Video Article

Examining the Characteristics of Episodic Memory using Event-related Potentials in Patients with Alzheimer's Disease

Erin Hussey[1], Brandon Ally[1]

[1]Department of Neurology, Vanderbilt University

Correspondence to: Brandon Ally at brandon.ally@vanderbilt.edu

URL: https://www.jove.com/video/2715
DOI: doi:10.3791/2715

Keywords: Medicine, Issue 54, recognition memory, episodic memory, event-related potentials, dual process, Alzheimer's disease, amnestic mild cognitive impairment

Date Published: 8/30/2011

Citation: Hussey, E., Ally, B. Examining the Characteristics of Episodic Memory using Event-related Potentials in Patients with Alzheimer's Disease. *J. Vis. Exp.* (54), e2715, doi:10.3791/2715 (2011).

Abstract

Our laboratory uses event-related EEG potentials (ERPs) to understand and support behavioral investigations of episodic memory in patients with amnestic mild cognitive impairment (aMCI) and Alzheimer's disease (AD). Whereas behavioral data inform us about the patients' performance, ERPs allow us to record discrete changes in brain activity. Further, ERPs can give us insight into the onset, duration, and interaction of independent cognitive processes associated with memory retrieval. In patient populations, these types of studies are used to examine which aspects of memory are impaired and which remain relatively intact compared to a control population. The methodology for collecting ERP data from a vulnerable patient population while these participants perform a recognition memory task is reviewed. This protocol includes participant preparation, quality assurance, data acquisition, and data analysis. In addition to basic setup and acquisition, we will also demonstrate localization techniques to obtain greater spatial resolution and source localization using high-density (128 channel) electrode arrays.

Video Link

The video component of this article can be found at https://www.jove.com/video/2715/

Protocol

1. Set up the EEG Equipment

1. Our laboratory uses the 128-channel BioSemi ActiveTwo EEG acquisition system with "active" electrodes (Amsterdam, The Netherlands; http://www.biosemi.com) and the ActiveTwo electrode cap (Behavioral Brain Sciences Center, Birmingham, UK) to obtain ERP data.
2. Make sure that the battery is fully charged and attached to the amplifier.
3. Gather all materials necessary to complete participant set-up, including: syringe, gel, tape measure, various sized EEG caps, alcohol swabs, facial electrode stickers, and velcro straps to secure the electrode cables.
4. Place stickers on five facial electrodes.

2. Set up the Stimuli Presentation and Data Acquisition Computers

1. Turn on both the stimuli presentation computer and the data acquisition computer.
2. Our Laboratory uses E-Prime software (Pittsburgh, PA) to present stimuli and acquire behavioral data.
3. Check to make sure that the experiment is sending the appropriate trigger codes to the data acquisition computer.
4. To do this:
    - Turn on the amplifier in the participant chamber (Note: no electrodes or cables need to be plugged in to do this), open data acquisition software on the data acquisition computer, hit start (do not save).
    - Go to the stimuli presentation computer, open your experiment file, and hit run.
    - You should now see the appropriate trigger codes that you programmed into your experiment file showing up on the data acquisition software program.

3. Participant Preparation

1. Detail all study procedures with the participant and address any safety concerns. Further, assure that patients fully understand the protocol by having them report the protocol back to the researcher in their own words.
2. Have participant seated comfortably in medium height hard-backed chair.

3. Once the participant is seated, ensure that his/her line of vision from the display is standard for the experiment (here we use 48 inches).
4. Measure the circumference of the participant's head in order to determine which EEG cap should be used.
5. Ask the participant to remove any jewelry or hair accessories so as to ensure proper fit of the EEG cap and accurate recording. Also, if the participant wears glasses, it is best to have him/her take them off at this point until all of the facial electrodes have been applied.
6. It is also important to review the following with each subject:
   - Remove any chewing gum or candy/mints to reduce motor movements
   - Ask participants to use facilities before starting as to not interrupt the EEG recording
   - Ask participant to try and keep movements and eye blinks to a minimum, but not be overly concerned about doing so
7. Using the alcohol swab, cleanse the participant's skin of oil and/or makeup, where the facial electrodes will be placed: one on each mastoid, one on each temple, and one directly below the left eye.
8. Place a small amount of conducting gel onto each facial electrode, remove the backing from the sticker and place on the participant, applying a small amount of pressure to ensure that the electrode will stay in place.
9. Now place the EEG cap onto the participant's head and fasten the strap under his/her chin. If the participant wears glasses, have him/her put these on before putting on the cap.
10. Next, measure (in centimeters) from the nasion (bridge of the nose) to the inion (protrusion on the lower back of the head). Multiply this measurement by .5 (finding the midpoint) and this is where electrode A1 should be placed from front to back. Next, measure from the pre-auricular on one ear to the other (indents above cartilage on ear). The midpoint of this measurement is where electrode A1 should be placed from side-to-side.

4. Digitizing for Source Localization and Electrode Placement

1. Our laboratory uses the Polhemus Patriot Digitizer / Locator (Colchester, VT) to obtain three-dimensional representations (or head models) of electrode positions on each participant's head. This controls for variability in skull shape for each participant and makes for more accurate source localization. Further, these head models can be co-registered with structural magnetic resonance images to tie together the superior spatial resolution of MRI and the superior temporal resolution of ERPs.
2. First, place the localization transmitter under the cap behind the left ear, with excess cord tucked in under the chinstrap to keep in place.
3. Attach receiver to a wooden chair in a position below the participant's head, approximately 6 inches from the transmitter.
4. Open digitizing software and take measurements of electrode locations with stylus as prompted by the software.
5. Generate 3D head model of electrode positions using MR Locator software and accept for localization of raw EEG data.
6. Once the 3D head model for the participant has been verified on the computer display, we are ready to place the electrode at each pre-defined location on the ActiveTwo cap.
7. Fill the electrode wells on the cap with the conducting gel and plug in all electrodes. Gather all cables and facial electrodes behind the participant and plug them into the amplifier.
8. Offer older participants a break, especially patients with Alzheimer's disease, who may require frequent breaks to maintain focus and sustained attention to the experimental task.
9. ActiView software is used to assure that all electrodes are free of artifact and resistance levels are acceptable. After all electrodes are placed, and the participant is ready to begin the experiment, resistance levels of the electrodes should be checked on the data acquisition computer using ActiView software. Offset levels should be within +/-25μV.
10. Once all resistance levels are acceptable, the experiment is ready to be run.

5. Data Acquisition for both EEG Data and Experiment

1. Our laboratory uses BioSemi's ActiView software to view and acquire raw EEG data.
2. Load behavioral data presentation file. Enter participant number. The experimental software saves the participant's responses and automatically generates a data file once the experiment finishes running with this participant number.
3. Perform a check to ensure the participant is seated 48 inches from the center of the display monitor.
4. Once the experiment has loaded, behavioral instructions should be read and verified with participant.
5. In our current recognition memory design, the experiment begins with the study phase, where the participant will be presented with either a series of pictures or words.
6. Begin saving raw EEG data file on the data acquisition computer.
7. Start stimulus delivery on the stimulus presentation computer.
8. Have a researcher work with older adults to input responses on button box. This is particularly important for patients with cognitive impairment.
9. Monitor participant during behavioral task, including need for breaks.
10. Once all behavioral stimuli have been presented, raw EEG data must be saved. Again, behavioral data are automatically saved by E-Prime software.
11. After saving the study or encoding data, the previous 9 steps will be repeated for the test phase, where the participant will again be presented with either a series of pictures or words. During the test phase, half of the items will be from the study phase and half of the items will be novel. Participants will identify the old/new status of the item by reporting their answer aloud to the researcher. The researcher will then input the participant's response on the button box.

6. Data Post-Processing Pipeline

1. Our laboratory uses EMSE Suite 5.3
2. The raw data must first be prepared and digitally filtered to remove noise and artifact from the signal before any type of analysis can be completed.
3. First, temporal filters, such as infinite impulse response and bandpass filters must be applied.

4. Next, the data must be referenced to some point on the head. Select reference. In the current protocol, we use the common average reference.
5. Next, the data must be filtered spatially and bad channels interpolated. Visual inspection of the data is performed and appropriate filters are put in place.
6. Finally, ocular artifact correction methods must be utilized to correct the signal for eyeblink and eye movement artifact.

7. Representative Results

Our work has shown that the early frontal old/new effect (hits > correct rejections), typically associated with conceptual processing or memorial familiarity, remain intact for pictures in patients with mild Alzheimer's disease compared to healthy older adults, but not for words (Ally, McKeever, Waring, & Budson, 2009). Ally et al. (2009) have shown that the parietal old/new effect, typically associated with recollection, is impaired in patients for both pictures and words compared to their peers. In other words, the frontal memorial processes associated with recognition appear to be similar for pictures between the patients with AD and healthy older adults. In contrast, these processes are impaired for words in patients when we examine differences between the two groups. This significant difference between the groups is evident for posterior memory processes for both pictures and words. Although there has been considerable debate as to the cognitive process associated with the early frontal effect, we hypothesize that patients with mild Alzheimer's disease can successfully utilize conceptual processing or memorial familiarity to increase their discrimination for pictures compared to words, and these processes likely underlie the robust picture superiority effect in patients with Alzheimer's disease.

Frontal ERP activity associated with the successful retrieval of words and pictures is demonstrated for patients with very mild Alzheimer's disease and healthy older controls (Figure 1). These images were taken during the 300 to 500 ms time interval typically associated with conceptual processing or memorial familiarity. Notice the similar frontal old/new effect for pictures (red pseudocolor) but diminished effect for words between groups. (cyan pseudocolor).

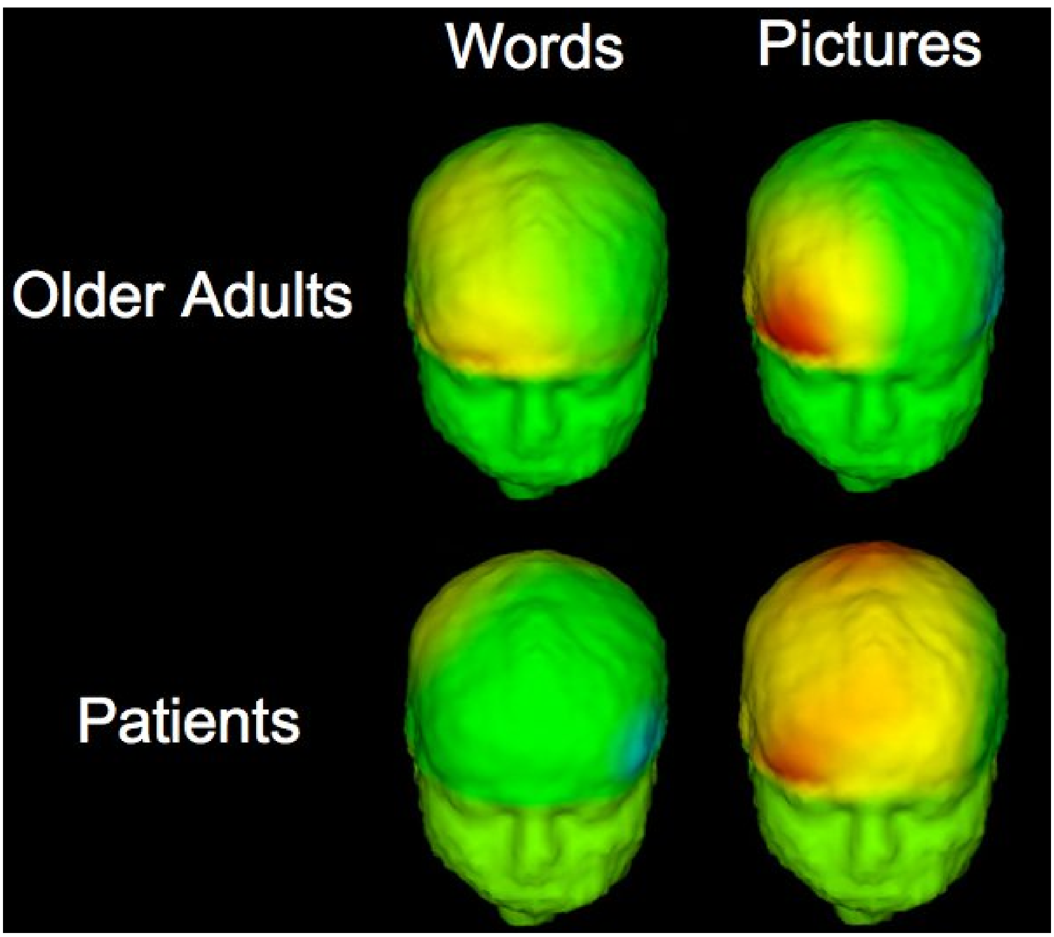

Figure 1: Representative ERP Activity During Retrieval Task in Alzheimer's Patients and Healthy Subjects.

Discussion

ERPs and behavioral data can provide us with different and complementary information. Whereas behavioral data informs us about the patients' performance, ERPs allow us to record discrete changes in brain activity. Due to their excellent temporal resolution, ERPs have proven very useful in dissociating and understanding the role of memorial processes (e.g., conceptual processing and familiarity, recollection, post-retrieval monitoring processes) that have been previously associated with specific old/new components of the ERP wave (early frontal, parietal, late frontal, respectively) (see Ally & Budson, 2007). In studying patients with cognitive impairment, event-related potentials (ERPs) are extremely useful in understanding brain physiology, particularly when obtaining meaningful behavioral data is difficult (Ally, 2011). However, there are many pitfalls faced when interpreting ERP data in these populations. For example, due to the heterogeneity of Alzheimer pathology, ERP data from patients often have significant variance between subjects. The current protocol highlights ways in which the variance can be minimized. The results from this protocol help to understand the cognitive and neural underpinnings of memory loss associated with mild Alzheimer's disease, and to help elucidate which memorial processes are impaired and which are relatively intact in mild Alzheimer's disease. Our work reveals that some frontally-mediated memory processes, perhaps conceptual processing or memorial familiarity, remain intact for pictures in patients (Ally et al., 2009). This understanding may in turn allow new drug therapies and early behavioral interventions to be developed and keep patients engaged and living in the community for longer periods of time.

Disclosures

No conflicts of interest declared.

Acknowledgements

This protocol was supported by the National Institute on Aging grant K23 AG031925 and R01 AG038471.

References

1. Ally, B.A. & Budson, A.E. The worth of pictures: Using high density event-related potentials to understand the memorial power of pictures and the dynamics of recognition memory. *Neuro Image*. **35**, 378-395 (2007).
2. Ally, B.A., McKeever, J.D., Waring, J.D., & Budson, A.E. Pictures preserve frontal memorial processes in patients with mild cognitive impairment. *Neuro psychologia*. **47**, 2044-2055 (2009).
3. Ally, B.A. Using EEG and MEG to understanding brain physiology in dementia. In Budson, A.E. & Kowall, N.W. Eds. *The Handbook of Alzheimer's disease and other dementias.* (Blackwell Publishing, 2011).