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2013 Humaine Association Conference on Affective Computing and Intelligent Interaction

ACII 2013

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Development of a Binary fMRI-BCI for Alzheimer Patients

A semantic conditioning paradigm using affective unconditioned stimuli

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Abstract— **With the aim of developing a brain-computer interface for the communication of basic mental states, a classical conditioning paradigm with affective stimuli was used, assessing the possibility to discriminate between affirmative and negative thinking in an fMRI-BCI setting. 6 Alzheimer patients and 7 healthy control subjects participated to the study. Congruent and incongruent word-pairs were respectively associated to pleasant (baby laughter) and unpleasant (scream) affective stimuli. A Support Vector Machine classifier focusing on insula, amygdala and anterior cingulate cortex was used to discriminate between the activations relative to congruent and incongruent word-pairs (eliciting respectively affirmative and negative thinking), following the conditioning process. Classification accuracy was on average 70% for Alzheimer patients, reaching 85%, and on average 69% for control subjects, reaching 83%. This study shows that it is possible to extract information on individuals' mental states by exploiting affective responses, overcoming the typical obstacles of traditional BCIs, which generally require time-consuming trainings and intact cognition.**

Keywords—Affective BCI; Alzheimer; Classical conditioning; Support Vector Machine

I. INTRODUCTION

Communication deficits can be pervasive in Alzheimer's disease (AD). In the most advanced stages of the neuropathology, patients may be left with the ability to utter only few words, or regress to mutism [1-3]. Despite the remarkable difficulty in oral communication, patients may still seek social contact [4].

AD patients who have lost the ability to communicate verbally may benefit from a brain-computer interface (BCI) that could allow them to convey basic thoughts and emotions. So far, there has been lack of research in this direction, since BCIs are traditionally considered to require an intact cognitive system to function as a communication method. Moreover, most BCI systems require users' active participation and long trainings to learn to self-regulate their own brain activity.

It has been recently proposed that not only self-regulated brain signals, but also signals that are independent from users' effort, could provide useful information related to users' mental states. The recently introduced 'affective BCIs', by relying on emotions, do not require users to actively perform a cognitive task [5]. Such interfaces could be particularly useful for individuals with cognitive impairment, such as mental retardation or dementia.

Given that BCIs based on operant conditioning are generally problematic for cognitively impaired individuals, we performed a paradigm shift to classical conditioning, using affective stimuli as unconditioned stimuli (US) and simple word-pairs as conditioned stimuli (CS). Using affective stimuli is particularly convenient because affectivity is generally preserved in the course of dementia [6]. More specifically, we assessed the feasibility of an auditory classical conditioning paradigm within an fMRI-based BCI setting, designed to condition AD patients to associate negative and positive affective sounds with incongruent and congruent word-pairs. We decided to use auditory stimulation since it has been shown that although AD patients differ significantly from healthy subjects in emotional processing of visual stimuli, there are no consistent differences in processing emotions through the auditory domain [7].

Our main goal was to ascertain whether the brain activations relative to congruent and incongruent word-pairs, respectively eliciting affirmative ("yes") and negative ("no") responses, could be classified using a linear Support Vector Machine (SVM) after the conditioning process. The possibility to discriminate positive and negative emotional states using a SVM was already demonstrated by Sitaram and colleagues [8]. We hypothesized that the differentiation between affirmative and negative responses would be evident, following the conditioning with affective stimuli, in brain regions that are mostly involved in emotional processing, such as insula, amygdala and anterior cingulate cortex (ACC) [9].

II. METHODS

A. Participants

6 AD patients recruited at the Memory Clinic of Ulm (2 males, 4 females, age: 69-91, average Mini Mental State Examination score: 22.5), and 7 healthy controls (5 males, 2 females, age 62-83), all native German speakers, participated to the study. All participants gave written informed consent prior to participation to the fMRI experiment. The study was approved by the Ethics Committee of the University of Ulm and was performed in compliance with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

B. Stimuli

Stimuli consisted of 300 German word-pairs, half congruent (e.g. "Tier-Katze", "Animal-Cat") and half incongruent (e.g. "Tier-Apfel", "Animal-Apple"), recorded using a SpeedLink USB microphone and QuickTime Player 7 program for Macintosh. Word-pairs included very simple terms belonging to common categories (such as animals or fruit), so that the recognition of their congruence or incongruence take place, at least implicitly, in mild AD patients [10-14]. Each word-pair lasted 1.5 s. The negative and affirmative responses to the word-pairs constituted the conditioned stimuli (CS). The unconditioned stimuli (US) were two standardized emotional sounds drawn from the International Affective Digitized Sounds (IADS, [15]): a pleasant emotional stimulus (a baby-laughter) and an unpleasant emotional stimulus (a scream). The duration of each US was also 1.5 s. To ascertain that all stimuli had the same precise length, their duration was adjusted using the software program Audacity 1.3.14 Beta for Mac OS X. Stimuli presentation in the fMRI scanner was performed with a software interface developed in Matlab v. 6.5 (Mathworks, Inc., Sherbon, MA). Participants heard all auditory stimuli through MRI-compatible headphones with efficient gradient noise suppression (up to 45 dB).

C. Experimental paradigm

The paradigm consisted of a single session divided into three blocks (Fig 1). In the first block, congruent (CS1) and incongruent (CS2) word-pairs were presented aurally, immediately followed by an affective pleasant (baby-laughter, US1) or unpleasant (scream, US2) sound, respectively. In the second and third blocks, only half of the word-pairs were followed by affective stimulation. While the first block was necessary to associate affirmative and negative thinking to positive and negative emotions, the remaining blocks served to verify the possibility to discriminate between affirmative and negative thinking when the affective stimulation was not present anymore.

Participants were simply instructed to listen to the word-pairs, and to think 'yes' if a word-pair was congruent, 'no' if it was incongruent.

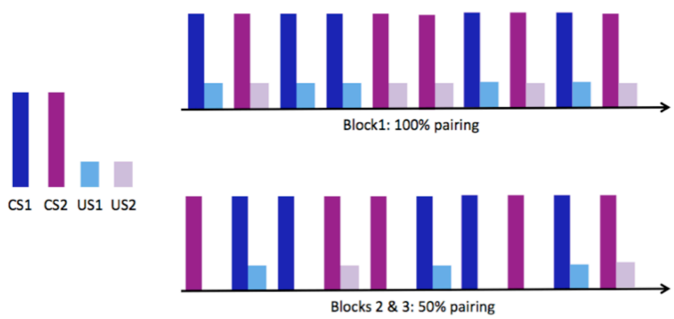

Fig. 1. In the first block incongruent and congruent word-pairs (CS1, CS2) were always followed by a pleasant or unpleasant affective stimulus (US1, US2), in order to associate negative and affirmative thinking to negative and positive emotions respectively. In the second and third blocks, only 50% of the word-pairs were followed by affetive stimuli, to verify the possibility to discriminate between the activation elicited by affirmative and negative thinking when affective stimulation was no more present.

D. fMRI data acquisition

The measurements took place in a 3.0 Tesla body scanner, with standard 12-channels head coil (Siemens Magnetom Tim TRIO, Siemens, Erlangen, Germany). A standard echo-planar imaging sequence was used (EPI; TR = 1.5 s, matrix size = 64×64, TE = 30 ms, flip angle = 70°). Sixteen oblique slices (voxel size = 3.3 times; 3.3×5.0 mm^3 , slice gap = 1 mm), AC/PC aligned in axial orientation were acquired. For superposition of functional maps upon brain anatomy, a high-resolution T1-weighted structural scan of the whole brain was collected from each participant (MPRAGE, matrix size = 256 times; 256, 160 partitions, 1 mm^3 isotropic voxels, TR = 2300 ms, TE = 3.93 ms, TI = 1100 ms, flip angle = 8°). The first 10 volumes of every block were discarded to permit T1 equilibrium.

E. *fMRI data analysis*

Data were pre-processed using Statistical Parametric Mapping (SPM8, Wellcome Department of Imaging Neuroscience, London, UK) run on Matlab R2008b (Mathworks, Inc., Sherborn, MA, USA). Images of each partcipant were normalized to a standard Echo-Planar Imaging (EPI) template in Montreal Neurological Institute (MNI) space. Prior to statistical analyses, data were high-pass (cutoff 128 s) and low-pass (AR(1)) filtered.

We performed a classification analysis using a linear SVM by selecting the fMRI signals from each voxel within insula, ACC and amygdala as input vector. Signals corresponding to various conditions, namely, congruent and incongruent word-pairs from the late acquisition and extinction phases were classified. A 'searchlight approach' [16] was adopted, employing a cubic searchlight algorithm (3x3x3 cube) which moved over each voxel of the insula, ACC and amygdala in an incremental sweep. 1000 voxels were selected for feature extraction using a smoothed Fisher Score. Only the fourth and the fifth volumes after the presentation of the word-pairs were considered, based on the empirical observation that such time points produced the highest differences between conditions. Subsequently, the features were submitted to the SVM, which operated using a linear kernel function. Classification accuracy was computed by averaging the classification accuracies from 35 replications of a leave-one-out cross validation principle.

III. RESULTS

Table 1 and Table 2 show the individual classification accuracies, sensitivities and specifities relatively to the second and third blocks (when the affective stimulation was not present anymore). Offline classification accuracies for AD patients reached up to 85%, with an average of 71%. Offline classification accuracies for healthy controls reached up to 83%, with an average of 69%.

TABLE I.

	Accuracy	Sensitivity	Specificity
Patient 1	0.70	0.70	0.70
Patient 2	0.53	0.50	0.55
Patient 3	0.78	0.70	0.85
Patient 4	0.63	0.55	0.70
Patient 5	0.85	0.80	0.90
Patient 6	0.75	0.80	0.70
Average	0.71	0.68	0.73

a. Offline classification results of the unpaired word-pairs in blocks 2 and 3 for Alzheimer patients.

b.

TABLE II.

	Accuracy	Sensitivity	Specificity
Control 1	0.70	0.70	0.70
Control 2	0.63	0.65	0.60
Control 3	0.63	0.60	0.65
Control 4	0.58	0.55	0.60
Control 5	0.78	0.80	0.75
Control 6	0.83	0.85	0.80
Control 7	0.68	0.70	0.65
Average	0.69	0.69	0.68

c. Offline classification results of the unpaired word-pairs in blocks 2 and 3 for control subjects

d.

IV. DISCUSSION

We assessed a novel affective-BCI approach using classical conditioning with emotional stimuli in combination with brain state classification. The paradigm allowed to extract information on the participants' mental states, namely affirmative and negative thinking, by exploiting affective responses. AD patients and healthy controls comparably responded to the conditioning process, showing that responses related to congruent and incongruent word-pairs could be discriminated after associating them to pleasant and unpleasant affective stimuli. The study shows that the typical hindrances of standard BCIs, which generally require time-consuming trainings and an active effort of the user in order to learn to self-regulate brain signals, can be overcome thanks to the use of affective stimuli.

In order to develop an affective BCI, some points need to be taken into consideration. Firstly, although useful for the identification of very specific cortical and subcortical brain regions, fMRI is not a system that could be used in everyday life. More portable systems, such as near-infrared spectroscopy based BCIs (NIRS-BCISs) [17] could be adopted for online classification of mental states. Secondly, it is possible that the conditioning effect extinguishes very quickly, meaning that several acquisition sessions could be necessary for its maintenance.

In our study only mildly affected AD patients were considered. However, patients at different stages of the disease may have different acquisition and extinction timings. These differences could be exploited for diagnostic aims, for instance by measuring the conditioned response in subjects with mild cognitive impairment who have not yet developed dementia. Testing with patients affected by other kinds of dementia (e.g. frontotemporal dementia) could also be used for differential diagnosis. Moreover, affective BCIs could open up new opportunities for cognitive rehabilitation.

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