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RESEARCH ARTICLE | *Higher Neural Functions and Behavior*

Predicting memory from study-related brain activity

Sucheta Chakravarty,[1] Yvonne Y. Chen,[2] and Jeremy B. Caplan[1,3]

[1]*Department of Psychology, University of Alberta, Edmonton, Alberta, Canada;* [2]*Department of Neurosurgery, Baylor College of Medicine, Houston, Texas; and* [3]*Neuroscience and Mental Health Institute, University of Alberta, Edmonton, Alberta, Canada*

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Chakravarty S, Chen YY, Caplan JB. Predicting memory from study-related brain activity. *J Neurophysiol* 124: 2060–2075, 2020. First published October 21, 2020; doi:10.1152/jn.00193.2020.—To isolate brain activity that may reflect effective cognitive processes during the study phase of a memory task, cognitive neuroscientists commonly contrast brain activity during study of later-remembered versus later-forgotten items. This "subsequent memory effect" method has been described as identifying brain activity "predictive" of memory outcome. However, the modern field of machine learning distinguishes between descriptive analysis, subject to overfitting, and true prediction, that can classify untrained data. First, we tested whether classic event-related potential signals were, in fact, predictive of later old/new recognition memory (N = 62, 225 items/participant); this produced significant but small predictive success. Next, pattern classification of the multivariate spatiotemporal features of the single-trial EEG waveform also succeeded in predicting memory. However, the prediction was still small in magnitude. In addition, topographic maps suggested individual differences in sources of predictive activity. These findings suggest that, on average, brain activity, measured by EEG, during the study phase is only marginally predictive of subsequent memory. It is possible that this predictive approach will succeed better when other experimental factors known to influence memory outcome are also integrated into the models.

NEW & NOTEWORTHY For both basic and applied reasons, an important goal is to identify brain activity present while people study materials that enable us to predict whether they will remember those materials. We show that this is possible with the conventional event-related potential "subsequent-memory-effect" signals as well as with machine learning classifiers, but only to a small degree. This is in line with behavioral research, which supports many determinants of memory apart from the cognitive processes during study.

event-related potential; pattern classification; prediction; recognition memory; subsequent memory effect

INTRODUCTION

To analyze brain activity underlying successful memory formation, cognitive neuroscientists have adopted the so-called "subsequent memory effect" (SME; Sanquist et al. 1980), contrasting brain activity during the study phase of a task for subsequently remembered (hits) versus forgotten (misses) items. The SME is a major advance over prior methods that compared activity between different encoding conditions rather than relating it to eventual memory outcomes (for reviews of the SME, see Wagner et al. 1999; Paller and Wagner 2002; Kim 2011). The SME approach has produced several highly replicated findings, including the late positive component (LPC) and the slow wave (SW) of the event-related potential (ERP) of the EEG, both more positive for subsequent hits than misses (e.g., Chen et al. 2014; Fabiani et al. 1990; Friedman 1990; Karis et al. 1984; Kim et al. 2009; Sanquist et al. 1980; Smith 1993). The robustness of the SME could be due to the fact that it indexes brain activity that is coupled with behavior. For example, the "levels of processing" concept (Craik and Lockhart 1972) holds that the likelihood of an item being remembered depends on the conceptual depth with which the participant evaluates or interacts with the item during encoding. Evidence has suggested different SME ERPs reflect these different processing-levels (Fabiani et al. 1990; Paller et al. 1987; Sanquist et al. 1980).

Notably, the SME is often described as identifying brain activity "predictive" of memory success (Brewer et al. 1998; Wagner et al. 1998). If truly predictive, the SME could form the basis of important learning applications, such as tracking learning progress or testing the effectiveness of different training protocols (Arora et al. 2018; Fukuda and Woodman 2015). Here, we examine whether "predictive" is an accurate characterization of SME ERP signals. Consider that in the traditional approach SME ERPs are analyzed by the difference in brain activity at study for subsequent hits and misses, averaged across many trials. The hits–misses contrast is tested for statistical significance, with participants as repeated measures. This captures the association between study phase brain activity and memory outcome, but such a descriptive model is not aimed at explaining the causal relationship or making predictions about new observations. To evaluate whether or not memory outcomes can indeed be predicted from the SME ERPs, it is important to apply predictive models, which remain underexplored in this context. Predictive models could be particularly helpful in bridging the gap between the existing theories and the potential learning applications.

Some recent studies suggest that prediction of memory from study activity could succeed with fMRI (Lee et al. 2013; Watanabe et al. 2011) as well as with intracranial EEG recordings (Arora et al. 2018; Ezzyat et al. 2017; Weidemann et al. 2019; Weidemann and Kahana 2019). With standard scalp-recorded EEG, Fukuda and Woodman (2015) showed that two preidentified SME EEG measures, amplitude of the frontal slow wave and occipital alpha band power, could predict the old/new confidence ratings given by the participants at test. Although this is a valuable finding, it skips predicting the memory outcome itself, our current aim. To classify subsequent memory

Correspondence: S. Chakravarty (sucheta@ualberta.ca).

from multivariate EEG activity at study, Noh et al. (2014) used two classifiers. One was trained with prestimulus spectral features. The other used during-stimulus features and was further divided into a time domain and a spectral-domain classifier. Overall classification accuracy was near 60%, but the authors did not report the success rate, alone, of the time-domain signal during stimulus. On the other hand, using only time domain features (pre- and poststimulus onset), Sun et al. (2016) found success in predicting subsequent memory for a majority of their participants ($N = 9$) with a convolutional neural network classifier (mean accuracy: 72.07%), whereas linear classifiers failed to classify the majority. Unlike linear classifiers, nonlinear classifiers (such as convolutional neural networks) can evaluate the interactions between features, which could have led to this difference in success rates. Notably, the number of examples available to build or train these models in this type of context is usually too small for such interactions to be captured reliably. Also, it is possible that in some cases the authors may have tried various variations of the classifier and for various reasons (including length limitations) reported only the best outcomes. This could result in inflated apparent success rates of classifiers (Skocik et al. 2016). In sum, for scalp-recorded EEG, it remains unknown whether highly replicated ERP SME features are predictive. This is an important step in estimating a "benchmark" of predictive strength for this purpose. It is also unclear whether the multivariate time domain EEG signal can be used predictively. One possible limitation of the time domain features is sensitivity to trial-to-trial variability in latency (Luck 2014), which could impact classifier training. Thus, it is possible that researchers have tried and failed in the time domain and opted to stop pursuing this goal in favor of spectral features (i.e., a file drawer problem).

In the present study, we sought to understand the general prospect of using study-related EEG time domain features to predict memory with the help of easy to interpret, linear predictive models. First, using concepts from signal detection theory (Green et al. 1966), we asked if it is possible to predict memory outcome (i.e., hit or miss) for each study item based on previously identified SME ERPs (mean amplitude of the LPC or the SW). We considered the probability distribution of the SME ERP for all the hits versus misses and tested for the amount of separability between these two distributions that could support predictions for individual trials. The predictions were made based on the rule that hits are more positive than misses (for LPC or SW, as per prior findings) and by varying the classification threshold across the two distributions.

Importantly, the SME ERPs were identified through trial averaging and planned comparisons, which could limit their use to predict memory. Trial averages in the traditional descriptive analysis can help raise the signal-to-noise ratio (SNR). But although this step can identify portions of the signal with low variability across trials, it can wash out components with greater variability, which could also carry meaningful information related to memory encoding. With planned comparisons, the electrodes of interest are based on prior studies, thus, possibly missing out on other relevant sources of activity. To move beyond these limitations, our next step was to use multivariate measures that include features beyond those known from the traditional research. The multivariate features were then analyzed with predictive models borrowed from the machine learning literature. These models can automatically learn useful patterns from multivariate measures (Norman et al. 2006) and are trained and tested on separate sets of data to evaluate its generalizability, a practice that checks for overestimation of a model and is not, in general, looked at in descriptive analyses. Thus, with this approach we can ask the more general question: does brain activity during the study phase predict memory at the test phase?

Another motivation for comparing the univariate predictors with multivariate, machine-learning classifiers was that the standard old/new recognition task is arguably impoverished. These kinds of judgments are highly likely to be driven by more than one process, which are reflected in more than one neural activity measure. The multivariate classifiers are designed precisely for problems such as this (multiple predictors). These have the potential to discover multiple processes and produce a combined prediction based upon this process-impure signal. Note that it is also possible to request additional subjective judgments, such as remember/know distinctions or confidence levels, to isolate multiple processes that are thought to underlie memory retrieval, such as recollection versus familiarity. This has frequently been done in previous classifier approaches to study phase as well as test phase activity (Fukuda and Woodman 2015; Liao et al. 2018; Noh et al. 2014, 2018; Sun et al. 2016). However, there is the risk that this approach may alter the way participants approach the task (Eldridge et al. 2002; Hicks and Marsh 1999). Also, this relies on subjects' ability to cleanly separate their own familiarity versus recollection processes (see Dunn 2008, whose state-trace analysis casts doubt on such ability). Moreover, the issue of process impurity likely goes far beyond the recollection/familiarity distinction. Thus, to avoid this, our task included simple instructions for the participants (simply to study for a later memory test) and a simple response (old versus new). This also welcomed subject variability that could reveal interesting individual differences.

Regarding the recollection/familiarity distinction, specifically, the common dual-process view of ERPs in recognition-memory paradigms is that the FN400, an ERP elicited during the test phase of the task, reflects familiarity-based retrieval and the late parietal positivity (LPP), also elicited during the test phase, reflects recollection-based retrieval (e.g., Rugg and Curran 2007). In our data set, both of these signals produced significant old/new effects (see Chen et al. 2014), suggesting that both familiarity and recollection processes appeared at test. This confirms the process impurity of the task. However, the FN400 (contrasting hits versus misses) covaried significantly with performance (d' and negatively with response time) across participants, whereas the LPP did not. This suggests that the putative recollection process, although clearly present, played a far more minor role in driving the old/new judgment than the putative familiarity (or conceptual priming; Voss and Paller 2009) process. This led to clear predictions for the current classifier approach. Because the LPC SME covaried significantly across participants (Chen et al. 2014), with both the FN400 and performance (d' and response time), we expected that the LPC would produce above-chance classification of subsequent hits versus misses. Because the SW SME covaried significantly across participants with the LPP but not with performance measures, we expected that the SW would not be able to classify subsequent old/new recognition above chance. Alternatively, variability reflected by the SW might be unrelated to individual differences but could still support classification above chance when attempted within subjects, as we do here.

MATERIALS AND METHODS

Behavioral Materials and Procedure

Data were from the 64 participants for whom the traditional analysis of ERPs was previously reported in Chen et al. (2014). Of these, two participants were excluded for having more than 15% of the total number of study trials (225) rejected due to artifacts. Participants provided written, informed consent for the procedures. The research was approved by a University of Alberta ethical review board.

The experiment involved alternating study and test phases (Fig. 1). Participants were given a very simple instruction: to study the words for later tests. No instructions related to study strategies were provided. For each study list, they were instructed that they would see 25 words that were to be studied. Participants were not required to make any response during study. For each test list, they were asked to make old/new judgments by pressing the relevant key (1 for old, 2 for new). Words were presented one at a time, both at study and at test. Each study word was displayed on the screen for 1,500 ms with a jittered intertrial interval (300–500 ms). Each study list consisted of 25 words and was followed by a short math distractor task, consisting of five addition or subtraction problems involving integers from 1 to 9. The math problem remained on the screen until the participant made a response. Each test list immediately followed the math distractor task and consisted of 50 words, 25 of which were from the study (i.e., "old") and 25 were lures or "new" words. Each test word remained on the screen until the participant pressed either key. Hits were correctly responded study trials, and misses were incorrectly responded study trials.

EEG Methods

EEG was recorded in an electrically shielded, sound-attenuated chamber, from high-density 256-channel Geodesic Sensor nets (Electrical Geodesics, Inc., Eugene, OR). Signal was amplified at a gain of 1,000 and was sampled at 250 Hz (impedance below 50 kΩ and referenced to the vertex electrode, Cz). EEG signal was preprocessed with the EEGLAB toolbox (https://sccn.ucsd.edu/eeglab; Delorme and Makeig 2004), running in MATLAB. It was bandpass filtered to 0.5–30 Hz and average re-referenced. Independent component analysis (ICA) was used to look for artifacts in the signal (such as eye blinks, muscle noise, etc.). EEG trials were then epoched from 100 ms prestimulus to 1,200 ms poststimulus intervals. After removing the baseline, we used a voltage threshold of 50 μV to remove epochs with large drifts. Additionally, for each epoch, we calculated the difference in voltage between adjacent time samples or the point-to-point difference to detect artifacts. We rejected epochs for which the point-to-point difference exceeded 25 μV. With the voltage and point-to-point difference thresholds in place, more than 15% of epochs were rejected for two participants (16% and 43% epochs rejected, respectively). Data from these two participants were excluded. For all other participants included in this study ($N = 62$), on average, 2 of 225 epochs were rejected (min = 0, max = 23).

EEG Classification

We seek a function f that can predict discrete class labels Y (hit or miss in this case) to each trial X, i.e., $f(X) = Y$. X is a $N \times T$ matrix where N denotes the number of electrodes and T denotes the number of voltage samples as a function of time; $N \in \mathbb{Z}$ and $T \in \mathbb{R}$. Elements of X are called "features." Thus, f transforms the high dimensional space of EEG features to a one-dimensional decision space; f is called a classifier. First, we tested whether classic SME ERPs, such as the LPC or the SW, when computed for individual trials, would be able to predict memory outcome for individual trials better than chance. Next, we tested whether multivariate pattern analysis of EEG trials from the study phase could predict memory outcomes.

Classification based on SME ERPs. Two study-related ERPs were considered, consistent with prior research dating back to Karis et al. (1984): the LPC and the SW, from the centroparietal electrode Pz. LPC is positive going, occurs between 400 and 700 ms after stimulus onset, and more positive for hits than misses. SW is relatively sustained activity, occurring between 700 and 1,200 ms. Across different SME studies, SW is reported for both centroparietal and frontal electrodes. But frontal SW is thought to reflect item-item associations (Kim et al. 2009) or processing of emotional stimuli (Diedrich et al. 1997; Simon-Thomas et al. 2005). Because we used isolated common nouns, we did not expect to see the frontal SW. The SW was subdivided into an early (700–900 ms poststimulus) and a late (900–1,200 ms) component (see Chen et al. 2014).

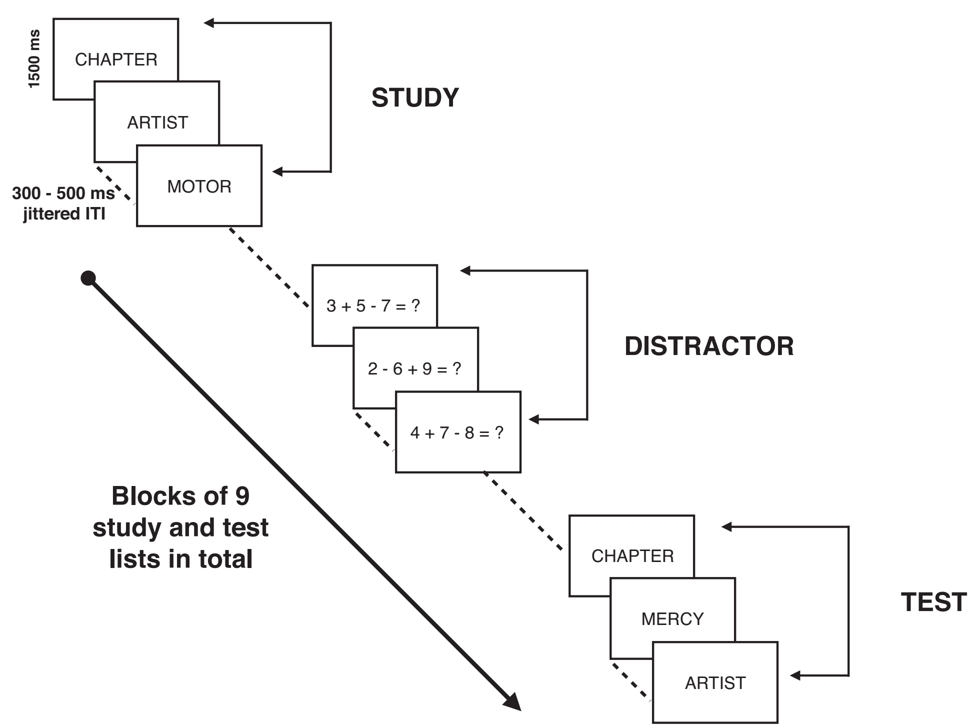

Fig. 1. Experimental paradigm. Participants were asked to study a list of 25 words, presented one at a time at the center of the screen. This was followed by a short distractor task with simple math problems. Participants were then given a set of item recognition tests, judging each word as "old" (targets) or "new" (lures). There were equal numbers of targets and lures in the test phase. This whole process was repeated 9 times, yielding 225 study and 450 test trials. Each study list was unique. The order of the items during study was same as the order of the targets at test, with lures being presented at random positions in the list; lure items were not repeated across lists nor within lists.

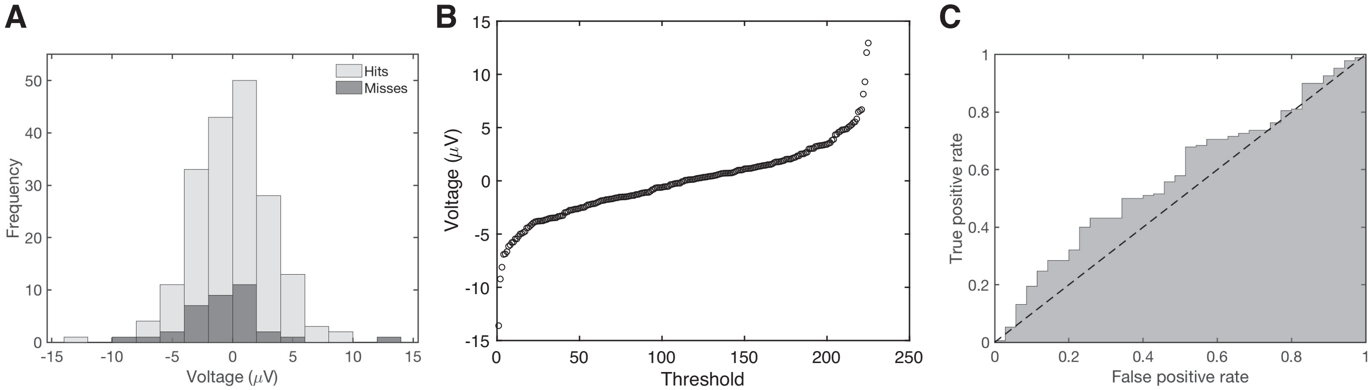

Fig. 2. Demonstration of classification based on subsequent memory effect event-related potentials. *A*: distribution of the late positive component amplitude (from electrode Pz) across all trials for a randomly selected participant. *B*: thresholds used for classification. *C*: receiver operating characteristic curve; shaded region represents the area under the curve. Dashed black line denotes chance.

For each SME ERP and for each study trial, we calculated the mean amplitude from electrode Pz over the respective time window. The classification rule or function, based on prior (descriptive) SME results, was that subsequent hits should have more positive voltage than subsequent misses (Chen et al. 2014; Karis et al. 1984). Then, the receiver operating characteristic (ROC) curve was traced by setting each observed mean amplitude value as a classification threshold and plotting true positives (subsequent hits that were greater than or equal to the threshold) against false positives (subsequent misses that were greater than or equal to the threshold). After obtaining the ROC, the area under the curve (AUC) of the ROC was calculated through trapezoidal numerical integration implemented by the perfcurve function in MATLAB R2018a (see Fig. 2 for a demonstration). AUC indexed the capability of the classifier to make more hits and fewer false alarms. AUC = 0.5 would reflect random predictions (chance), and a perfect classifier would achieve AUC = 1. Also, in this case, AUC < 0.5 would indicate that subsequent misses were on average more positive than subsequent hits.

Multivariate classification. Here, we used multiple EEG features per trial, with the speculation that other study-related EEG features (beyond the known SME measures) could also be informative for making memory predictions. Each EEG epoch had 257 electrodes, sampled at 250 Hz for 1,200 ms; thus, there were over 80,000 features per trial. For computational simplicity, we selected a subset of those. First, since correlations are very common across neighboring electrodes, we selected a set of 10 electrodes that spanned the recording coverage (Fig. 3). Second, we averaged the signal for each electrode over 100-ms time bins, from 0 to 1,200 ms poststimulus onset. The resulting EEG signal consisted of 10 spatial $\times$ 12 temporal = 120 features.

When multiple EEG features are used to make predictions, the classification rule is not known a priori (unlike as above). However, we can learn this through predictive modeling. We used two models, linear discriminant analysis (LDA; Fisher 1936) and linear support vector machine (SVM; Cortes and Vapnik 1995). In general, linear models are advantageous because they are easy to interpret; the weight of a feature in the model indicates its relative importance in the classification. Each model has a set of parameters, values of which are set through examples, also known as "training set." Once trained, the model can generate examples on its own; thus, it can be used for predictions for unseen examples, also known as "testing set."

It is crucial to test the model on unseen examples; for the model could be too specific to the training examples, often by capturing the noise in it (also known as "overfitting") and thus cannot generalize. To reduce overfitting, the weights of the features in the model can be scaled, also known as "regularization." We used a regularized LDA classifier (fitcdiscr, MATLAB 2018a) where the covariance matrix was calculated as:

$$\hat{\Sigma}_\gamma = (1-\gamma)\hat{\Sigma} + \gamma \mathrm{diag}\hat{\Sigma},$$

where $\hat{\Sigma}$ is the empirical, pooled covariance matrix for the two classes, and γ is a regularization parameter lying between 0 and 1. SVM uses support vectors to draw hyperplanes that discriminate between the two classes. The support vectors are examples (here, EEG trials) that maximize the distance between the classes. We can reduce the chance of overfitting of an SVM model by setting a penalty (the box constraint parameter of fitcsvm; MATLAB R2018a) for misclassifying examples that are on the class boundary. The default value for box constraint is 1, and in general, smaller values allow for more regularization. In this study, for all LDA models, we set $\gamma = 1$, i.e., the maximum. For SVM, since a fixed maximum or minimum for the box constraint parameter does not exist, we chose a value that is reasonably smaller than the default value of 1: we set box constraint = 0.05. Importantly, the choice of regularization parameter values was independent of the test sets used to evaluate performance of the classifiers. Note that it is also possible to tune the regularization parameters for individual models. However, this did not alter the results substantially (see Fig. 7).

We tested model performance through 10-fold cross-validation. Trials were randomly split into 10 equal-size folds, with nine folds being used to "train" the model and the remaining fold to "test" it. This

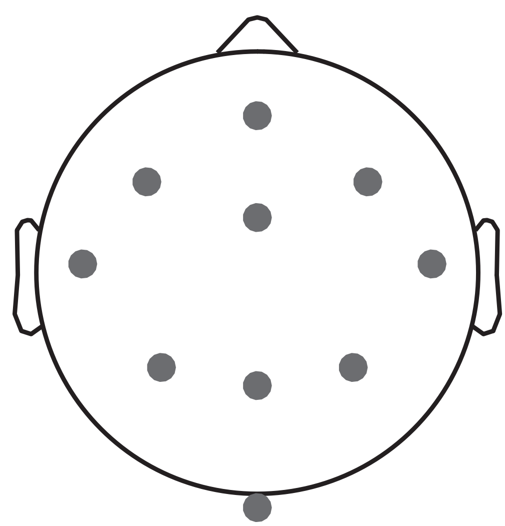

Fig. 3. Selected electrodes for the multivariate classification, roughly distributed equally between the frontal and posterior scalp regions.

was repeated 10 times, ensuring that each trial was once used as a test trial. Cross-validation folds were stratified such that the number of examples for the two classes was the same across all training folds. For each trial in a test fold, the trained classifier computed a "score," which readily translated into the posterior probability of that trial belonging to each class. Probability estimates across all trials for a test fold were then sorted and set as thresholds for calculating the corresponding true-positive and false-positive rates, to trace the ROCs, and to compute the AUC. Average AUC across the 10 test folds was used as the final estimate of the classifier performance.

Note that classifier success can also be evaluated by "accuracy," calculated as: $\frac{(TP+TN)}{(P+N)}$; TP = true positives, TN = true negatives, P = positives, and N = negatives. However, in our data, the two classes, hits and misses, were imbalanced (described in detail in the next paragraph, *Class imbalance*). Since accuracy does not take false alarms into consideration, for imbalanced sets it is possible to achieve very high accuracy when the classifier has a bias to predict the overrepresented class. Thus, we did not use accuracy as the measure for classifier performance.

Class imbalance. In our data, hits were more frequent than misses, making the training sets class imbalanced. This could lead to the classifier getting biased toward learning more about and predicting more frequently the overrepresented class. If this was true, rebalancing the classes either by undersampling the overrepresented class or by oversampling the underrepresented class could be helpful. Due to the small sample size of our data ($\leq$225 in total per participant) we did not use undersampling. Instead, we used the synthetic minority oversampling technique (SMOTE; Arora et al. 2018; Chawla et al. 2002) to create new examples from the existing underrepresented class examples. To create a new example, the algorithm *1*) randomly selects an existing example from the underrepresented class, *2*) randomly selects one example from its k-nearest neighbors (from the same class), *3*) calculates the distance between the two chosen examples, *4*) adds a random number between 0 and 1 to this distance, and *5*) adds the distance (with added random noise) to the first chosen example. The new example, created this way, lies between the original example and its chosen neighbor. We set the number of nearest neighbors in the SMOTE algorithm to four but note that the first nearest neighbor is the example itself. Thus, the effective number of nearest neighbors considered for each example was three. Synthetic minority samples were computed until the total number of examples in the two classes matched. Importantly, we used SMOTE to balance only the training sets. If SMOTE is used to balance the entire data set, it is possible to end up with very similar trials in the training and testing sets, creating a double-dipping problem.

Cluster analysis of LDA weights. For LDA, we can assess the importance of a feature from its coefficient or weight in the model. To check whether any pattern existed in the distributions of feature weights across participants, we performed a cluster analysis in MATLAB (R2018a) using the k-means algorithm (kmeans function from the Statistics and Machine Learning toolbox; Martinez et al. 2017). For a specified number of clusters, n, the algorithm minimizes the within-class variance or the sum of distance of each point in a cluster from the centroid of the cluster. We ran the cluster analysis separately for two, three, four, and five clusters. To avoid local minima, each clustering solution was minimized over 100 replications. For each clustering solution, we calculated the following distance measure for each participant (using the function silhouette in MATLAB R2018a):

$$S_i = \frac{(y_i - x_i)}{\max(y_i, x_i)},$$

where x_i is the average of all distances from the ith participant in one cluster to all other participants in the same cluster, and y_i is the minimum of the average distances from the ith participant to all other participants in all clusters other than its own cluster. This measure can range from -1 (indicating probable wrong assignment of a participant in a cluster) to 0 (participant can belong to either of the neighboring clusters) and up to 1 (participant is distant from the neighboring clusters). A set of two clusters was found to be the best possible solution, with the highest average value for this measure (0.11) across all participants (see Fig. 10 for a visual representation of the distance measures across all participants, separately for the cases of 2, 3, 4, and 5 clusters). To visualize the feature weight pattern for each cluster, we used spline-interpolated topographic plots, created by the topoplot function of the EEGLAB toolbox (Delorme and Makeig 2004). An inverse distance weighting interpolation was used. This means that feature weight values for electrodes that were not used in the classification were calculated from the weighted averages of the same for the electrodes used in the classification.

All analyses were done using built-in and custom-written functions and scripts in MATLAB R2018a. Specific functions from the Statistics and Machine Learning toolbox (Martinez et al. 2017) were also used. Although the classification problem was set up for each participant individually, to gauge overall success of the methods, one-sample t tests (against chance level, 0.5) were done. We also carried out Bayesian t tests using a MATLAB function by SamPenDu (2015). The Bayes factor is the ratio of Bayesian probabilities for the alternative and the null hypotheses: $BF_{10} = \frac{p(H_1)}{p(H_0)}$. By convention (Kass and Raftery 1995), $BF_{10} > 10$ provides strong evidence for the alternate, and $BF_{10} < 0.1$ provides strong evidence for the null. For $BF_{10} > 3$ and $BF_{10} < 0.3$, there is some evidence for the alternate or the null, respectively. Effect sizes of the classifiers were estimated from the 95% confidence intervals (CI). To ensure that our results can be reproduced over multiple runs of the scripts, a pseudorandom number generator algorithm was specified in MATLAB R2018a (Mersenne twister, seed = 0).

RESULTS

We start with the traditional ERP analysis of the subsequent memory effect. Figure 4 presents these ERPs at electrode Pz, averaged across all participants (N = 62), whereby hits appeared to be more positive than misses. Paired t tests between the mean voltage for hits and misses for the LPC was significant; $t(61) = 2.89$; $P < 0.05$. We first examined two measures of the slow wave (see METHODS), as had been reported previously (Chen et al. 2014). The difference was also significant for the early SW; $t(61) = 3.04$; $P < 0.005$. Note that these effects were comparable to those reported by previous studies. For example in Paller et al. (1987),

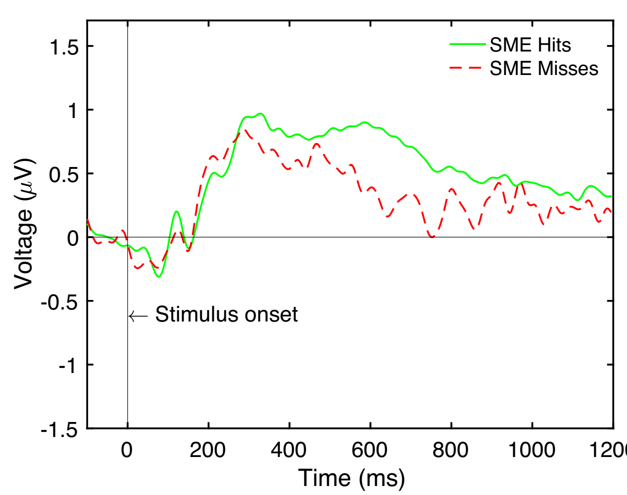

Fig. 4. Grand averaged event-related potentials at electrode Pz for subsequently remembered (hits) and forgotten trials (misses). SME, subsequent memory effect.

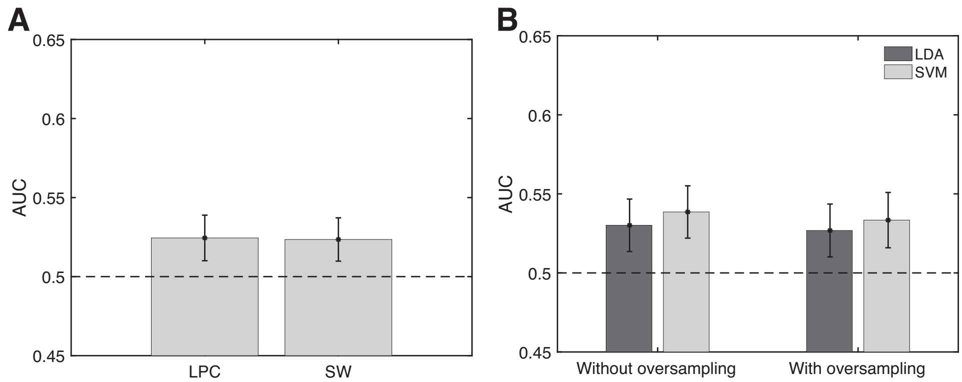

Fig. 5. *A*: classification based on subsequent memory effect (SME) event-related potentials (ERPs): late positive component (LPC) and slow wave (SW) (computed from electrode Pz). Maximum area under the curve (AUC) observed was 0.69 for both LPC and SW (for the same participant). *B*: multivariate classification with linear discriminant analysis (LDA) and support vector machine (SVM) (*left*) and with oversampling to produce balanced classes (*right*). Maximum AUCs observed were 0.69 for LDA and 0.73 for SVM (same participant for LDA and SVM and also same as above). With balanced classes, maximum AUC for both LDA and SVM was 0.69 (same participant for LDA and SVM but different from above). Error bars are 95% confidence intervals. Dashed black line denotes chance level (0.5).

the reported F ratio for the LPC was 8.6; thus, the corresponding t statistic can be estimated to be 2.93 (i.e., square root of the F ratio), which is very similar to that of the present study. However, the ERP effect was not significant for the late SW; $t(61) = 1.82$; $P = 0.07$. We also calculated the Bayes factor, BF_{10}, which showed some evidence for the subsequent memory effect for the LPC ($BF_{10} = 6$) and the early SW ($BF_{10} = 9$) but was inconclusive for the late SW ($BF_{10} = 0.7$).

Next, we tested whether these known SME ERP measures could predict subsequent memory for individual trials. Since the ERP effect for the late SW was not significant, we did not include it in this analysis. Accordingly, from here on, we refer to the early SW simply as SW. We found that for both ERP measures (Fig. 5), AUCs (across all participants) were significantly above chance (0.5); $t(61) = 3.31$; $P < 0.005$; $BF_{10} = 18$ for LPC, and $t(61) = 3.35$; $P < 0.005$; $BF_{10} = 19$ for SW. However, in each case, the 95% CIs for the AUCs were close to chance; [0.51 0.54] for both LPC and SW. Also, across participants, AUCs were significantly correlated between the LPC and SW measures, $r(60) = 0.65$; $P < 0.0001$ (Fig. 6). This could be due to the general temporal autocorrelation property of the EEG signal. In sum, classification of single trials from the study phase using a priori measures achieved small but significant success.

Next, we tested whether multivariate brain activity from the study phase, as measured with EEG, could predict subsequent memory and whether it can do so better than the individual SME ERPs. As noted in METHODS, we selected a set of 10 electrodes and 12 time samples, i.e., 120 features in total. We used two linear classifiers: LDA and linear SVM, along with a stratified 10-fold cross validation technique. AUCs were averaged across the 10 folds. To reduce chances of overfitting, we used regularization; the regularization parameters were set to be constant across the models (also, optimizing these parameters for individual models did not alter our results; see Fig. 7). Across participants, the AUCs for both LDA and SVM (Fig. 5*B*, *left*) were significantly better than chance, $t(61) = 3.54$; $P < 0.001$; $BF_{10} = 33.54$ for LDA, and $t(61) = 4.55$; $P < 0.0001$; $BF_{10} > 500$ for SVM. The corresponding 95% confidence intervals were [0.51 0.55] for LDA and [0.52 0.56] for SVM. Also, pairwise one-tailed t tests showed that SVM performance was significantly greater than the SME ERP-based classifiers [SVM versus LPC: $t(61) = 1.83$; $P < 0.05$; $BF_{10} = 1.28$; SVM versus SW: $t(61) = 1.76$; $P<0.05$; $BF_{10} = 1.13$]. However, this was not true for LDA [LDA versus LPC: $t(61) = 0.62$; $P = 0.27$; $BF_{10} = 0.24$; LDA versus early SW: $t(61) = 0.70$; $P = 0.24$; $BF_{10} = 0.26$]. Given that the multivariate models had more degrees of freedom than the SME ERP-based classifiers, these results suggest that, overall, the time domain EEG signal during the study phase is only marginally predictive of subsequent memory success. Moreover, predictive success was positively correlated between LDA and SVM (Fig. 8*A*), $r(60)=0.74$, $P < 0.0001$, suggesting that participants who were easier to classify by one method were also easier to classify by the other.

Notably, for both LDA and SVM, a small subset of participants was found to have AUCs far below chance (Fig. 8*A*). This is possible, for the assumption of a symmetric null distribution for the classifier performance may not hold in the case of small sample size data with small effect size (Jamalabadi et al. 2016). In that case, nonparametric tests may be better suited. Following up on this, for each participant we conducted a Mann–Whitney U test between the AUC values for all of the 10 folds and chance (0.5). Then, we calculated the z transform of the U statistic.

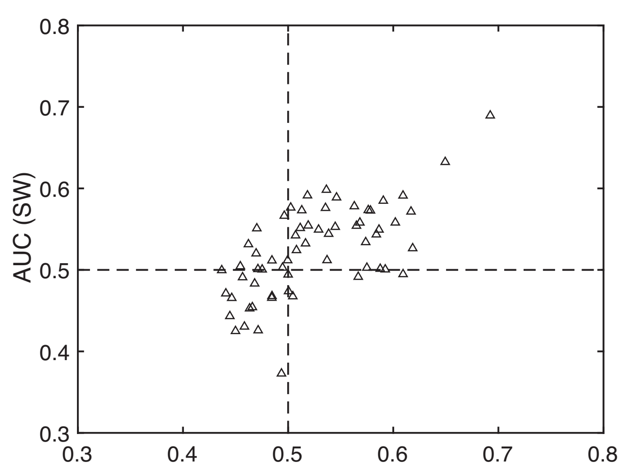

Fig. 6. Correlation between areas under the curve (AUCs) for late positive component (LPC) and slow wave (SW). Dashed lines denote chance.

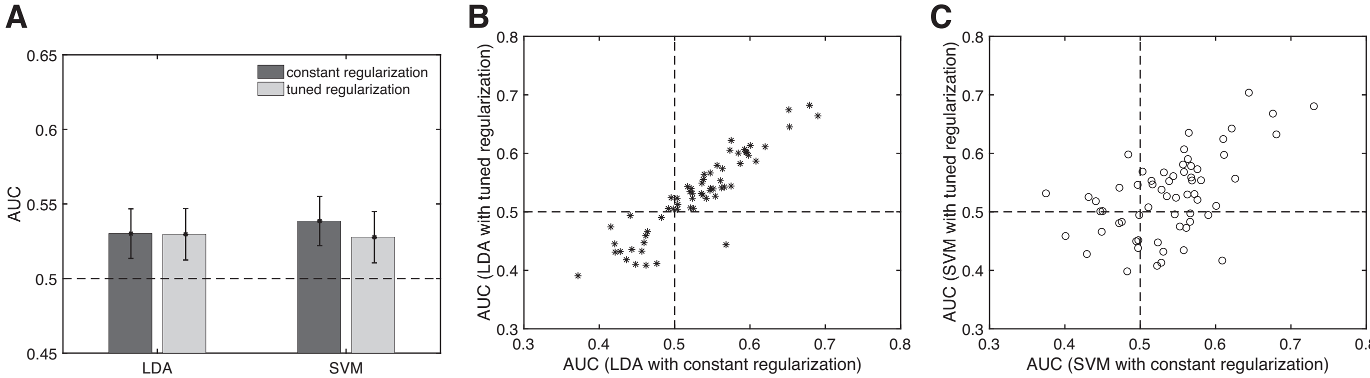

Fig. 7. Effect of tuning the regularization parameters gamma of linear discriminant analysis (LDA) and box constraint of support vector machine (SVM). We used a nested cross validation procedure. For the outer cross-validation, data were randomly partitioned into 10 stratified folds, 9 folds being used for training and 1 for validation. Then, the training data were subjected to an inner 9 fold stratified cross-validation to tune the regularization parameter. For each training set of the inner cross-validation, separate LDA models were trained for gamma = (0, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1). Similarly, for SVM, separate models were trained for box constraint = (0.001, 0.005, 0.01, 0.05, 0.1, 0.5, 1, 5, 10, 50, 100). Then, performance for these models was computed for the test folds of the inner cross validation. Value of the regularization parameter corresponding to the model with best performance was selected. Then, this value was used in the model for the training data of the outer cross-validation and then tested with the left-out validation set. Finally, areas under the curve (AUCs) were averaged across the 10 validation sets. *A*: overall effect of tuning the regularization parameters for each model. *B* and *C*: AUCs for individual participants with constant and tuned regularization parameters.

Finally, we used *t* tests to check if the *z* scores across all participants were significantly different from zero. This showed that the *z* scores for both LDA and SVM were significantly positive: [LDA: $t(61) = 2.55$; $P < 0.05$; $BF_{10} = 3$, SVM: $t(61) = 3.13$; $P < 0.005$; $BF_{10} = 11$]. This confirms that even if the assumption of symmetry for the null distribution was relaxed, the LDA and SVM classifiers in our study were overall better than chance.

Imbalanced classes might have challenged classifier training. Alternatively, participants with better memory may have a greater signal-to-noise ratio (SNR) that the classifier could identify. Across participants, a weak positive trend (Fig. 9, *A* and *B*) was observed between AUCs and the proportion of hits. This trend was significant for SVM: $r(60) = 0.38$, $P < 0.005$ but not for LDA, $r(60) = 0.21$, $P < 0.09$. We also calculated the sensitivity index or d' of participants performance, which showed similar results as the proportion of hits [LDA: $r(60) = 0.14$, $P = 0.29$; SVM: $r(60) = 0.28$, $P < 0.05$]. To investigate whether the imbalance between the trial numbers for hits and misses influenced our classifier results, we balanced the trials by oversampling the misses with SMOTE (see METHODS; Chawla et al. 2002). AUCs (Fig. 5*B*, *right*) were yet again significantly above chance [LDA: $t(61) = 3.13$; $P < 0.005$; $BF_{10} = 10.91$, SVM: $t(61) = 3.72$; $P < 0.001$; $BF_{10} = 57$]. However, the 95% CIs were not better than that without oversampling (LDA: [0.51 0.54]; SVM: [0.52 0.55]). Predictive success remained positively correlated across LDA and SVM, $r(60) = 0.80$, $P < 0.0001$ (Fig. 8*B*). Thus, while imbalanced classes often pose a challenge to classifier training, in this case, it could not account for the relatively small prediction rate. Instead, participants with better recognition memory appeared easier to classify (see DISCUSSION for implications of this). The positive trend between classifier performance and proportion of hits was also observed after the classifiers were trained with balanced classes [LDA: $r(60) = 0.14$, $P = 0.29$; SVM: $r(60) = 0.13$, $P = 0.31$]. For SVM, when participants with very low AUCs (< 0.45) were excluded, this trend was significant, $r(51) = 0.28$, $P < 0.05$. However, classifier performance did not correlate with d' in this case.

For participants with LDA AUCs above 0.5 ($N = 43$), we wondered which features were deemed more important by the classifier for the classification. A cluster analysis of the LDA feature weights revealed two subgroups of participants with distinct patterns (see METHODS and Fig. 10). $N = 22$ participants were found to be in *cluster 1* and $N = 21$ in *cluster 2*. Figure 11 shows the topographic plots for the LDA feature weights, averaged across all participants in each cluster and for three different time windows: 0–100 ms, 501–600 ms, and 1,001–1,100 ms

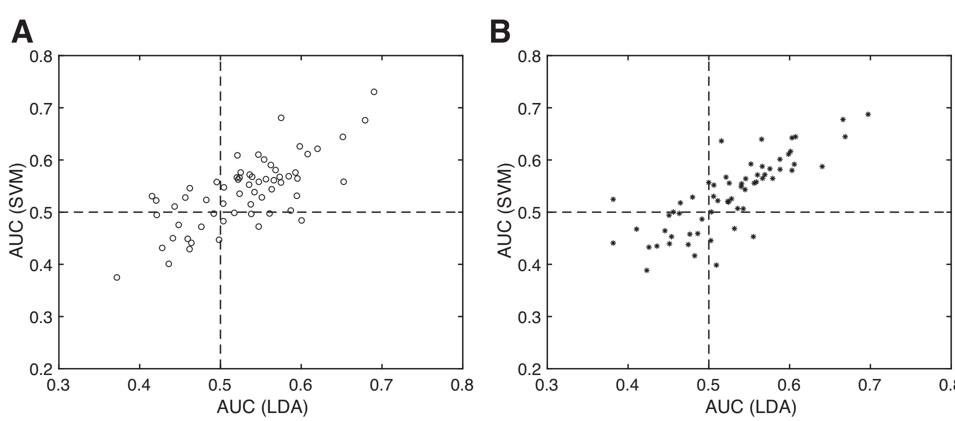

Fig. 8. Correlation between areas under the curve (AUCs) for the 2 classifiers linear discriminant analysis (LDA) and support vector machine (SVM) with (*A*) and without (*B*) balanced classes for training. Dashed black lines denote chance.

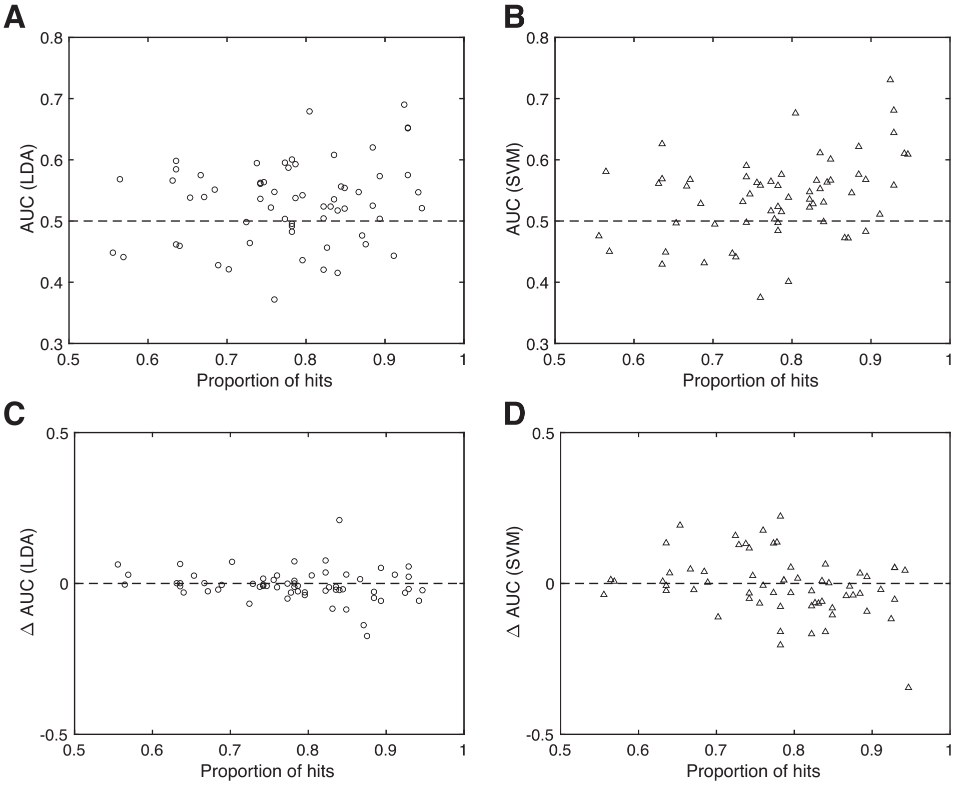

Fig. 9. Relationship between classifier performance [area under the curve (AUC)] and proportion of hits for linear discriminant analysis (LDA; *A*) and support vector machine (SVM; *B*). Percent change in classifier performance (ΔAUC) after oversampling, separately for LDA (*C*) and SVM (*D*).

(see Fig. 16 and Fig. 17 for the full version, i.e., for all the time windows). For *cluster 1*, for the very early 0- to 100-ms time window, greater feature weights were observed on the left and right parietal regions. On the other hand, for *cluster 2*, for the same time window, greater feature weights were observed in the frontocentral region. Given that these earlier time windows are more likely to reflect perceptual processing, one possibility is that these differences in feature weight patterns are indicative of the potential difference in attentional mechanisms between the two clusters. For a later time window, 501–600 ms, which is closer to the onset of LPC activity, only *cluster 1* showed greater weights for the central parietal scalp region, whereas for *cluster 2*, greater weights were observed more widely in the right frontal and parietal regions. Thus, the topographic plot for *cluster 2*, for 501–600 ms did not resemble the posterior positivity feature observed in the SME ERP analysis of this data set (see Chen et al. 2014). For an even later time window, 1,001–1,100 ms, the patterns for the two clusters were almost orthogonal: *cluster 1* showed greater weights in the left parietal region, whereas *cluster 2* showed greater weights in the frontal and slightly left parietal region. It is possible that this difference is indicative of potentially different spontaneous study strategies between the participants of the two clusters.

We were also curious as to whether the standard SME ERP effects might be different for the two clusters. Investigating this, follow-up analysis of the corresponding ERPs at electrode Pz (Fig. 12) showed a general trend for hits to be more positive than misses (i.e., the classic subsequent memory effect) for both clusters. However, this trend was clearly more pronounced for *cluster 1* than for *cluster 2*. We conducted a 2×2 ANOVA on mean LPC amplitude with the within-subject factor memory success (hit versus miss) and between-subject factor cluster (*1* and *2*). This revealed a significant interaction between the two factors $F(1,41) = 15.72$; $P < 0.001$; $\eta_p^2 = 0.28$; whereas the LPC effect was significant for *cluster 1*, it was not so for *cluster 2*. The same ANOVA design on the mean amplitude for SW also showed similar results. The average LDA AUC for *cluster 1* was similar to that of *cluster 2* (mean ± SD of AUC for *cluster 1* = 0.56 ± 0.05; for *cluster 2* = 0.57 ± 0.04), and the average proportion of hits was comparable between *clusters 1* and *2* (mean ± SD for proportion of hits for *cluster 1* = 0.79 ± 0.11; for *cluster 2* = 0.80±0.08). The d' values were also comparable between the two clusters (mean ± SD for d' for *cluster 1* = 2.13 ± 0.62; for *cluster 2* = 2.09 ± 0.87). Overall, this could suggest that there may be at least two different types of feature patterns that could form the basis for predicting memory.

DISCUSSION

The subsequent-memory approach is often referred to as identifying brain activity "predictive" of memory. However, limited attempts have been made to test this claim with actual predictive models. Here, using signal detection theory, we showed that two previously identified SME ERPs, namely, the LPC and the SW, could indeed predict memory (hit or miss) for individual trials in a word recognition task. However, across participants (N = 62), the success rate was small. Considering that the SME approach is limited by many factors, such as planned comparisons and trial averaging, the small success may be expected. Also, multiple processes could be at play for memory judgments in a recognition task, each associated with different sources of neural activity. Thus, instead of single ERPs, analysis of patterns in the multivariate EEG waveform at study may fare better at predicting memory. To test this, we employed

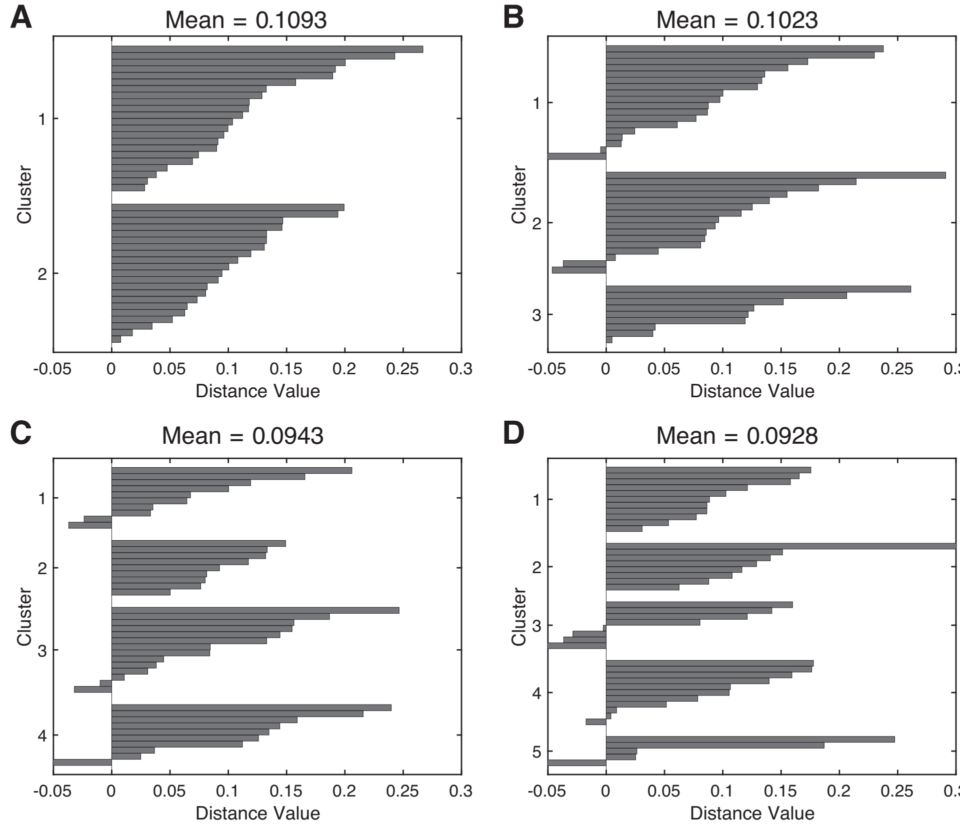

Fig. 10. Determining the correct number of clusters for the cluster analysis of linear discriminant analysis feature weights. Each plot shows the distance measure for each participant for their respective clusters: 2, 3, 4, and 5 clusters (*A–D*). Average distance scores across all participants are listed on *top* of the plot. For a set of 2 clusters (*A*), this measure was the highest. Also, all participants show positive distance scores for a set of 2 clusters.

machine learning classifiers (LDA and linear SVM), which are well suited to analyze multivariate structures. These models were used to learn memory-relevant patterns from a set of 120 spatiotemporal EEG features from individual study trials. Both LDA and SVM achieved significant success in predicting memory, albeit still with a small success rate. Since generalization was also accounted for in LDA and SVM with 10-fold cross validation, the success of these models further strengthens the possibility of predicting subsequent memory from EEG activity at study. However, when LDA and SVM performance was compared with that of the LPC- or SW-based classification, only SVM showed a small significant improvement. Thus, despite the considerably greater degrees of freedom, these models did not offer an obvious improvement over classification with LPC or SW alone. But, interestingly, exploratory analysis on the features of importance to the LDA classifier showed that there were two subgroups of participants with seemingly different activity patterns. On average, one of these subgroups (*cluster 1*; see Fig. 16) showed greater feature weights for the posterior scalp region, which is similar to the findings from the univariate ERP analysis of the same data set (see Chen et al. 2014). It also agrees with previous SME ERP studies that have shown that memory success can be associated with a greater positive going signal over the parietal region (for a review, see Paller and Wagner 2002). However, for the other subgroup (*cluster 2*; see Fig. 17), greater weights were observed in the frontal region. Furthermore, post hoc analysis of SME ERPs at electrode Pz, separately for the two subgroups, showed significant LPC as well as SW effects for *cluster 1* but not for *cluster 2*. Interestingly, previous literature also suggests that a frontal slow wave may be invoked by associative processes whereas the posterior slow wave may reflect elaborate item-oriented processing (e.g., see Kamp et al. 2017). Although we cannot know this for sure, one possible reason for the involvement of the frontal region in *cluster 2* could be that it reflects some associative strategies for learning, spontaneously undertaken by the participants in this group. Notably, it would not be possible to identify these subgroups without the classifier models. Thus, both the univariate and the multivariate predictive analysis reported in the current study have their own merits. Below, we discuss potential improvements and limitations toward predicting memory.

We sought to understand the general level of challenge in predicting memory from EEG activity during the study phase. Unlike other approaches, where failed or less successful analyses might not be disclosed, so that the degree to which best cases are reported becomes impossible to judge, we report a systematic sequence of classification analyses to avoid apparently inflated success rates. We did not exclude participants based on their performance in the task, which is commonly done (Noh et al. 2014; Sun et al. 2016; Watanabe et al. 2011). Thus, although the 95% CIs of our classifier success are modest for the aggregate, the regression (Fig. 9*B*) suggests meaningfully large classification success rates. Also, to avoid any possible circularity in the analysis, we did not select the multivariate features based on the univariate SME results (Coutanche 2013; Noh et al. 2014). Instead, we selected those features based on the general EEG knowledge (scalp coverage, correlations, etc.), which

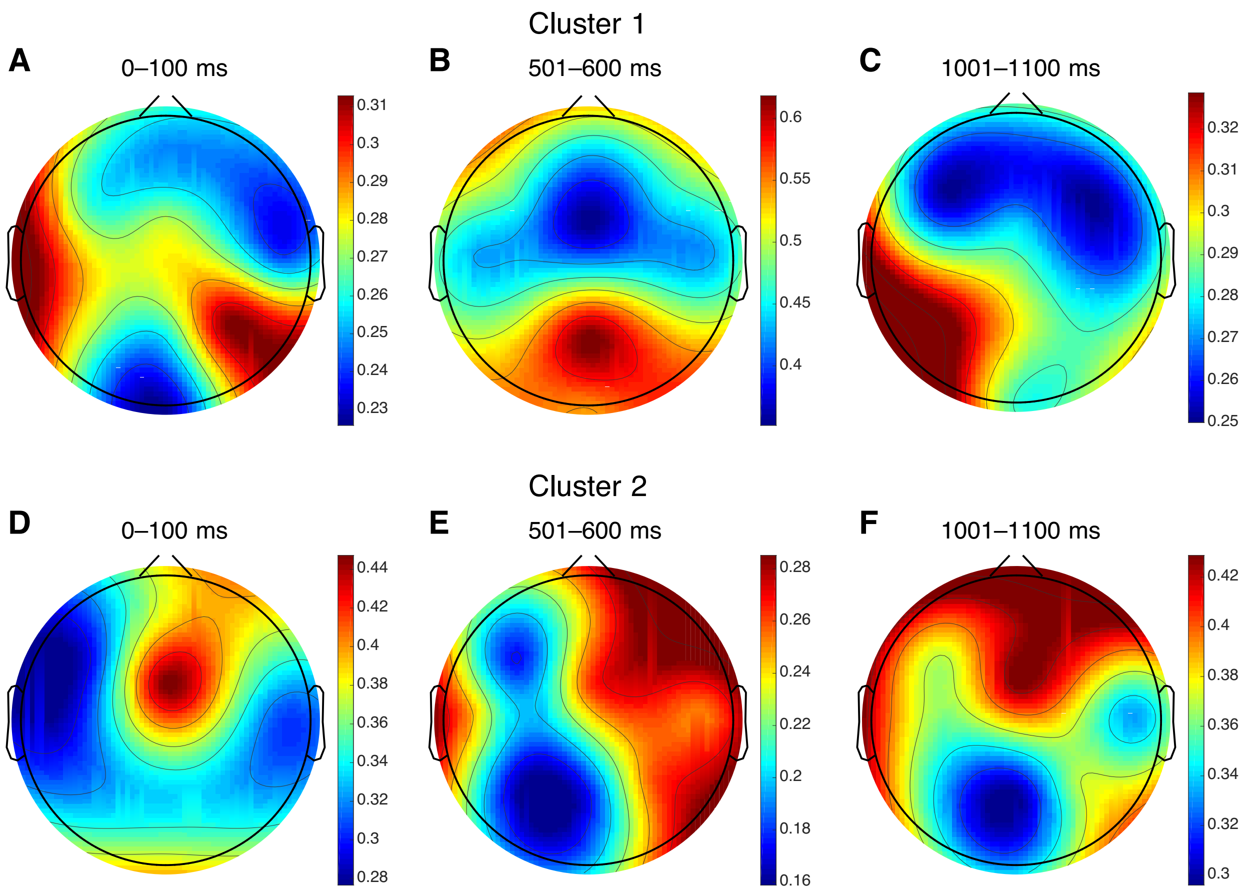

Fig. 11. Cluster analysis of feature weights for all participants with linear discriminant analysis area under the curve> 0.5. Set of 2 clusters best explained our data ($N = 22$ for *cluster 1* and $N = 21$ for *cluster 2*). *A–C*: *cluster 1*. *D–F*: *cluster 2*. Colors are range scaled. Note that the color scale varies across panels. See Figs. 16 and 17 for full version of this figure.

substantially minimizes the chance of overestimating the effect. Thus, our results provide a benchmark for the effect size for this type of classification to be compared against. This could improve with more fine-grained analysis, for example, through other feature selection or feature reduction methods or even with the help of nonlinear classifiers including state-of-the-art neural networks. Including EEG spectrogram features, which are more resilient to trial-to-trial latency fluctuations, may also lead to better performance (Ezzyat et al. 2017; Weidemann et al. 2019).

Notably, class imbalance (hits versus misses) was common in our data set, and this could have biased the training of LDA and SVM toward the overrepresented class (hits). However, rebalancing classes offered no improvement, allaying such concerns, at least in our case. Alternatively, it is possible that participants with more hits also had high-SNR brain activity, which could have helped the classifier. We found some support for the latter, as SVM performance increased significantly as the proportion of hits increased (for similar evidence, see Arora et al. 2018). Whenever memory was close to chance, the corresponding brain

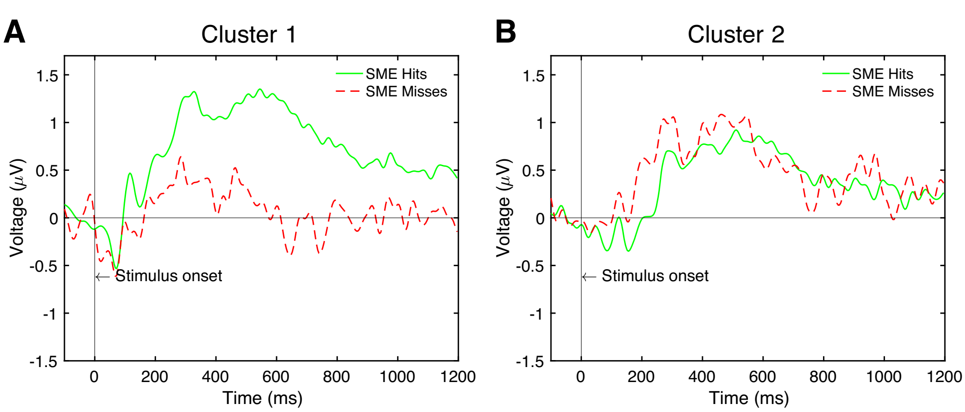

Fig. 12. Event-related potentials at electrode Pz for the 2 clusters obtained through k-means clustering of linear discriminant analysis feature weights.

activity may have had less information for the classifier to pick up on. Conversely, participants who performed better might, to some degree, have been those who (and whose brains) were more engaged in the task, producing higher task relevance of their brain activity.

Although we cannot know for sure why better-performing participants may be easier to classify, two causes come to mind. First, some lower-performing participants might have low motivation, a plausible possibility, given that participants did not self-select as research participants but were recruited from a course-based research participation pool, in exchange for partial course credit. There was no disincentive to speed through the experiment or disengage from the task. For such participants, brain activity may simply not be task relevant. Second, participants who struggle with the task more, genuinely finding the task challenging, may have task-related brain activity that is more variable or obscured by cognitive processes related to frustration or strategic exploration, etc. Both causes could lead to lower SNR. In future studies, this could be addressed by precalibrating the task for each participant to equate difficulty across the sample and to increase the level of motivation across participants, for example, through rewards. Both of these modifications might produce substantially higher levels of classifier success as well across the sample.

One may conclude that, due to individual variability in performance and likely in brain activity too, a large sample size, as in our study, is essential to obtain overall significant results with the classifiers. To test this idea, we estimated the minimum sample size we might have needed for the classifier analysis to succeed. With bootstrap techniques, we tested significant effects for the SVM classifiers for different sample sizes, ranging from 6 to 62 participants, who were selected at random and without replacement. For each sample size, we generated 100 sets of participants and for each set we calculated one sample t test to check whether the corresponding SVM AUCs were significantly better than chance. Then, across the 100 sets, we calculated the average effect or the probability of obtaining AUCs that were not overall significantly better than chance. This showed that the probability of obtaining a nonsignificant effect for SVM decreases very sharply with increasing sample size (Fig. 13), up to $\sim$30 participants. For sample sizes greater than 30, this probability is very close to zero. Thus, we were not after a result that was only made possible by a large sample size. In fact, in many cases, a sample size of $\sim$15 participants may be enough to obtain significant results (probability for a nonsignificant effect < 0.5; see Fig. 13), provided that the number of trials per participant is high or at least comparable to that in our study. Thus, it is conceivable that Sun et al. (2016) failed to find overall success with simple linear classifiers due to small sample size ($N = 9$). Interestingly, some of the early, influential, SME ERP studies do not pass this sample size ($N > 15$) criterion (Brewer et al. 1998; Karis et al. 1984; Neville et al. 1986; Sanquist et al. 1980; Wagner et al. 1998). Others do so (Friedman 1990; Otten and Rugg 2001; Paller et al. 1987; Smith 1993; Van Petten and Senkfor 1996); however, many of these also have considerably lower trial counts.

Many decades of behavioral research (Humphreys et al. 1989; Kahana 2012; Lewis 1979; Neath 1998) points to numerous factors that determine memory success that should not be visible through the lens of study-related activity alone (for an alternate account, see Weidemann and Kahana 2019). Examples

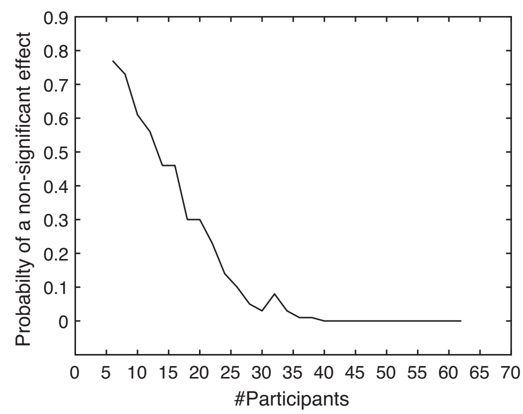

Fig. 13. Effect of sample size on overall significant results for support vector machine (SVM). With 1-sample t tests, we calculated whether SVM performance was significantly better than chance for different sample sizes, ranging from 6 to 62 participants. For each sample size, participants were selected at random and without replacement. In addition, for each sample size, we collected 100 sets of participants. The y-axis shows the probability of obtaining a nonsignificant effect, calculated across these 100 sets and for each sample size.

include competition from other items at retrieval, nature of the retrieval task (such as recognition, free recall, serial recall, cued recall, word stem completion, word fragment completion, lexical decision), retrieval time, output encoding, rehearsal, and response criterion (recognition tasks). The serial positions of the items in the studied list can also influence subsequent memory (for example, primacy and recency effects) and are possibly reflected in brain activity as well (Rushby et al. 2002; Sederberg et al. 2006; Talmi et al. 2005). However, these factors are usually not accounted for in the SME approach. In addition, the Encoding Specificity principle (Tulving and Thomson 1973) suggests that remembering will be more successful when there is a good match of context between study and test than when they mismatch (for an alternate account, see Nairne 2002). Context could be spatial/environmental, temporal, or internal mental or physical state (Howard and Kahana 2002). This study-test contextual match is also overlooked with the SME. Brain activity indexed by the SME may also relate to experimental manipulations such as attention (Otten and Rugg 2001; Paller et al. 1987; Summerfield and Mangels 2006), intentional learning (Karis et al. 1982; Paller 1990), use of different learning strategies (Karis et al. 1984; Rugg and Curran 2007), etc. Semantic congruity of the to-be-remembered stimuli (Neville et al. 1986) as well as the type of the stimulus (for example, verbal, pictorial, abstract patterns, etc.; see Fabiani et al. 1990; Friedman 1990; Paller et al. 1987; Van Petten and Senkfor 1996) can also influence the SME. Also, study and test phases are temporally distinct, but some aspect of brain activity may covary across these two phases (Chen et al. 2014), and test activity (Rugg and Curran 2007) is also an important determinant of memory. Brain activity at retrieval may even be more reflective of important determinants of memory success (Polyn et al. 2005; Weidemann et al. 2019), including item distinctiveness (LaRocque et al. 2013). Clearly, memory encoding is multifaceted, and thus, a more extensive model that incorporates different cognitive measures as well as measures of brain activity may be more effective in predicting memory (Halpern et al. 2018).

Accordingly, it is likely that our current classifiers are underperforming their potential. One important factor missing from

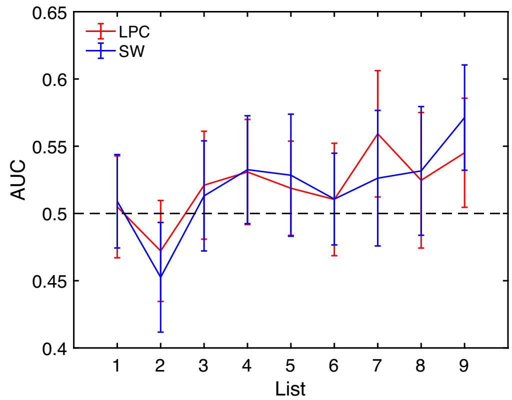

Fig. 14. Classification of hit versus miss trials for each list in the task, based on the late positive component (LPC) and slow wave (SW) event-related potential measures. Error bars are 95% confidence intervals. Dashed line refers to chance performance. Lists with all hits or all misses were excluded. AUC, area under the curve.

the SME approach and possibly influencing our classifiers is that retrieval performance is, to a large extent, competitive. Thus, the probability of remembering an item depends not only on the corresponding EEG activity for that item at study but also on the EEG activity during the study of other items. Also, over the course of an EEG recording session, there is usually drift in the signal, mainly due to the electrodes drying out or sliding. Additionally, it is also possible that, as the task progresses, the participant shifts their strategy or approach toward the task. All of these factors could influence the classification. To test this, with the LPC and SW classifiers, we calculated classification performance separately for each of the nine lists studied by each participant (Fig. 14). Lists with all hits or all misses were not included. Indeed, the classification improved as the task progressed. Linear regressions between average AUC (across participants) for each list and list number (1 to 9) were significant, for both LPC [$F(1,7) = 6.34$; $P < 0.05$] and SW [$F(1,7) = 7.35$; $P < 0.05$]. Similar trends may also be possible for the multivariate classifiers, but due to the very small number of trials available per list for training the models, we did not follow up on that. However, performance measures such as d' or the proportion of hits for individual lists did not vary significantly with list number.

Also, given the wealth of research on distinctions between recollection- and familiarity-based retrieval, one important future direction could be to incorporate those distinctions into the classification, as indeed has been done by some previous studies (Fukuda and Woodman 2015; Liao et al. 2018; Noh et al. 2014, 2018; Sun et al. 2016). As with incorporation of other relevant variables (previous two paragraphs), this could improve classification accuracy. Two classifiers could be trained, one to classify based on a familiarity-like signal and one based on a recollection-like signal. The two classifiers could then be combined to produce a higher overall classification success rate. However, the subjective responses distinguishing recollection versus familiarity might be variable, in themselves, and thus introduce noise into the classification. Moreover, Dunn (2008) showed that remember/know judgments themselves appear to be based on a summation of recollection and familiarity evidence. Thus, alternatively, it could be more effective to let a multivariate classifier "discover" the two (or more) neural processes and their optimal summation weights.

Importantly, in the traditional ERP or other similar univariate analysis, brain activity is averaged over many trials to increase the signal to noise ratio. Then, measures from this averaged brain activity signal are computed for behavioral conditions of interest and are compared across participants. With this approach, we may be able to identify some components of brain activity relevant to that behavior; it should also be considered that the brain itself does not compute such averages to produce the behavior. Instead, this is produced by the firing of networks of neurons. In that sense, the classifiers, which learn from the multivariate pattern of brain activity specific to individual events, may be closer to the way the brain works than the traditional approach. However, since the classifiers are driven by the data only, it is also possible for them to learn relations that are different from what actually produces behavior. Thus, obtaining a function-to-structure map of memory may also be inaccessible with present methods of obtaining brain activity measures (Henson 2005). The two different clusters of participants identified here could reflect individual variability in studying the same information, for example, use of different strategies. Classifiers could also be showing differences due to the word stimuli (frequency, imageability, etc.).

Also, if the EEG activity from study can predict memory, then, hypothetically, it could also be used to guide restudy, as attempted by Fukuda and Woodman (2015). But in their case, the restudy rerandomized the relationship between initial study-related EEG activity and eventual memory outcome. It is possible that, when enforcing better learning for stimuli tagged as "likely to be forgotten" by the classifier, stimuli that were initially more likely to be remembered become weakened. If the goal is only to be able to predict memory, it may be possible to find differences that lead to some classifier success, which is appreciated, but to be employed in a memory training framework, we may need to isolate EEG activity that taps into truly effective encoding processes.

In doing so it may also be possible to find memory-relevant neural activity patterns that generalize not only within the trials for one participant but also across multiple participants. This is an interesting future direction, and very few studies have attempted

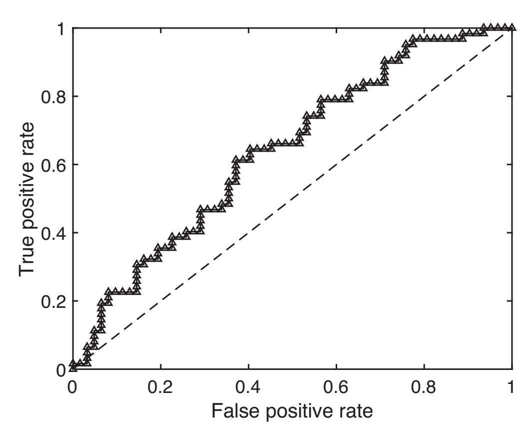

Fig. 15. Receiver operating characteristic curve obtained from between-subject classification of the average EEG waveform at study for hit versus miss events, with linear support vector machine. Dashed line denotes chance.

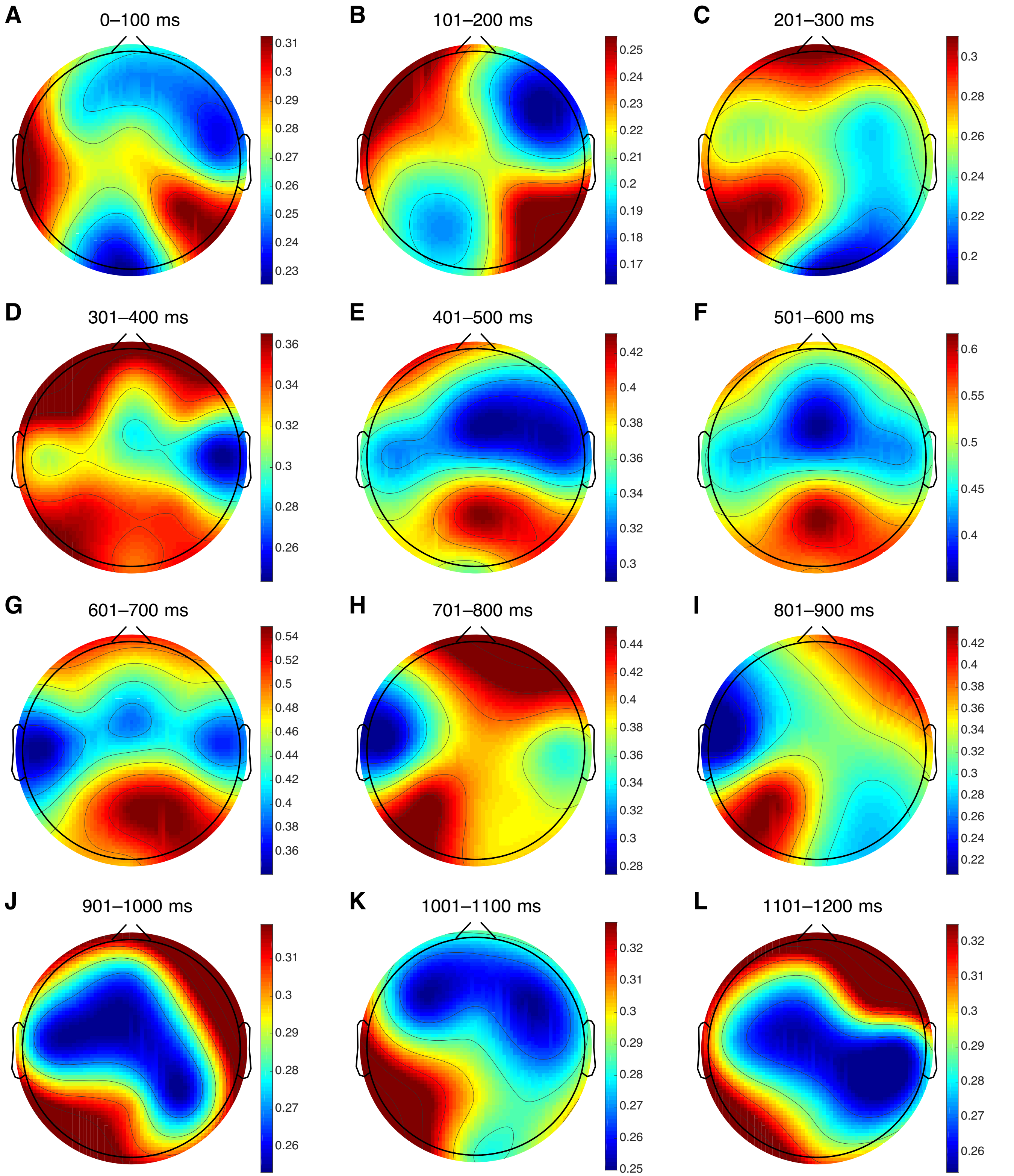

Fig. 16. Topographic plots showing linear discriminant analysis feature weights averaged across all participants in *cluster 1* ($N = 22$). Colors are range scaled and the scale varies across panels.

"between-subject" prediction of memory (Koch et al. 2020; Liao et al. 2018). Specific to EEG, Liao et al. (2018) found some success with the test phase activity. However, their experiment requested additional subjective judgments from the participants, such as remember-know as well as source and confidence judgments. Accordingly, the between-subject classifiers were set up to predict memory outcomes that were constrained to these additional judgments rather than simple old/new responses. Thus,

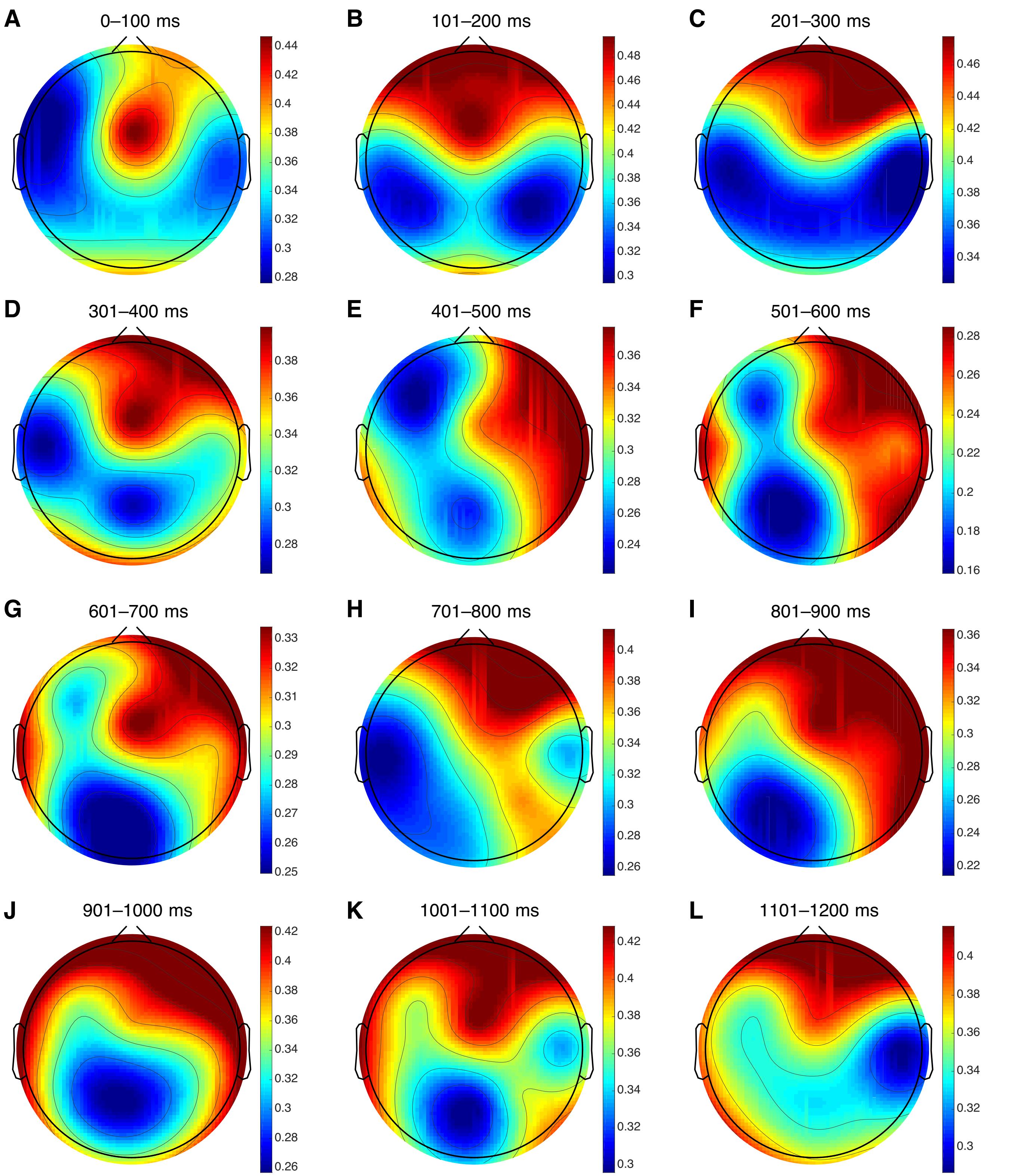

Fig. 17. Topographic plots showing linear discriminant analysis feature weights averaged across all participants in *cluster 2* ($N = 21$). Colors are range scaled and the scale varies across panels.

although their results cannot be compared directly with the current study, we were curious whether between-subject prediction for hits versus misses is possible with the study phase EEG activity in our data set. However, given the small success rates of the within-subject classifiers, we suspected that this might fail. We tested this with a leave-one-subject-out cross-validation procedure. Data from one participant were selected at random and used as the test set. Data from all other participants were used to train the classifier. We chose linear SVMs, as our results show these may be better than the LDA. The leave-one-subject-out cross-validation was repeated 62 times, i.e., until data from each participant were used as the test set. This produced AUCs greater than 0.5 for 34 of the 62 participants, i.e., for ~54% of the total sample, thus it was not significant across participants: $t(61) = 0.98$; $P = 0.33$; $BF10 = 0.22$.

Also, with fMRI, Koch et al. (2020) were able to predict the average encoding pattern between their participants. Following this idea, we checked whether we could predict the average EEG waveform at study for hit and miss events for a participant, based on the same for the other participants. Once again, we used leave-one-subject-out cross-validation and linear SVM classifiers. Also, since in this case east test set had only two trials (averaged waveform for hit and miss), instead of calculating AUCs for individual participants, we pooled together the classifier scores across subjects to calculate the ROC and the AUC of the ROC. Furthermore, we used 1,000 bootstrap samples to calculate the 95% CI of the AUC. This produced an AUC of 0.64, along with a 95% CI of [0.54 0.74] (Fig. 15). Thus, it was possible to predict the average waveform for hit and miss events between participants. However, this may not be too surprising, as the variance of the miss waveform may, in general, be higher than the hit waveform due to the disparity in their trial counts, as we have discussed before under *Class imbalance*. The classifier may be able to learn based on this difference in variance. Regardless, this initial set of analyses suggests that there may be multiple interesting directions to follow up on in the future with between-subject classifications.

In sum, SME ERPs such as the LPC and SW may not only be related to memory success at the aggregate level but could also predict memory for individual trials, albeit with small effect size. Some increase in effect size was achieved by using more features of the study trial activity and through multivariate pattern classification. This also showed that two distinct patterns of activity could be related to subsequent memory success (see Figs. 16 and 17). Methodological improvements to the classification analysis may be able to increase the performance even further (for example, by using more complex algorithms and/or spectrogram information) and will be addressed by future research. Also, it is possible that, unlike the EEG signal, the SME measured by the fMRI may contain a better SNR to predict memory success for individual trials. Alternatively, it is also quite possible for the classification success to never approach the maximum possible outcome due to the numerous cognitive factors that are known to significantly influence memory success but are not directly taken into account in the subsequent memory approach. In that case, even a low, but above-chance, classification is important, and a small level of success is, in fact, expected.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

S.C., Y.Y.C., and J.B.C. conceived and designed research; Y.Y.C. performed experiments; S.C. and Y.Y.C. analyzed data; S.C., Y.Y.C., and J.B.C. interpreted results of experiments; S.C. prepared figures; S.C. drafted manuscript; S.C., Y.Y.C., and J.B.C. edited and revised manuscript; S.C., Y.Y.C., and J.B.C. approved final version of manuscript.

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