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## Studying memory processes at different levels with simultaneous depth and surface EEG recordings

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19 **analysis**

### 20 Abstract

21 Investigating cognitive brain functions using non-invasive electrophysiology can be challenging due  
22 to the particularities of the task-related EEG activity, the depth of the activated brain areas, and the  
23 extent of the networks involved. Stereoelectroencephalographic (SEEG) investigations in patients  
24 with drug-resistant epilepsy offer an extraordinary opportunity to validate information derived from  
25 non-invasive recordings at macro-scales. The SEEG approach can provide brain activity with high  
26 spatial specificity during tasks that target specific cognitive processes (e.g. memory). A full  
27 validation is possible only when performing simultaneous scalp-SEEG recordings, which allows  
28 recording signals in the exact same brain state. This is the approach we have taken in 12 subjects  
29 performing a visual memory task that requires the recognition of previously viewed objects. The  
30 intracranial signals on 965 contact pairs have been compared to 391 simultaneously-recorded scalp  
31 signals at a regional and whole-brain level, using multivariate pattern analysis. The results show that  
32 the task conditions are best captured by intracranial sensors, despite the limited spatial coverage of  
33 SEEG electrodes, compared to the whole-brain non-invasive recordings. Applying beamformer  
34 source reconstruction or independent component analysis does not result in an improvement of the  
35 multivariate task decoding performance using surface sensor data. Investigating whether the two

36 types of signals carry complementary information that would improve the machine-learning classifier  
37 performance, part of the multivariate analysis, revealed that the results are driven by the modality  
38 with best separate performance, namely SEEG.

## 39 **1 Introduction**

40 Electroencephalography (EEG) is routinely used to understand cognitive processes (Kappenman and  
41 Luck, 2011). The ability of these non-invasive recordings to capture cognitive processes accurately  
42 and entirely is the subject of ongoing investigations. A primary challenge is the well-known ill-posed  
43 problem of source-reconstruction (Grech et al., 2008). Knowing the actual sources and their time-  
44 course in detail would provide invaluable information to disentangle brain activities. Clinical uses of  
45 EEG face a similar challenge, for example concerning the surface visibility of epileptiform activity,  
46 either ictal or inter-ictal. The challenge has been addressed through the simultaneous recording of  
47 intracranial and surface, both with EEG (Tao et al., 2005; Ray et al., 2007; Koessler et al., 2015;  
48 Antony et al., 2019; Barborica et al., 2021) and MEG (Pizzo et al., 2019). An asset of the clinical  
49 context is that many forms of epileptiform activity, sometimes paroxysmal, involve relatively large  
50 patches of cortical tissue that present synchronized activity, evoking potentials on scalp having  
51 reasonable signal-to-noise ratio (SNR). By contrast, cognitive processes evoke more subtle activities  
52 and variations, involving deep brain structures, and high frequency activity. These factors may  
53 cumulatively contribute to a poor scalp visibility of the corresponding EEG activity.

54 Recognition memory provides an ideal test case to explore how neural activities evoked by cognitive  
55 tasks are captured at the scalp by EEG. Recognition memory is complex cognitive function generally  
56 broken down into encoding, storage, and retrieval processes (Mandler, 1980; Besson et al., 2012).  
57 These are known to involve lateral and deep structures such the hippocampus (Rutishauser et al.,  
58 2006; Merkow et al., 2015). Recognition memory has been extensively studied with EEG, using  
59 recordings made either on the scalp (Ratcliff et al., 2016) or in the brain, but rarely both  
60 simultaneously. Here, we assess to what extent the postulated processes are visible on scalp EEG by  
61 validating the source localization results with simultaneous scalp-intracranial recordings. The data  
62 are from patients undergoing stereo-electroencephalographic (SEEG) presurgical evaluation for drug-  
63 resistant epilepsy; they performed a standard task requiring them to encode and later recognize  
64 pictures of objects (Besson et al., 2012; Despouy et al., 2020). We performed a high-sensitivity  
65 multivariate pattern analysis (MVPA) (Haxby et al., 2001; Grootswagers et al., 2017), not only on  
66 sets of signals of different modalities (intracranial, scalp or reconstructions), but also on combined  
67 sets, to evidence possible synergies between signals recorded at different scales.

## 68 **2 Methods**

### 69 **2.1 Subjects**

70 We selected 12 patients diagnosed with focal drug resistant epilepsy that underwent long-term  
71 simultaneous EEG and SEEG recordings in the Emergency University Hospital Bucharest between  
72 2020 and 2022 (Table 1). Patients were considered surgical candidates and underwent presurgical  
73 non-invasive evaluation using extended patient history, video-electroencephalography, brain  
74 structural and functional imaging (inter-ictal FDG-PET CT) and neuropsychological profile.  
75 Consequently, in these patients, invasive recordings were considered necessary to delineate the  
76 epileptogenic zone and to map functional cortex for tailoring the surgical resection (Munari et al.,  
77 1994; Kahane et al., 2003; Jayakar et al., 2016; Isnard et al., 2018). The details regarding the  
78 patients' gender, age, type of epilepsy and lateralization are provided in Table 1. In addition, part of

79 this research protocol, scalp electrodes were attached, allowing for simultaneous surface and  
80 intracranial long-term recordings.

81 The study has been performed under Bucharest University ethical committee approval CEC  
82 23/20.04.2019. All patients, or their legal guardian/next of kin, signed a written informed consent, in  
83 accordance with the Declaration of Helsinki, for the simultaneous recordings and data sharing  
84 procedures.

## 85 **2.2 Experimental paradigm**

86 We have used the same experimental visual memory paradigm as in López-Madróna et al. (2022). In  
87 summary, we used 168 images from the database of Duñabeitia et al., (2018) that were organized in  
88 blocks of 12 or 24 images, presented on a computer screen. There were two block types: encoding  
89 (“ENC”), where a set of 12 images were presented to the patient, followed by a recognition block  
90 type where the same 12 familiar images (“OLD”) were randomly interleaved with other 12 novel  
91 images (“NEW”). The patient was required to indicate by pressing two buttons on the keyboard,  
92 using two fingers of right hand, whether the images were familiar or not, within 1500 ms. A  
93 distracting video of 1 minute was presented in between encoding and recognition blocks. The  
94 sequence of 36 image presentations was repeated 7 times using different images from the 168-image  
95 set and pseudo-random distribution the OLD and NEW items, with the constraint that there were  
96 never more than 3 “old” or “new” items in a row. Stimuli presentation and response logging were  
97 controlled by the software E-Prime 3.0 (Psychology Software Tools, Pittsburgh, PA).

## 98 **2.3 Simultaneous scalp and intracranial recordings**

99 SEEG exploration was performed using depth electrodes (Dixi Medical, Chaudfontaine, France)  
100 with 8 to 18 contacts per electrode, 2 mm contact length, 3.5 mm center-to-center contact spacing and  
101 0.8 mm diameter. Multiple electrodes were placed following an individual hypothesis allowing for up  
102 to 258 contacts to be available in each patient. Electrodes were placed intracranially using the  
103 microTargeting™ Multi-Oblique Epilepsy STarFix Platform (FHC, Bowdoin, ME USA) (Dewan et  
104 al., 2018; Yu et al., 2018; Pistol et al., 2021) or the Leksell stereotactic frame (Elekta AB,  
105 Stockholm, Sweden). To determine the exact location of each electrode and contact, the post-  
106 implantation CT scan was loaded in the surgical planning software (Waypoint Planner, FHC,  
107 Bowdoin, ME USA), co-registered with the pre-implantation MRI, and adjustments to the initially  
108 planned trajectories were made to match the postop location of the electrodes. A manual labeling of  
109 the SEEG contacts has been performed using the following abbreviations: A – Amygdala; Hc –  
110 Hippocampus; TP – Temporal Pole; STG – Superior Temporal Gyrus; MTG – Middle Temporal  
111 Gyrus; ITG – Inferior Temporal Gyrus; W – Wernicke; F – Fusiform Gyrus; PHG –  
112 Parahippocampal Gyrus; LG – Lingual Gyrus; E – Entorhinal; SPL – Superior Parietal Lobule; IPL  
113 – Inferior Parietal Lobule; S – Postcentral Gyrus; AG – Angular Gyrus; SMG – Supramarginal  
114 Gyrus; IPS – Intraparietal sulcus; PrC – Pre – Cuneus; PCL – Paracentral Lobule; PCC – Posterior  
115 Cingulate; Ist – Isthmus; O – Lateral Occipital; TPO – Temporo-Parieto-Occipital; V1 – Primary  
116 Visual Cortex; C – Cuneus; aI – Anterior Insula; pI – Posterior Insula; OpF – Operculum Frontalis;  
117 OpR – Operculum Rolandis; OpP – Operculum Parietalis; OpT – Operculum Temporalis; R –  
118 Rolandic; B – Broca; PMC – PreMotor; DLPFC – Dorso-Lateral Prefrontal; VLPFC – Vento-  
119 Lateral Prefrontal; OF – Orbitofrontal; SMA – Supplementary Motor Area; preSMA – Pre-  
120 Supplementary Motor Area; SFG – Superior Frontal Gyrus; MOFC – Medial Orbito – Frontalis; FP –  
121 Frontal Pole; ACC – Anterior Cingulate; MCC – Middle Cingulate; DMPFC – Dorso-Medial  
122 Prefrontal Cortex; VMPFC – Vento-Medial Prefrontal Cortex; BG – Basal Ganglia; WM – White  
123 matter.

124 In view of the group analysis, the presurgical MRI of each patient was also used for running an  
125 analysis pipeline implemented in FreeSurfer (Fischl, 2012) that allowed us to obtain the patient's  
126 cortical surface reconstruction, used for visualization purposes, but also – more importantly -, for  
127 performing a non-rigid registration of the patient's MRI to the “cvs\_avg35\_inMNI152” FreeSurfer  
128 template (Postelnicu et al., 2009), providing us with the coordinates of each intracranial contact in a  
129 common MNI space.

130 One up to three days after the SEEG implantation, between 20 and 37 scalp electrodes were placed  
131 according to the 10-20 system. A few electrodes were repositioned on adjacent 10-10 grid location,  
132 due to interference with the SEEG electrodes and up to 10 electrodes could not be placed at all. The  
133 exact number of scalp electrodes in each patient is provided in Table 1.

134 Signals were collected using a setup as described in Barborica et al. (2021). In summary, two  
135 identical Natus Quantum 128-channel amplifiers (Natus Neuro, Middleton, WI) were used, one for  
136 each modality (scalp/intracranial) and having separate signal references. The reference for the SEEG  
137 recordings was chosen on one contact located in white matter exhibiting minimal activity, whereas  
138 for the scalp system the reference was Fpz. Raw data was acquired a sample rate of 4096 Hz. The  
139 hardware was synchronized using digital triggers to both systems and a 50 Hz sine reference signal,  
140 recorded simultaneously using DC inputs of the two systems. Patients 9 – 12 were recorded with a  
141 single Quantum 256-channel amplifier, that no longer required the external synchronization  
142 hardware. The data was combined and saved in a single file in AnyWave ADES format (Colombet et  
143 al., 2015), containing both types of signals. The analysis workflow is shown in Fig. 1.

144 The synchronization between stimuli presentation and (S)EEG recordings has been performed using  
145 a photodiode part of Chronos response box (Psychology Software Tools, Pittsburgh, PA) attached to  
146 a corner of the screen where trial start synchronization flashes were presented. The response time and  
147 correctness were merged into the AnyWave event file by reading the E-Prime log files using Matlab  
148 (Mathworks, Natick, MA) custom scripts.

149 The intracranial channels located in the seizure onset zone and in white matter were discarded.  
150 Additional artefacted trial removal, as well as bad channel removal was performed manually by  
151 visually inspecting the recordings.

## 152 **2.4 ERP Processing**

153 Signals were loaded into EEGLab (Delorme and Makeig, 2004) software, resampled at 256 Hz and  
154 filtered in the 0-45 Hz interval. Scalp EEG was re-referenced to common average and artifacts were  
155 removed using Independent Component Analysis (ICA). Only correct trials have been retained for  
156 further analysis.

## 157 **2.5 Source localization**

158 To test the inverse solution of scalp EEG for finding brain areas that are involved in task decoding,  
159 we have calculated source signals at the location of the intracranial electrodes. To achieve that, we  
160 have performed a beamformer analysis on the standard FreeSurfer's *fsaverage* template, brain  
161 electrical model and 10-20 electrode positions available in MNE-Python. The beamformer spatial  
162 filters calculated using Linearly Constrained Minimum Variance (LCMV) were used to calculate  
163 source time courses on a 5-mm grid covering the brain. The source time course on the grid point  
164 nearest to the midpoint between a pair of SEEG contacts that were part of a bipolar-recorded signal  
165 was considered to approximate the source signal at each intracranial site. We therefore obtained a set

166 of signals having a dimensionality identical to the one of the SEEG, that was analyzed through the  
167 common MVPA pipeline.

## 168 **2.6 Independent component analysis**

169 To test whether a method that is known to separate temporally correlated neuronal sources can  
170 enhance MVPA decoding results, we have performed an independent component analysis (ICA) of  
171 scalp signals using second-order blind identification (SOBI) blind source separation (Belouchrani et  
172 al., 1993, 1997; Tang et al., 2005), using EEGLab software.

## 173 **2.7 Multivariate Pattern Analysis**

174 For Multivariate Pattern Analysis we have generally followed the workflow described in  
175 Grootswagers et al., (2017). The processing has been performed using MNE-Python toolbox  
176 (Gramfort et al., 2013) and custom Python and Matlab (Mathworks, Natick, MA) scripts. A logistic  
177 regression linear classifier was trained to discriminate between responses for the OLD and NEW  
178 conditions using the L-BFGS-B – (Large-scale Bound-constrained Optimization) solver. The model  
179 was fitted to the data and its performance scored using receiver operating characteristic (ROC) area  
180 under curve (AUC). The scores were evaluated using 20-fold cross-validation and time regions where  
181 they were statistically different from chance were evaluated using a 1-sample permutation cluster test  
182 applied to the set of scores calculated for each fold (Maris and Oostenveld, 2007).

183 The processing pipeline was applied to SEEG bipolar signals, to the EEG signals or to the scalp  
184 source signals at SEEG sensor location obtained using beamformer. Specific to our study, the  
185 simultaneous collection of scalp and SEEG data allowed pooling of the signals for the two modalities  
186 to investigate whether combined data provides a classifier performance significantly different from  
187 analyzing individual sets.

188 We have calculated the contribution of signals at each intracranial sensor location (recorded or  
189 reconstructed) to the recognition process by calculating the activation patterns associated with fitting  
190 the data with a linear model (Haufe et al., 2014) using MNE-Python toolbox which in turn resorts  
191 extensively to scikit-learn Python toolbox (Pedregosa et al., 2011; Abraham et al., 2014).

192 To assess the contribution of various brain structures to decoding task conditions, we have repeated  
193 the MVPA analysis on subset of signals recorded or reconstructed within the same brain area or  
194 structure (Despouy et al., 2020), according to the labeling we have described earlier in this section.  
195 We will further refer to this analysis restricted to a region of interest (ROI) as “regional analysis”  
196 (Ebrahimi et al., 2022). Compared with activation patterns (Haufe et al., 2014), that have no  
197 significance associated with them, the regional analysis allows inferring, in a probabilistic way, the  
198 time intervals where the decoding performance is different from chance, evidencing the  
199 sequential/hierarchical processing of stimulus novelty within the brain.

## 200 **3 Results**

201 A total of 136 intracranial electrodes having 1885 contacts were implanted in 12 patients. Additional  
202 436 surface electrodes were attached to the scalp. After data curation and application of inclusion  
203 criteria, signals recorded at 965 intracranial sites and at 391 scalp locations were further included in  
204 the analysis. The subjects correctly identified stimulus novelty in 89.53% of the trials. The MVPA  
205 analysis was applied to 1729 correct recognition trials (OLD: 822, NEW: 907) having a mean±SD  
206 response time of 719.1±162.4 ms (OLD) and 765.0±191.2 ms (NEW).

207 **3.1 Responses on single scalp and SEEG electrodes**

208 The ERPs for the scalp sensor and SEEG sensor having the highest magnitude multivariate activation  
209 patterns among all scalp and  $m=965$  SEEG signals recorded in all  $n=12$  patients are shown in Figure  
210 2.

211 While a typical high-amplitude ERP presents prominent peaks either following the stimulus  
212 presentation ( $\sim 200$  ms) or around response time, depending on sensor location, these examples rather  
213 capture situations where the novelty of the stimulus is best captured, between 400 ms and 600 ms and  
214 around the response time ( $\sim 800$  ms).

215 **3.2 Single-subject Multivariate Analysis**

216 The results of the MVPA analysis of responses at the SEEG, scalp, source level and combined scalp-  
217 SEEG in patient 3 are shown in Fig. 3. The classifier performance for the SEEG signals is  
218 consistently above chance through the interval  $\sim 450$  ms through  $\sim 900$  ms (permutation cluster test,  
219  $p < 0.05$ ). By contrast, the scalp signals provide a statistically significant classification performance  
220 only during the memory retrieval and stimulus recognitions processes between  $\sim 500$  ms and  $\sim 600$   
221 ms. Computing source signals at SEEG sensor locations provide classification results that are similar  
222 in magnitude to the scalp sensor signals, with eventually better results in terms of the extent of the  
223 clusters reflecting the scores significantly different from chance ( $p < 0.05$ ).

224 A regional MVPA analysis presented in Fig. 3C,D highlights the regions that contribute most to the  
225 overall decoding performance, namely the anterior cingulate cortex and hippocampus. The ACC, as  
226 sampled by SEEG, exhibits sustained better-than-chance scores in the late interval  $\sim 500$  ms through  
227  $\sim 900$  ms, whereas Hc presents early ( $\sim 500$  ms), but limited duration ( $\sim 100$  ms) activations. The  
228 scalp, source and combined signals provide similar results in Hc, but rather different ones in ACC.

229 **3.3 Group Analysis**

230 At the population level ( $n=12$  subjects), the classifier performance based on intracranial signals was  
231 much higher than the one based on scalp or source signals, as shown in Fig. 4.

232 The use of source signals calculated at SEEG sensor locations provides slightly lower classifier  
233 performance than the one based on signals from which it was derived, i.e. scalp signal (Fig. 4). The  
234 MVPA analysis applied to the independent components of the scalp signal provides results that are  
235 virtually identical to the scalp ones. Combined scalp and SEEG scores follow closely the time course  
236 of the SEEG scores.

237 The time course of the classification performance using SEEG signals is consistent across subjects,  
238 as can be seen in Fig. 5 where we have plotted the scores for all subjects, in addition to the grand  
239 average. This is somehow unexpected, as the areas implanted with depth electrodes can be quite  
240 different. We have illustrated in Fig. 5A and Fig. 5C two implantation schemes providing similar  
241 scores, highlighted in Fig. 5E using green and blue colors.

242 In performing a regional analysis of the performance in decoding task conditions, we see that the  
243 findings at the level of all  $m=965$  sites in  $n=12$  subjects, shown in Fig. 4, are confirmed at a regional  
244 scale (Fig. 6), the scores significantly different from chance associated with SEEG signals being  
245 higher and more sustained over time, compared to source signals reconstructed at the same locations.  
246 Among the areas exhibiting the highest and earliest SEEG scores, we can count F, ITG, Hc, as well

247 as insular-opercular complex. One has to keep in mind that all these findings are strongly influenced  
248 by the coverage of each ROI with SEEG electrodes.

249 The 3D representation of multivariate activation patterns (Haufe et al., 2014) of SEEG and source-  
250 space data is shown in Figure 7. One has to keep in mind that these activation patterns do not reflect  
251 the magnitude of the ERPs, but rather represent a virtual signal corresponding to how well a site  
252 encodes the stimulus novelty, in our case. A wide-area brain activation (Fig. 7A) over the course of  
253 the recognition process is visible for the intracranial signals, whereas at a comparable amplitude  
254 scale, the source data shows much less activations. The activation patterns of various brain areas is  
255 sequential, following a posterior-to-anterior flow, as illustrated in Fig. 7 and in the Supplementary  
256 Data movie. The activations associated with EEG source signals show a roughly similar spatio-  
257 temporal pattern. At a closer visual inspection of Fig. 7 we can find evidence of known leakage-  
258 related effects (Schoffelen and Gross, 2009), as multiple contacts in several electrodes exhibit similar  
259 activation values.

260 In SEEG recordings (Fig. 7A) we can divide the activation in four clinically relevant time-intervals.  
261 The significant activation starts at ~200ms and between 200-400ms we can observe the recognition  
262 process that activates the network of structures that mainly involves temporal-basal and hippocampus  
263 on the right side. Then, between 400-600ms we can see the activations related to the decision making  
264 process that significantly involves bilaterally the peri-sylvian, prefrontal and mesial temporal lobe  
265 structures. The sensorimotor activation overlaps the 400-600ms and continues in the next interval  
266 600-800ms and represents the response phase of the task. The last time-interval (600-800ms)  
267 highlights the activation of the prefrontal cortex possibly related to self-evaluation or memory  
268 storage. The EEG source (Fig. 7B) displays a similar timeline of activation pattern in the 200-600ms.  
269 However, the late phase between 600-800ms is not informative.

#### 270 **4 Discussion**

271 While other studies that compared intracranial to scalp data used sequential recording of the two  
272 modalities (Ebrahiminia et al., 2022), or even different sets of participants (Haufe et al., 2018), we  
273 have simultaneously acquired data in the two modalities, approach that allowed us to validate the  
274 results of the EEG source reconstruction using SEEG recordings in decoding task conditions, and  
275 investigate the possible synergy between invasive and non-invasive recording in decoding stimulus  
276 novelty.

277 Our results show that our task requiring the subjects to categorize visual stimuli based on novelty,  
278 involving memory encoding and retrieval, activates large areas of the brain. This finding is supported  
279 by the widespread activation visible in Fig. 7, as well as by the fact that SEEG implantations at  
280 totally different locations result in decoding performances over time that are close to each other and  
281 to the group average (Figure 5).

282 The decoding performance of the ML classifier is maximal when using intracranial signals,  
283 regardless of the fact that the SEEG implantation has limited spatial coverage of the brain, compared  
284 with the scalp EEG which is supposed to provide full-brain coverage, as visible in Figs. 3 and 4. The  
285 relatively poor decoding performance of the classifier that uses scalp signals can be attributed, in our  
286 opinion, to significantly lower signal-to-noise ratio (SNR) of the scalp EEG compared to SEEG. It  
287 may also be possible that scalp EEG provides poor visibility of the activity in deep structures of the  
288 brain, whereas SEEG samples with undegraded SNR all implanted locations, no matter how deep  
289 they are. A previous study by Ebrahiminia et al. (2022) performing sequential scalp and



290 electrocorticographic (ECoG) recordings have shown that scalp EEG provides slightly better  
291 classification performance of passively viewing visual stimuli of different categories (Liu et al.,  
292 2009). Not counting the differences in the tasks, one reason for this discrepancy may relate once  
293 again to the fact that ECoG does not record activity in deep brain structures, therefore both modalities  
294 provide information from outer cortex, with scalp EEG providing a slightly better spatial coverage.  
295 One other factor that may favor EEG in other studies is that in our simultaneous protocol, the EEG  
296 electrodes were glued to the scalp one day or more before running the memory task (part of a wider  
297 set of investigations), presenting a degradation of the quality of the contact within this interval, non-  
298 correctable due to the requirement of maintaining sterility at the scalp level. Also, due to spatial  
299 constraints related to pre-existing SEEG electrode anchors, the coverage with scalp electrodes was  
300 non-uniform.

301 Interestingly, using SEEG electrodes, the classifiers were always able to decode the task conditions  
302 using task-evoked intracranial EEG recorded 300 to 1000ms post stimuli presentation. This was true  
303 not only at the group, but also at individual subject level, even when the spatial sampling of the  
304 SEEG electrodes was completely different (Fig. 5). Recent studies have shown the “traveling wave”  
305 behavior of brain activity (Lubenov and Siapas, 2009; Muller et al., 2014; Liang et al., 2021;  
306 Bhattacharya et al., 2022), and it is possible that we have observed such effects in our analysis.  
307 Under the assumption that the task-evoked intracranial EEG activity is recorded on a critical number  
308 of electrodes, sufficient for the classifier to learn the propagation patterns of the traveling wave, we  
309 may decode the task conditions from various brain regions, without a loss in decoding performance.  
310 Similar effects have been observed by groups that studied the representation and processing of  
311 emotion in the brain with machine learning methods, concluding that emotion representation is  
312 encoded as patterns of activations over widely-distributed brain networks (Wager et al., 2015; Donos  
313 et al., 2022).

314 The process of reconstructing the EEG source signals using beamforming does not result in a  
315 significant improvement at the population level of the classifier’s performance, yielding results  
316 comparable to signals on scalp sensors, as visible in Fig. 4. There are exceptions to that general  
317 finding in some individual patients, as illustrated in Fig. 3B, where the decoding performance of a  
318 classifier operating on source signals show earlier and longer statistically significant above-chance  
319 scores than sensor-based analysis, at a significance level  $p < 0.05$ . However, such results have to be  
320 treated with caution, given the probabilistic nature of the statistical tests applied (Sassenhagen and  
321 Draschkow, 2019). The regional analysis of the classification performance shown in Fig. 6 is in  
322 agreement with the overall results in Fig. 4, where source signals result in more sparse and limited-  
323 duration significant scores than the intracranial signals.

324 The beamformer source reconstruction is based on linear matrix operations on the responses  
325 (Westner et al., 2022), which is equivalent to an affine transformation in the  $n$ -dimensional response  
326 space, which is the space in which the MVPA operates (Grootswagers et al., 2017). An affine  
327 transformation is equivalent to a series of elementary transformations like rotation, scaling, shear etc.,  
328 that do not change the relationships between points representing the set of  $n$  responses at a particular  
329 point in time, therefore it is not expected to significantly affect the performance of a ML classifier  
330 operating on the transformed set of points. In line with this finding, we have also tested whether  
331 performing an Independent Component Analysis (ICA) of the scalp EEG responses, that also uses  
332 linear matrix transformations, results in a set of independent components that provide a better  
333 decoding of the task conditions. The results, presented in Fig. 4 show that classifier performance  
334 operating on the independent components is virtually identical to the one for the original signals on  
335 the scalp sensors.

336 In investigating whether scalp and intracranial signals contain complementary information that might  
337 contribute to a classifier performance, we did find that the modality providing best performance (i.e.  
338 SEEG) is determining the combined performance (Figs. 3 and 4).

339 A limitation of the study is the partial and non-uniform spatial sampling of both scalp and intracranial  
340 sensors, due to objective reasons. Another limitation is that our analysis pipeline is the most  
341 conservative one, being based on wide-band single-trial data. Creating “super-trials” or “pseudo-  
342 trials” by averaging several trials (Despouy et al., 2020; Ashton et al., 2022) might improve the SNR  
343 of EEG and correspondingly of the source reconstruction signals. Further measures for improving  
344 SNR can be possibly implemented (Grootswagers et al., 2017), alleviating some of the apparent  
345 limitations of non-invasive recordings.

## 346 **5 Conclusion**

347 Analysis of invasive EEG provides highest amount of information related to stimulus novelty,  
348 compared with scalp recordings, despite the limited spatial sampling of the brain with depth  
349 electrodes. This may be related to the limited scalp visibility of the activity related to memory  
350 processes in deep brain structures, particularly if containing higher frequency components. The  
351 synergy between the two modalities - enabled by pooling data recorded simultaneously- is limited,  
352 the SEEG sensors providing best decoding performance driving the combined, overall, performance.

353

## 354 **6 Conflict of Interest**

355 The authors declare that the research was conducted in the absence of any commercial or financial  
356 relationships that could be construed as a potential conflict of interest.

## 357 **7 Author Contributions**

358 AB: conceptualization, methodology, software, formal analysis, resources, data curation, writing,  
359 visualization, supervision, funding acquisition; IM: methodology, investigation, writing, supervision;  
360 VJLM: methodology; FXA: methodology, writing – review and editing; AT: methodology; CD:  
361 methodology, software, formal analysis, writing – initial draft; IO: investigation; CP: investigation,  
362 formal analysis, data curation; FM: investigation, data curation; CGB: Conceptualization,  
363 methodology, writing – review and editing, funding acquisition. All authors contributed to the article  
364 and approved the submitted version.

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370 performing the SEEG implantations and surgical procedures, as well as Flavius Bratu and Camelia  
371 Lentoiu for their contribution to collecting the clinical data.

## 372 **10 Data Availability Statement**

373 The datasets for this study can be found at <http://epi.fizica.unibuc.ro/scalesoldnew/>.

374

375

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518

519

## 520 12 Figure Captions

521 Figure 1. Signal collection and analysis workflow.

522 Figure 2. A) ERP image for the scalp sensor PO2 in subject 1, exhibiting the highest multivariate  
523 activation pattern; trials are grouped by condition and sorted by response time, which are marked  
524 using black lines; average ERPs for each condition as well as the contrast between OLD and NEW  
525 conditions are shown; the statistical significance of the univariate (permutation cluster test)  
526 difference, if present, between OLD and NEW conditions at a significance level  $p < 0.05$  is shown  
527 using thick horizontal lines; B) same as A, but for the intracranial sensor X04-X05 located in right  
528 anterior insula in subject 9.

529 Figure 3. Task decoding performance expressed as the area under curve of the receiver operating  
530 characteristic of the classifier for SEEG, scalp and source signals in patient 3. A) SEEG electrode  
531 locations in the left hemisphere; B) ROC-AUC for sensors of different types, as well as for combined  
532 scalp and SEEG; C) same as (B), but for the contacts located in the anterior cingulate cortex; C) same  
533 as in (B), but for contacts located in the hippocampus.

534 Figure 4. Classifier performance for SEEG, scalp, source, ICA and combined scalp-SEEG signals for  
535 all  $n=12$  subjects. The dashed areas show standard error interval for the set of classifier scores for all  
536 patients. The horizontal bars indicate the intervals where the scores are statistically different from  
537 chance (1-sample permutation cluster test,  $p < 0.05$ ).

538 Figure 5. Classifier performance using intracranial signals for two patients having SEEG  
539 implantation covering different areas of the brain; A) Bilateral implantation in subject 8, covering  
540 temporal lobe, including mesial structures; B) mean magnitude of activation patterns in subject 8  
541 across the entire trial duration; C) Electrode locations in subject 12, frontal, parietal and cingulate  
542 areas; D) Same as B, but for subject 12; E) Average and individual classifier scores.

543 Figure 6. A) Timeline of decoding performance significantly different from chance ( $p < 0.05$ ) for  
544 signals recorded on subsets of intracranial contacts implanted in different brain structures. The color  
545 of the bars indicate the maximum value of the AUC score within a cluster. The numbers at the right  
546 of each bar indicate the number of sites and number of patients for clusters in each ROI; B) same as  
547 (A), but for scalp sources calculated at the location of intracranial contacts using beamformer.

548 Figure 7. MVPA timeline of activation patterns for SEEG signals (A) and in EEG source space (B)  
549 for all 965 contacts implanted in 12 patients, shown on the glass brain. The mean values for  
550 activation values within a 200 ms bin are represented.

551

552

553 **13 Tables**

554 Table 1. Patients included in this study

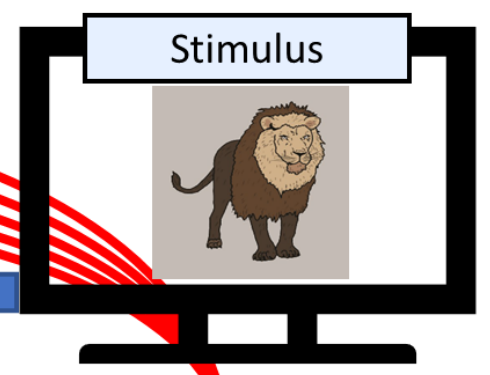
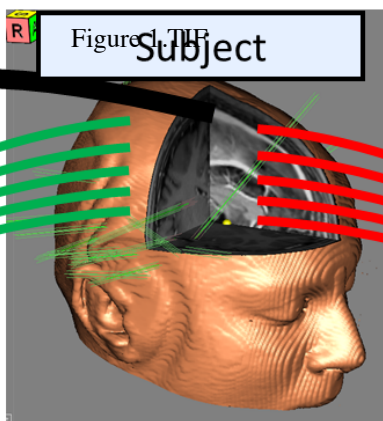
Patient	ID	Age	Epilepsy	Lateralization	Language organization	SEEG electrodes	SEEG contacts	Scalp electrodes	SEEG electrode location
1	89	37	Insular	R	Left typical	14	172	30	Left, posterior
2	90	17	Insular-opercular	L	Left typical	9	86	30	Left, central
3	92	27	Insular	L	Left typical	10	145	30	Left, posterior
4	96	26	Temporal	R	Left typical	11	152	38	Right, anterior
5	97	26	Rolandic Operculum	L	Atypical bilateral	10	135	35	Left, central
6	98	39	Temporal	R	Left typical	9	129	38	Right, posterior
7	99	24	Insular	L	Left typical	13	189	38	Left, anterior
8	101	31	Temporal	B	Left typical	14	187	40	Bilateral, central
9	102	31	Temporo-insular	B	Left typical	16	229	40	Bilateral, posterior
10	104	20	Insular	L	Left typical	10	124	40	Left, central
11	105	26	Frontal	R	Left typical	12	161	37	Right, anterior
12	107	26	Frontal	L	Left typical	8	176	40	Left, anterior



555

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In review

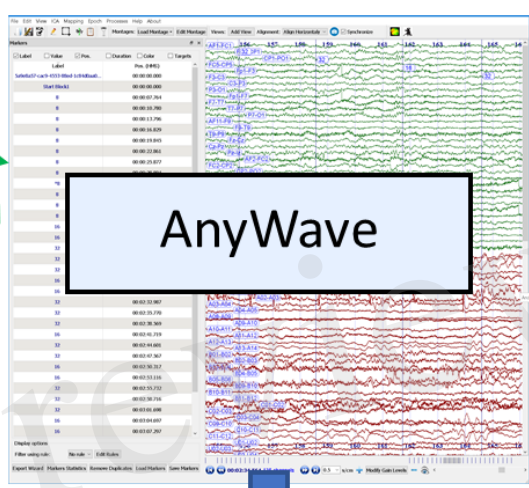


**Scalp**  
Quantum EEG  
128

Synchronization  
Box

**SEEG**  
Quantum EEG  
128

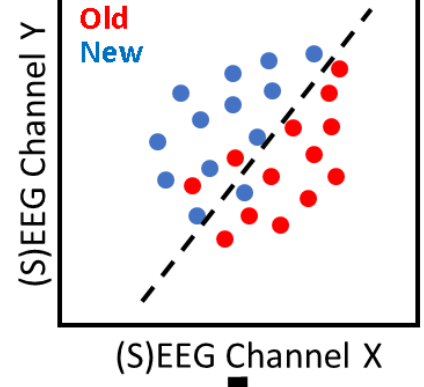
SEEG  
Electrode  
Localization



AnyWave

Beamformer  
Source  
Reconstruction

ML Classifier



Overall  
Performance

Regional Analysis

Activation Patterns

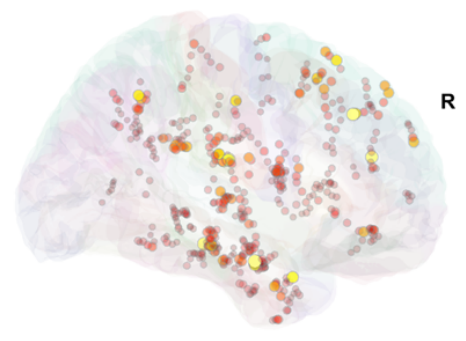
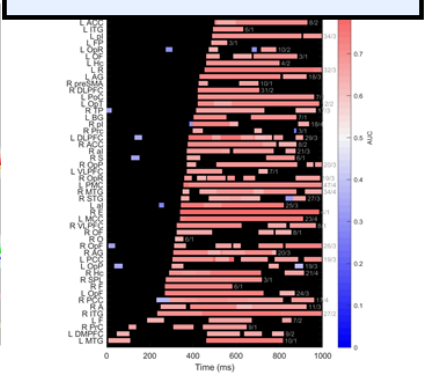
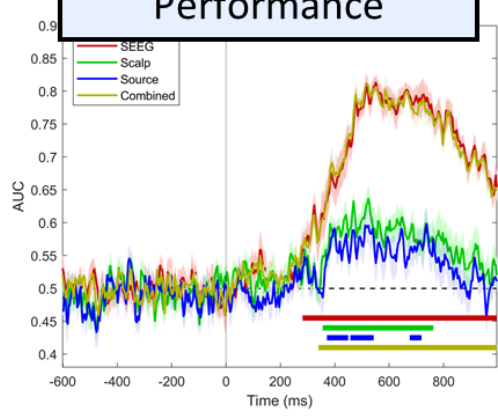


Figure 2.TIF

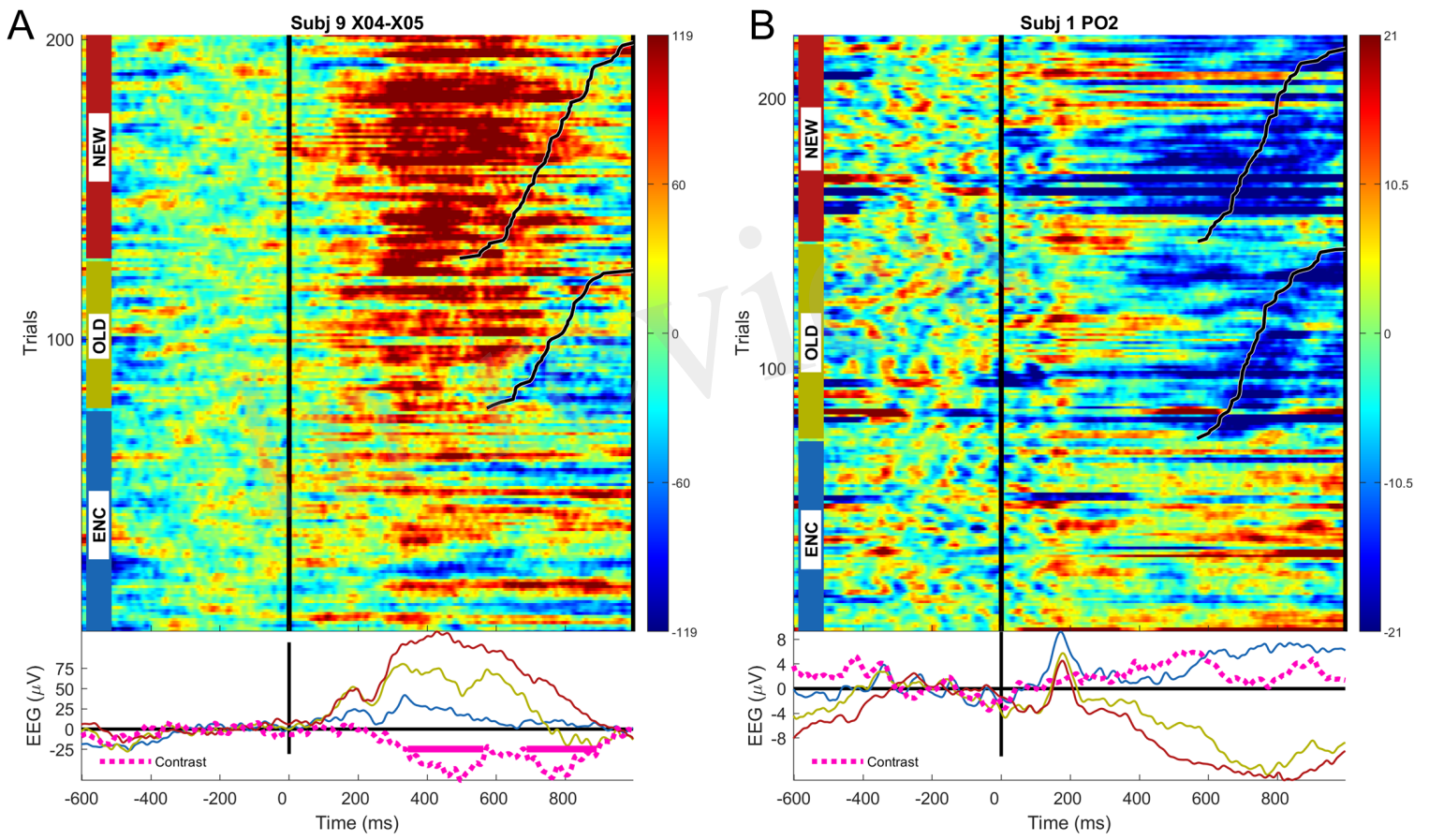


Figure 3.TIF

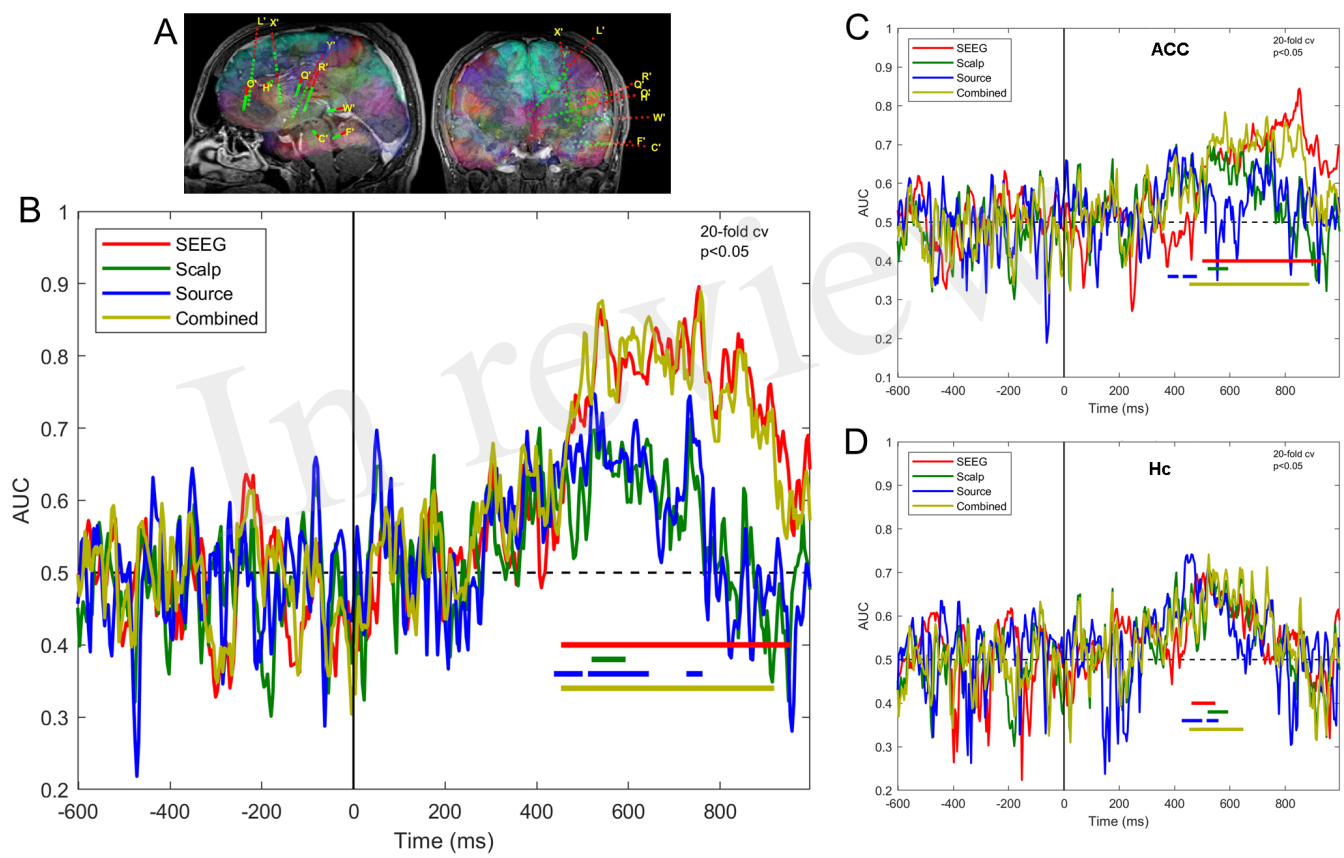


Figure 4.TIF

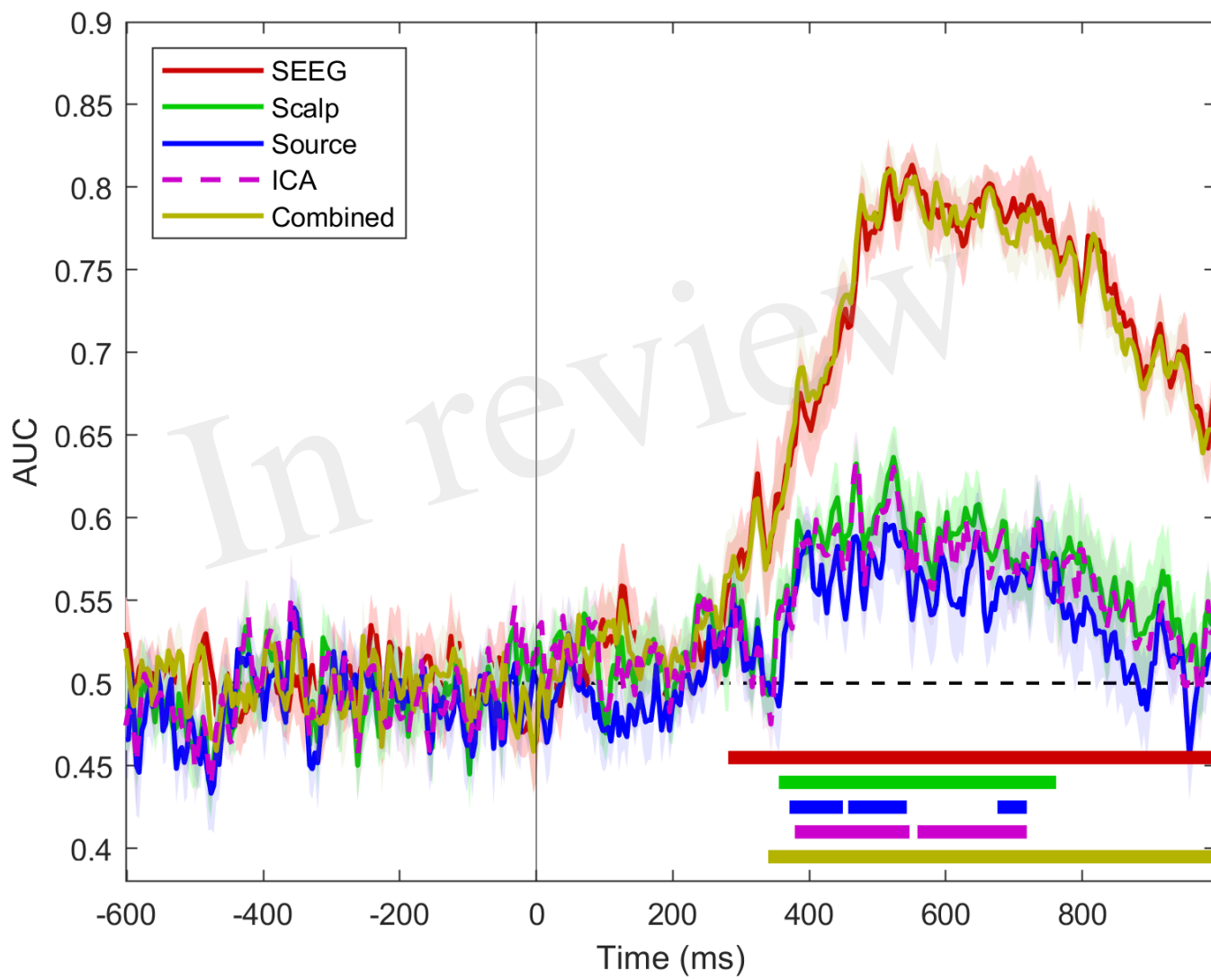


Figure 5.TIF

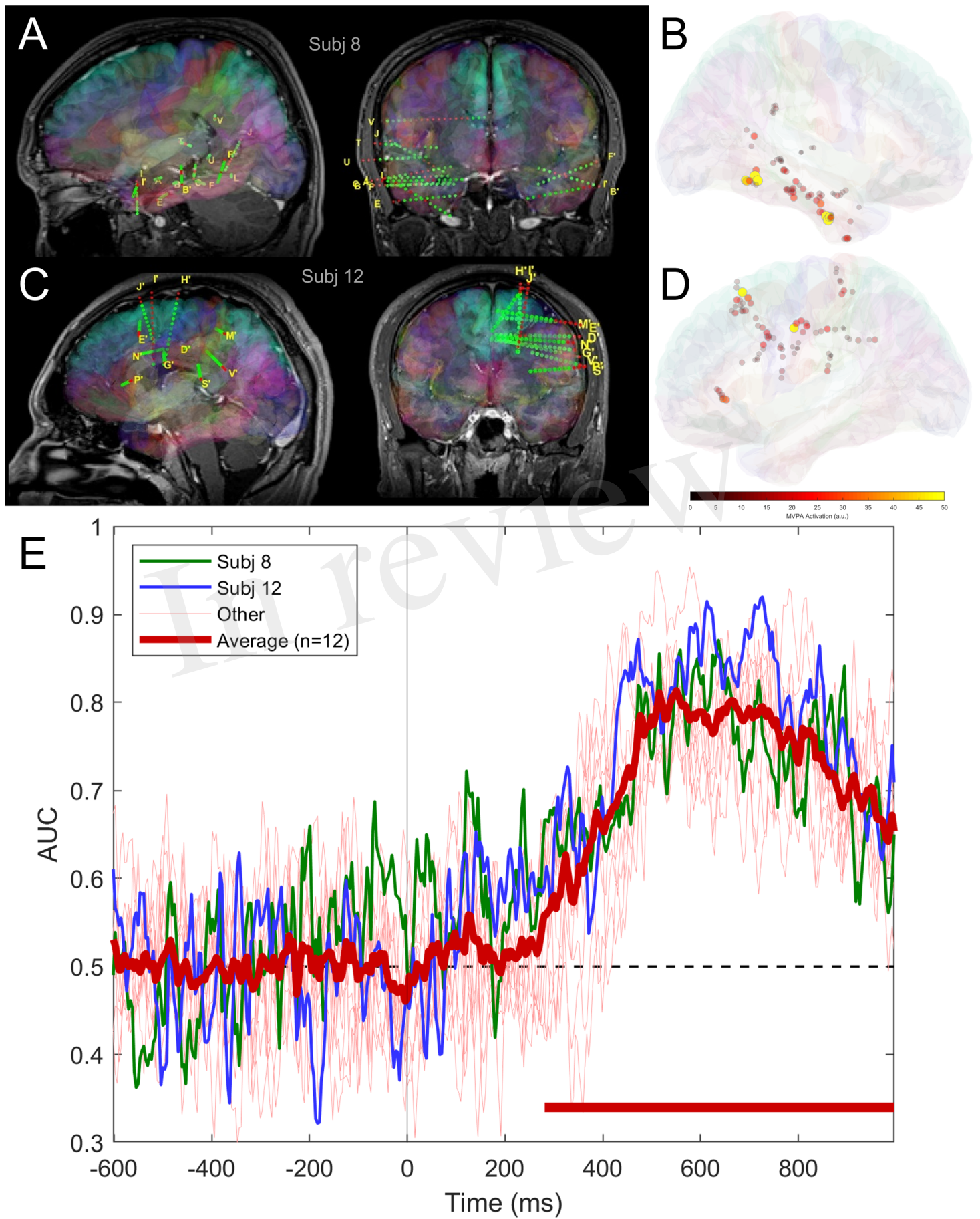


Figure 6.TIF

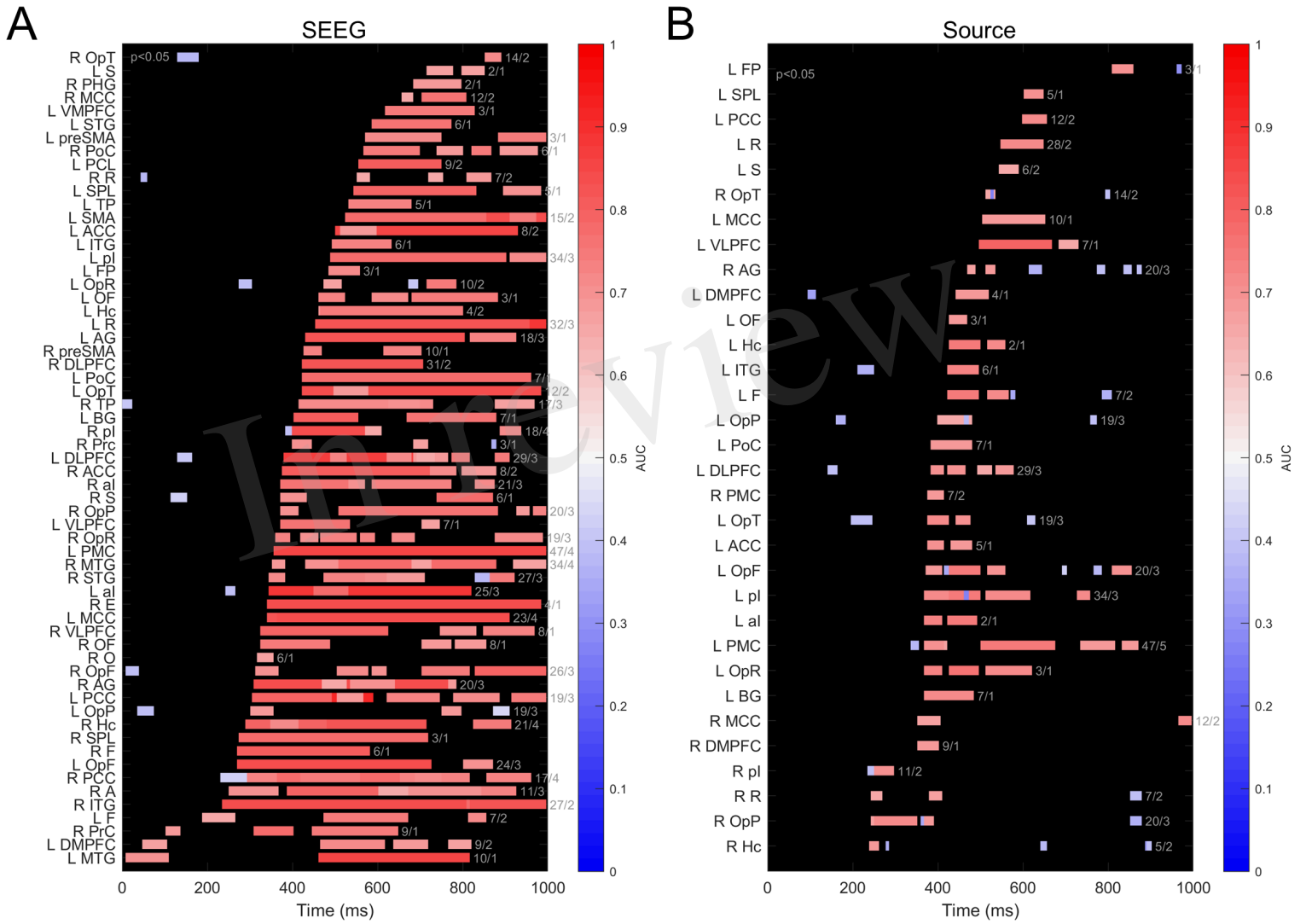


Figure 7.TIF

