive view(/listen) conditions, thus controlling for basic perceptual processing (**Figure 4**).
      1. Calculate the Measurements such that a positive value always indicates greater enhancement above baseline or greater suppression below baseline. For P100, calculate neural suppression by subtracting quantified neural activity to the distracting

stimulus (DS) from that evoked by the passively viewed stimulus (PV) (*i.e*: PV - DS). Calculate enhancement in fMRI by subtracting quantified BOLD activity to the baseline passively viewed stimulus from that evoked by the interrupting stimulus (IS) (*i.e*: IS – PV).

4. Statistically compare neural modulations elicited by ignored distractions versus activity during attended interruptions to begin to ascertain the specific impact of top-down attention on the resolution of different types of interference in working memory.

Representative Results

This interference paradigm has enabled generation of important findings regarding the distinct behavioral impact and neural mechanisms of distraction and interruption on working memory in younger and older adults (see **Table 2** for summary).

Behavior. Behaviorally, in line with the existing literature, interruption consistently imparts a greater detrimental impact versus distraction on working memory performance [2-5, 10,11,12]. Older adults exhibit even greater interference-deficits relative to younger adults, especially in versions of this paradigm using complex visual object stimuli (faces and scenes) [2,3,4]. However, age did not exacerbate interference deficits in the low-level auditory motion paradigm variant [5], nor in the low-level visual motion variant [5] (re-analysis of a previously published dataset [10,11]). Of note, the low-level visual and auditory motion variants of the task used perceptually thresholded stimuli in each individual, young or old, which may have contributed to the age-equivalent behavioral results.

Neural Correlates of Interference. Neural data using fMRI and EEG recordings show distinct processing of passively viewed versus to-be-ignored and to-be-attended interference stimuli. In most paradigm variants, several neural markers predict WM performance, as well as neural processing differences between older and younger adults that may underlie the age-related interference deficits. fMRI evidence suggests that encoded items are maintained throughout the delay via middle frontal gyrus (MFG) - visual association cortex (VAC) connectivity in NI and DS conditions; but upon occurrence of an interrupting stimulus, this MFG-VAC connection is disrupted, and subsequently reactivated upon probe appearance [2]. The severance and subsequent re-activation of this functional connection appears critical for visual recognition WM performance. Furthermore, older adults fail to disengage from the interruption and do not as effectively re-establish functional connections within the disrupted MFG-VAC memory network [3]. Converging evidence from several other fMRI and EEG studies strengthens the hypothesis that excessive or prolonged processing of the interruptor underlies interference-related deficits in WM. Also of note, less neural enhancement to the interruptor in IS (relative to activity during PV) correlates with improved WM accuracies and response times [2,4,10 11].

Modulating Resolution of Interference. Accumulating evidence points to some malleability of interference resolution abilities in both youth and in aging [10,11,12]. Within a single session, younger adults demonstrate significant improvement in interference-induced WM disruption [10]. This behavioral improvement is correlated with decreased processing of interruptions across experimental blocks, providing evidence for a inverse relationship between neural activations to interruptions and their immediate influence on WM.

Recent evidence indicates that extended cognitive training might transfer benefits to improvements in interference-processing during working memory tasks in older adults. After 12 sessions of multi-tasking training, older adults improved WM performance on the high-level visual (faces and scenes) version of this task in DS and NI conditions relative to participants completing single-tasking training. The multi-tasking training group also improved WM performance relative to a no-contact controls in IS, DS, and NI conditions [12]. Also of note, in a different training experiment probing the effects of 10 sessions of perceptual discrimination training on the low-level visual motion variant, older adults showed improvement in NI but not IS condition, indicating general working memory improvement driven by low-level perceptual learning, but no improvements in interference-resolution abilities [11].

Figure 1. Keyboard with Yes/No Key. A keyboard for behavioral and EEG experiments with stick-on ‘Y’ and ‘N’ labels on neighboring keys to indicate ‘Yes’ and ‘No’ responses. Please click here to view a larger version of this figure.

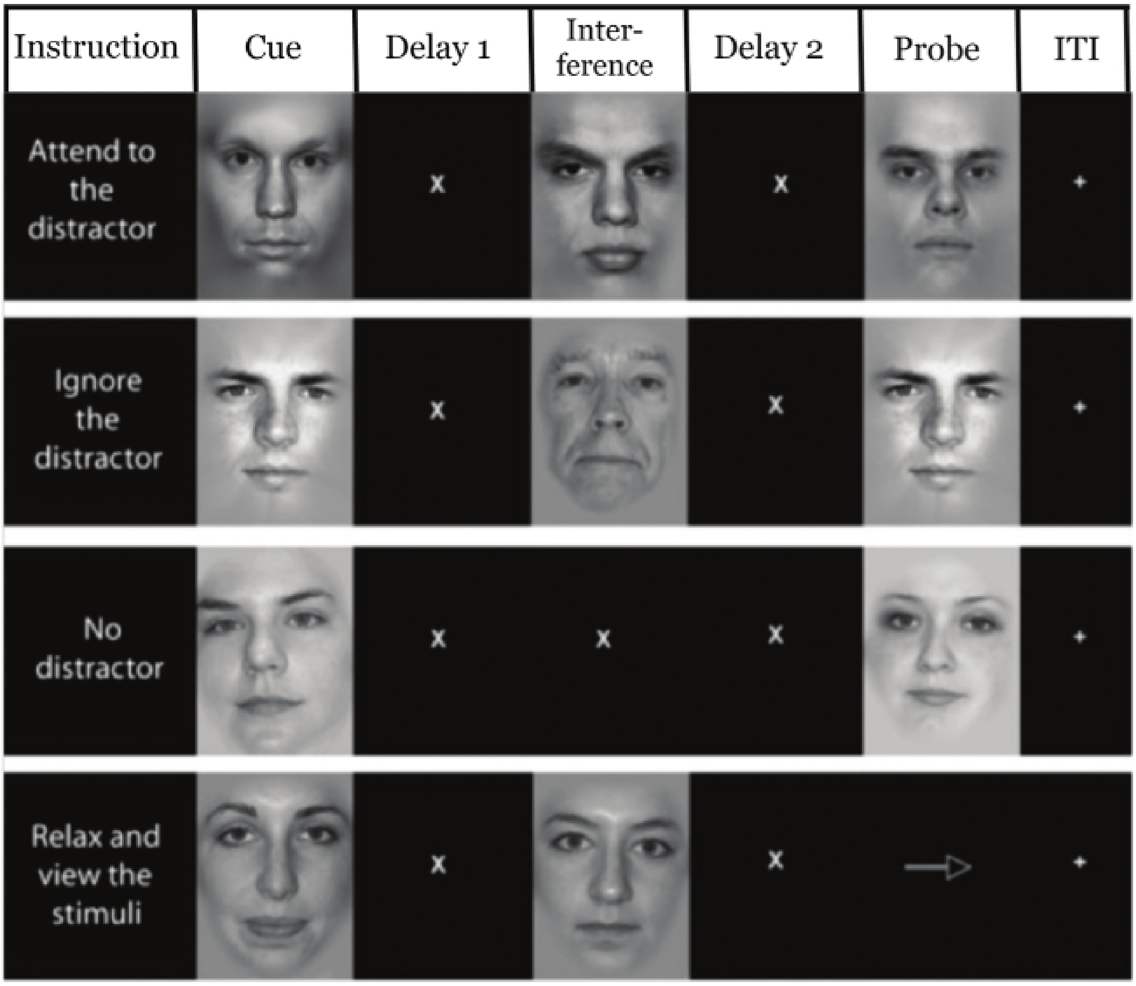

Figure 2. High-level Visual (Congruent) Experiment Design. The flow of a trial for each of the four interference conditions (by row), with stimuli from the High-Level Visual (Congruent) paradigm variant. Each rectangle depicts what is shown on screen at a particular portion of the trial (columns). ITI = inter-trial interval. For timing parameters, please refer to **Table 1**. This figure has been modified from Clapp *et al.*, 2010.[2] Please click here to view a larger version of this figure.

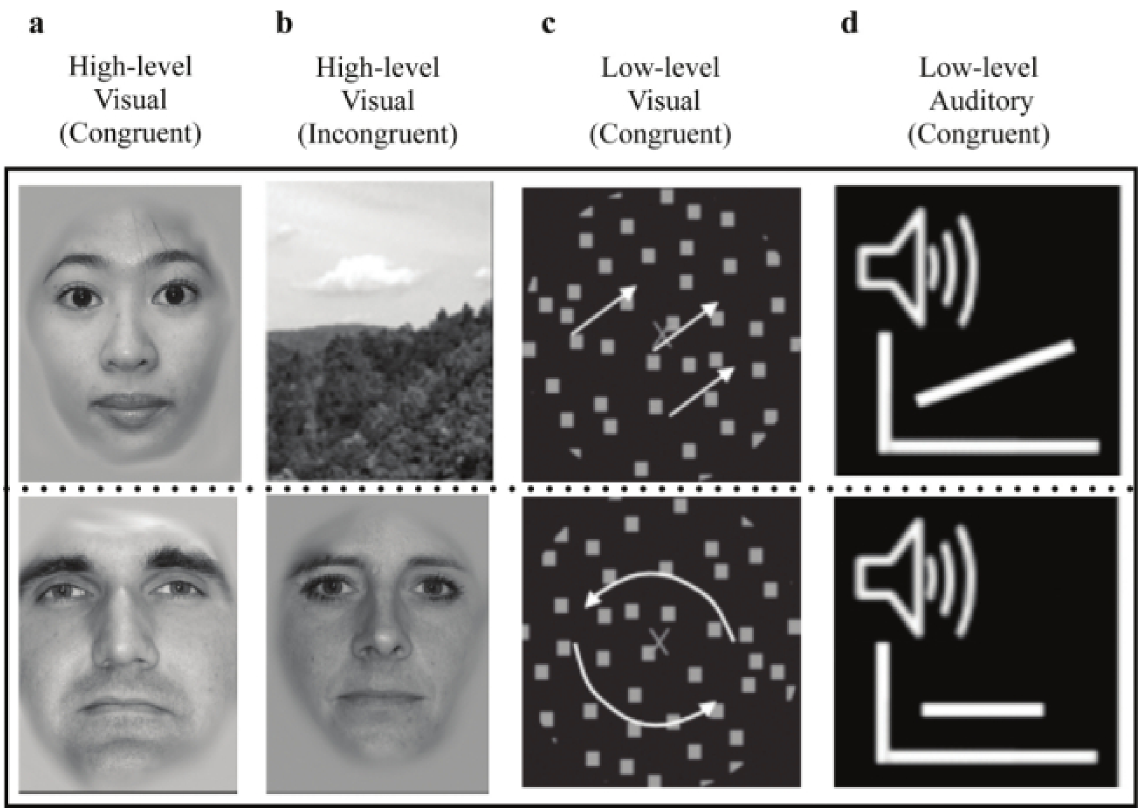

Figure 3. Stimuli by Paradigm Variant. Representative cue/probe (top row) and interfering stimulus (bottom row) for each paradigm variant (demarcated by column). In the high-level visual congruent variant (1a), a face is used as the cue/probe stimulus (top row) and another face is used as the interfering stimulus (bottom row). 1b: High-level visual incongruent variant: Cue/Probe is a natural scene; Interfering Stimulus is a face. 1c: Low-level visual motion: Cue/Probe is a dot motion kinematogram in which the dots flow together diagonally (arrows are depicted here to convey motion, but do not appear on the screen); Interfering Stimulus is a dot motion kinematogram that rotates either quickly or slowly (as above, arrows are depicted here to convey motion, but do not appear on the screen). 1d: Low-level auditory motion: Cue/probe is a sound sweep, which moves up or down one octave (only a fixation cross appears on screen); Interfering Stimulus is a stationary high frequency tone. Please click here to view a larger version of this figure.

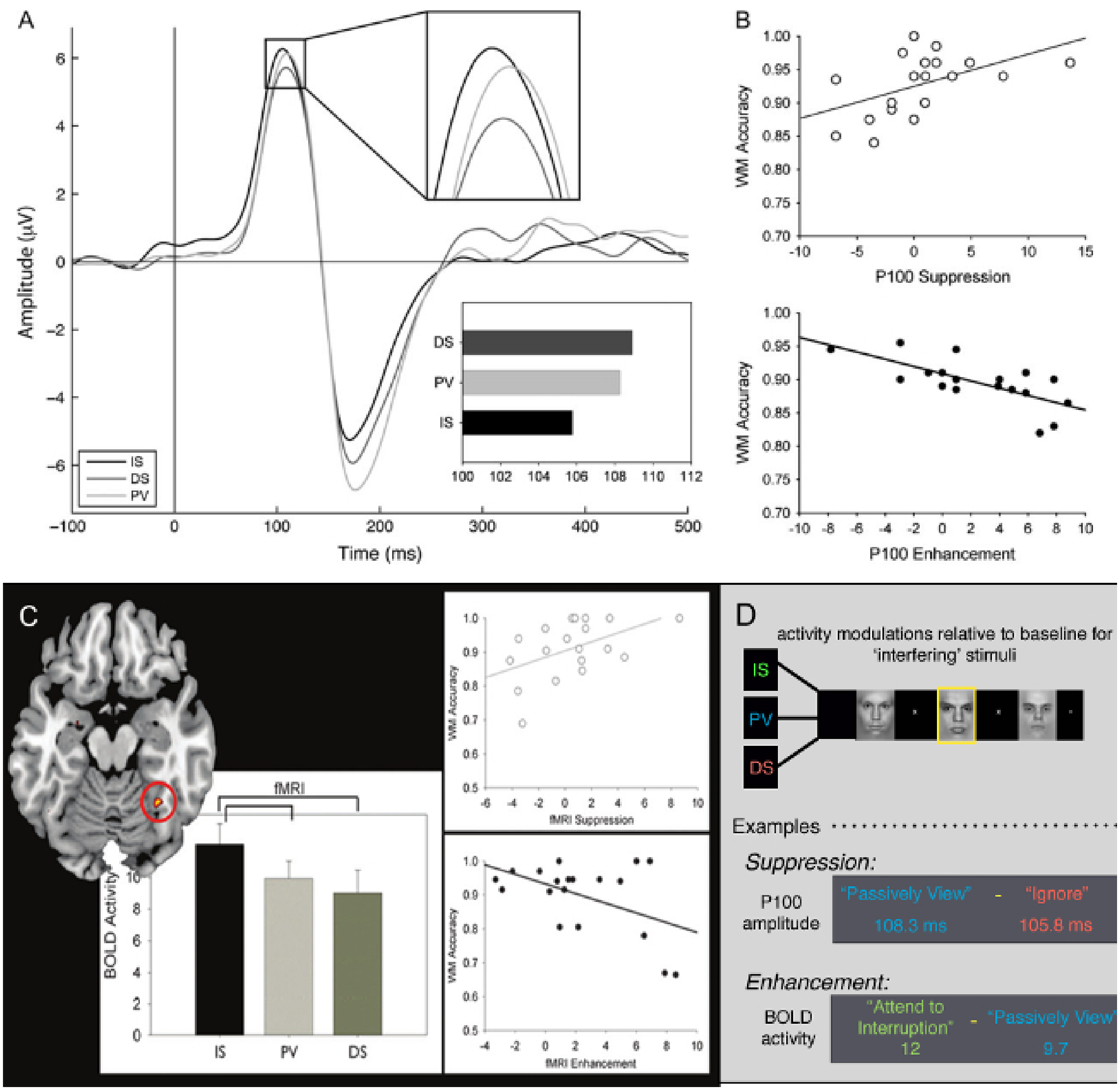

Figure 4. Representative Data: Neural Activity Comparisons between Interference Condition. Modulation of neural activity to interruptors (IS), passively viewed stimuli (PV), and distractors (DS). A: Event-related potential (ERP) data showing the latency (msec) and amplitude (µV) of the average evoked response in occipitotemporal electrodes to the 'interfering' face. ERP component P100 latency reveals significant enhancement to interruptors (IS – PV). B: Correlation between the amplitude modulation of ERP component P100 and working memory accuracy. The amount that participants allocate attention toward an interruptor (IS - PV, enhancement) negatively correlates with their WM performance (R 5 = -0.7, P<0.001). Likewise, the amount of attention allocated away from a distractor (PV - DS, suppression) positively correlates with WM (R = 0.5, P<0.05). C. fMRI BOLD (blood-oxygen-level dependent) activation in the Fusiform Face Area (FFA) in response to the 'interfering' face are presented in the bar graphs. The BOLD response was highest in response to the interruptors and lowest to the distractors (enhancement [IS>PV, P<0.01]), demonstrating enhanced processing of interrupting stimuli. D: Template and examples for neural comparisons. Measures are calculated such that a positive value always indicates greater enhancement above baseline or greater suppression below baseline. For P100, neural suppression is calculated by subtracting quantified neural activity to the distracting stimulus (DS) from that evoked by the passively viewed stimulus (PV) (ie: PV - DS). Enhancement is calculated in fMRI by subtracting quantified BOLD activity to the baseline passively viewed stimulus from that evoked by the interrupting stimulus (IS) (ie: IS – PV). This figure has been modified from Clapp *et al.*, 2010 [2]. Please click here to view a larger version of this figure.

	Cue	Delay 1	Inter-ference	Delay 2	Probe	Feed-back	ITI	Trials
Low-level auditory motion (Mishra et al., 2013)	100 ms	2800-3000 ms	100 ms (congruent)	2800-3000 ms	100 ms	yes	response prompt 400ms from probe onset	2 runs of 40 trials (80) x 4 conditions
Low-level visual motion (Berry et al., 2009, 2010; Mishra et al., 2013)	800 ms	2800-3000 ms	800 ms (congruent)	2800-3000 ms	800 ms	yes	<4000 ms to respond	2 runs of 40 trials (80) x 4 conditions
High-level visual - EEG or behavioral (Clapp et al., 2010, 2011, Clapp and Gazzaley, 2012, Anguera et al., 2013)	800 ms	2800-3200 ms (Clapp 2012) 3000 ms (Clapp 2010, Anguera 2013)	800 ms (congruent)	2800-3200 ms	1000 ms	no	self-paced	2 runs of 40 trials (80) x 4 conditions
High-level visual - fMRI (Clapp et al., 2010, 2011)	800 ms	7200 ms	800 ms (incongruent)	7200 ms	1000 ms	no	9000 ms	2 runs of 16 trials (32) x 4 conditions

Table 1: Timing Parameter. Experimental Timing for each paradigm variant (rows). A range of times (*i.e*: 2,800 - 3,200 msec) indicates that the timing of this portion of the trial is 'jittered', with timing randomly chosen from within the given range. A congruent interfering stimulus is of the same type as the cue/probe (*i.e*: face cue/probe and face interference), whereas an incongruent interfering stimulus is of a different type (*i.e*: scene cue/probe and face interference). ITI = inter-trial interval. Each row from cue to ITI represents one trial (for depiction of trial flow, please refer to **Figure 1**).

Table 2: Interference Paradigm Key Behavioral and Neural Results

	Stimuli	Inter-ference	Age (YA: Younger Adults/ OA: Older Adults)	Key Results
Berry et al, 2009	low-level visual motion, thresholded	congruent	YA	Behavior: across a single session, interference-induced performance decrements in accuracy and response time (RT) were diminished by rapid learning. EEG: a. interruptors and distractors elicited differential event-related potential (ERP) P1 and N1 component modulation. b. Extent of early interference processing in visual cortex was found to correlate with improvements in working memory (WM) accuracy and response times (RT). Specifically, relative to PV baseline, increased suppression of DS and decreased enhancement of IS resulted in improved WM performance.
Berry et al., 2010	low-level visual motion, thresholded	congruent; *DS condition absent*	OA	Behavior: a. Overall WM performance impaired in OA relative to YA (comparison with YA in Berry 2009). b. Perceptual discrimination training improved performance on the untrained NI condition of the WM task, but not the IS task condition. EEG: Perceptual discrimination training led to changes in WM stimulus encoding (decreased ERP N1 amplitude) during the NI task; N1 amplitude change correlated with improved working memory performance.
Clapp et al., 2010	high-level visual	EEG: congruent fMRI: incongruent	YA	Behavior: WM performance impaired by interference; with greater impairment during IS relative to DS. EEG: Magnitude of processing of interfering stimuli in visual cortex negatively impacted subsequent WM recognition accuracy. fMRI: In DS condition, encoded items are maintained throughout the delay via functional connectivity between middle frontal gyrus (MFG) and visual association cortex (VAC). In contrast during IS, this MFG-VAC connectivity was not maintained, but was reactivated upon probe appearance.
Clapp et al., 2011	high-level visual	incongruent	OA	Behavior: WM performance was more disrupted by interference in OA than in YA (comparison with fMRI study in YA (Clapp et al., 2010)) fMRI: OA failed to disengage from the interruption and reestablish functional connections with the disrupted memory network between MFG and VAC.

Table 2: Interference Paradigm Key Behavioral and Neural Result. Key behavioral and neural results obtained with this interference paradigm are presented by study and categorized by stimuli parameters, participant age-group, and imaging modality.YA = Younger Adults; OA = Older Adults.

Discussion

A novel cognitive paradigm has shown efficacy in investigating working memory interference by distractions and interruptions. This paradigm and its several variants, extending its use across sensory modalities, stimulus complexity levels, and imaging methods, are detailed.

Before beginning the experiment, pre-screen all participants to ensure appropriate cognitive and perceptual abilities. For experiments using low-level perceptual stimuli, administer an adaptive thresholding procedure to calibrate the stimuli to a perceptual discrimination level of equivalent difficulty between participants. Adhere to the experiment variant parameters for the intended imaging modality and stimulus type. Run all interference conditions (No Interfering Stimuli, Ignore Distraction, Attend to Interruption, and Passive View (only necessary for neural recordings)) in a counterbalanced, block design, and compare behavioral and neural data between conditions as described above. To explore working memory interference with different stimuli types, simply substitute the desired stimuli in the presentation script.

The existing research using this paradigm has several limitations. While the low-level visual and auditory motion variants both use perceptual-discrimination thresholds established by an adaptive staircase procedure completed by each participant, the high-level visual face and scene variant is not thresholded and instead uses identical stimuli between all participants. Further work is required to better understand the impact of perceptual thresholding on this interference task. In addition, congruent interference is used in all of the behavioral and EEG experiments, while fMRI experiments due to their low temporal resolution, utilized incongruent interfering stimuli that could be distinctly spatially localized in the brain. Interfering stimuli that are congruent with the probe/cue are known to evoke a greater interference cost relative to that of incongruent stimuli [2]. Incongruent distractors may even have no interference costs in some circumstances [34]. Thus, when selecting which paradigm variant to use, which maybe partially constrained by the neuroimaging tools being used, or comparing between studies, the differences between congruent and incongruent stimuli must be taken into account.

The paradigm described in this paper offers a novel, elegant method for differentiating between interference by distraction or interruption in a working memory task. Comparing stimulus-locked neural data between the four interference conditions (**Figure 4**) offers a significant advantage over other techniques in its targeted elucidation of neural mechanisms of top-down attention in processing and resolving external interference. In addition, the flexibility of this paradigm framework to address diverse stimulus types enables efficient comparison of interference across domains. Further, this paradigm's use of perceptual thresholding for low-level visual and auditory experiments is superior to many alternative methods in that it establishes comparable perceptual difficulties across participants, ensuring that differences in the interference experiment are due to specific deficits with interference resolution, rather than confounding baseline differences in stimulus perception.

Future studies are needed to continue to explore the distinctions in processing and resolving interference by distraction and interruption, and how these capacities might be improved. For instance, in each of the current paradigm variants, accuracy on the interrupting task was very high in both younger and older adults (90% [3]; 93% [4]; 100% [5]), *i.e.*, this secondary task was not cognitively demanding. In the future, researchers may choose to modulate the difficulty of the primary and/or the secondary (interrupting) task in order to reveal how working memory load or interference load interacts with performance and neural activity. In addition, to supplement the comparisons between low-level visual and auditory stimuli and high-level visual stimuli, future variants on this paradigm could investigate the role of interference with high-level auditory stimuli (ie: speech), and its possible that a future version may perceptually threshold the high-level visual stimuli. Finally, this paradigm could be used to test the efficacy of different interventions, in diverse clinical populations, to improve specific aspects of interference-resolution. For instance, use of this paradigm with ADHD or schizophrenia patients may enable more precise measurement of the specific interference deficits involved in these disorder. Additionally, this paradigm can be used as a therapeutic assessment, *i.e.,* administered before and after an intervention to assess whether interference deficits in a certain population may be alleviated with behavioral therapy or drug or other interventions. Future studies may also investigate how results on this paradigm correlate to other individual differences such as in mind-wandering and working memory span.

To summarize, this interference paradigm has clear utility as a tool for understanding behavioral and neural correlates of the different types of external interference (distraction and interruption), and can help to elucidate distinctions between interference in the visual and auditory domains, as well as the impact of stimulus complexity and congruence on interference.

Disclosures

The authors have nothing to disclose.

Acknowledgements

Many thanks to the developers of this paradigm, especially Wesley Clapp, Anne Berry, Jyoti Mishra, Michael Rubens, and Theodore Zanto. This work was supported by NIH grant 5R01AG0403333 (AG).

References

1. Baddeley, A. Working memory: Looking back and looking forward. *Nature Reviews Neuroscience.* **4**, (10), 829-839 (2003).
2. Clapp, W. C., Rubens, M. T., Gazzaley, A. Mechanisms of working memory disruption of external interference. *Cerebral Cortex.* **20**, (4), 859-872 (2010).
3. Clapp, W. C., Rubens, M. T., Sabharwal, J., Gazzaley, A. Deficit in switching between functional brain networks underlies the impact of multitasking on working memory in older adults. *PNAS.* **108**, (17), 7212-7217 (2011).
4. Clapp, W. C., Gazzaley, A. Distinct mechanisms for the impact of distraction and interruption on working memory in aging. *Neurobiology of Aging.* **33**, (1), 134-148 (2012).

5. Mishra, J., Zanto, T., Nilakantan, A., Gazzaley, A. Comparable mechanisms of working memory interference by auditory motion in youth and aging. *Neuropsychologia.* **51**, (10), 1896-1906 (2013).
6. Sakai, K. Reactivation of memory: role of medial temporal lobe and prefrontal cortex. *Rev Neurosci.* **14**, (3), 241-252 (2003).
7. Sakai, K., Roye, J., Passingham, R. E. Active maintenance in prefrontal area 46 creates distractor-resistant memory. *Nature Neuroscience.* **5**, (5), 479-484 (2002).
8. Yoon, J. H., Curtis, C. E., D'Esposito, M. Differential effects of distraction during working memory on delay-period activity in the prefrontal cortex and the visual association cortex. *Neuroimage.* **29**, (4), 1117-1126 (2006).
9. Sreenivasan, K. K., Jha, A. P. Selective attention supports working memory maintenance by modulating perceptual processing of distractors. *Journal of Cognitive Neuroscience.* **19**, (1), 32-41 (2007).
10. Berry, A. S., Zanto, T. P., Rutman, A. M., Clapp, W. C., Gazzaley, A. Practice-related improvement in working memory is modulated by changes in processing external interference. *Journal of Neurophysiology.* **102**, (3), 1779-1789 (2009).
11. Berry, A. S., *et al.* The influence of perceptual training on working memory in older adults. *PLoS One.* **5**, (7), e11537 (2010).
12. Anguera, J. A., *et al.* Video game training enhances cognitive control in older adults. *Nature.* **501**, (7465), 97-101 (2013).
13. Gazzaley, A., Clapp, W., Kelley, J., McEvoy, K., Knight, R. T., D'Esposito, M. Age-related top-down suppression deficit in the early stages of cortical visual memory processing. *PNAS.* **105**, (35), 13122-13126 (2008).
14. Hasher, L., Zacks, R. T. Working memory, comprehension, and aging: A review and a new view. *The Psychology of Learning and Motivation.* Bower, G. H. **22**, 193-225 Academic Press San Diego, CA (1998).
15. Lustig, C., Hasher, L., Tonev, S. T. Inhibitory control over the present and past. *European Journal of Cognitive Psychology.* **13**, (1-2), 107-122 (2001).
16. Lustig, C., Hasher, L., Zacks, R. Inhibitory deficit theory: Recent developments in a "new view. *Inhibition in Cognition.* Macleod, C. M., Gorfein, D. S. 145-162 American Psychological Association Washington, DC (2007).
17. Solesio-Jofre, E., Lorenzo-Lopez, L., Gutierrez, R., Lopez-Frutos, J. M., Ruiz-Vargas, J. M., Maestu, F. Age effects on retroactive interference during working memory maintenance. *Biological Psychiatry.* **88**, (1), 72-82 (2011).
18. Zacks, R. T., Hasher, L. Directed ignoring: Inhibitory regulation of working memory. *Inhibitory Mechanisms in Attention, Memory and Language.* Dagenback, D., Carr, T. H. 241-264 Academic Press New York, NY (1994).
19. Guerreiro, M. J. S., Murphy, D. R., Van Gerven, P. W. M. Making sense of age- related distractibility: The critical role of sensory modality. *Acta Psychologica.* **142**, (2), 184-194 (2013).
20. Verhaeghen, P., Zhang, Y. What is still working in working memory in old age: dual tasking and resistance to interference do not explain age-related item loss after a focus switch. *J Gerontol B Psychol Sci Soc Sci.* **68**, (5), 762-770 (2013).
21. García-Pacios, J., *et al.* Early prefrontal activation as a mechanism to prevent forgetting in the context of interference. *Am J Geriatr Psychiatry.* **21**, (6), 580-588 (2013).
22. Guerrerio, M. J. S. *The role of sensory modality in age-related distraction.* Maastrict University the Netherlands (2013).
23. Li, L., Daneman, M., Qi, J. G., Schneider, A. B. Does the information content of an irrelevant source differentially affect spoken word recognition in younger and older adults. *Journal of Experimental Psychology, Human Perception and Performance.* **30**, (6), 1077-1091 (2004).
24. Murphy, D. R., McDowd, J. M., Wilcox, K. A. Inhibition and aging: Similarities between younger and older adults as revealed by the processing of unatteneded auditory information. *Psychology and Aging.* **14**, (1), 44-59 (1999).
25. Schneider, B. A., Daneman, M., Murphy, D. R., See, S. K. Listening to discourse in distracting settings: the effects of aging. *Psychology and Aging.* **15**, (1), 110-125 (2000).
26. Alain, C., Woods, D. L. Age-related changes in processing auditory stimuli during visual attention: evidence for deficits in inhibitory control and sensory memory. *Psychology and Aging.* **14**, (3), 507-519 (1999).
27. Chao, L. L., Knight, R. T. Prefrontal deficits in aging and inhibitory control with aging. *Cerebral Cortex.* **7**, (1), 63-69 (1997).
28. Fabiani, M., Low, K. A., Wee, E., Sabble, J. J., Gratton, G. Reduced suppression or labile memory? Mechanisms of inefficient filtering of irrelevant information in older adults. *Journal of Cognitive Neuroscience.* **18**, (4), 637-650 (2006).
29. Passow, S., *et al.* Human aging compromises attentional control of auditory perception. *Psychological Aging.* **27**, (1), 99-105 (2012).
30. Sommers, M. S., Danielson, S. M. Inhibitory processes and spoken word recognition in young and older adults: the interaction of lexical competition and semantic context. *Psychology and Aging.* **14**, (3), 458-472 (1999).
31. Tun, P. A., Wingfield, A. One voice too many: adult age differences in language processing with different types of distracting sounds. *J Gerontol B Psychol Sci Soc Sci.* **54**, (5), P317-P327 (1999).
32. Tun, P. A., O'Kane, G., Wingfield, A. Distraction by competing speech in young and older adult listeners. *Psychology and Aging.* **17**, (3), 453-467 (2002).
33. Conway, A. R. A., Engle, R. W. Working memory and retrieval: A resource-dependent inhibition model. *Journal of Experimental Psychology: General.* **123**, (4), 354-373 (1994).
34. Cashdollar, N., Lavie, N., Duezel, E. Alleviating memory impairment through distraction. *The Journal of Neuroscience.* **33**, (48), 19012-19022 (2013).
35. Folstein, M. F., Folstein, S. E., McHuge, P. R. Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research.* **12**, (3), 189-198 (1973).
36. Reisberg, B., Ferris, S. H., de Leon, M. J., Crook, T. The Global Deterioration Scale for assessment of primary degenerative dementia. *American Journal of Psychiatry.* **139**, (9), 1136-1139 (1982).
37. Delis, D. C., Freeland, J., Kramer, J. H., Kaplan, E. Integrating clinical assessment with cognitive neuroscience: Construct validation of the California Verbal Learning Test. *Journal of Consulting and Clinical Psychology.* **56**, (1), 123-130 (1988).
38. Gregoire, J., van der Linden, M. Effect of age on forward and backward digit spans. *Aging, Neuropsychology, and Cognition: A Journal on Normal and Dysfunctional Development.* **4**, (2), 140-149 (1997).
39. Conway, A. R. A., Kane, M. J., Bunting, M. F., Hambrick, D. Z., Wilhelm, O., Engle, R. W. Working memory span tasks: A methodological review and user's guide. *Psychonomic Bulletin & Review.* **12**, (5), 769-786 (2005).
40. Holdnack, J. A., Zhou, X., Larrabee, G. J., Millis, S. R., Salthouse, T. A. Confirmatory factor analysis of the WAIS-IV/WMS-IV. *Assessment.* **18**, 178-191 (2011).
41. Hill, B., Elliott, E., Shelton, J., Pella, R., O'Jile, J., Gouvier, W. Can we improve the clinical assessment of working memory? An evaluation of the WAIS-III using a working memory criterion construct. *Journal of Clinical Experimental Neuropsychology.* **32**, (3), 315-323 (2011).

42. Homack, S., Lee, D., Riccio, C. A. Test review: Delis-Kaplan Executive Function System. *Journal of Clinical and Experimental Neuropsychology.* **27**, (5), 599-609 (2005).
43. Benton, A. L., Hamsher, K. D. S., Rey, G. J., Sivan, A. B. *Multilingual aphasia examination.* AJA Associates Iowa City, IA (1994).
44. Strauss, E., Sherman, E. M. S., Spreen, O. *A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary 3rd ed.* 501-526 Oxford University Press New York (2006).