Published in final edited form as:
Clin Neurophysiol. 2013 January ; 124(1): 2–4. doi:10.1016/j.clinph.2012.07.012.

New horizons in brain-computer interface research

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1. Extending the utility of brain-computer interface communication

The last decade has shown a large increase in the number of P300-based BCI publications. The majority of these studies have used non-disabled subjects; far fewer studies have been conducted with people suffering from amyotrophic lateral sclerosis (ALS) or other neuromuscular disorders. Although the field has matured significantly, most research has focused on improving classification through signal processing algorithms (Hoffmann et al., 2008; Kaper et al., 2004; Lenhardt et al., 2008; Manyakov et al., 2011; Rakotomamonjy and Guigue, 2008; Serby et al., 2005), or paradigm manipulations (Frye et al., 2011; Hong et al., 2009; Jin et al., 2011; Salvaris and Sepulveda, 2009; Takano et al., 2009; Townsend et al., 2010). To be sure, signal processing and paradigm improvements are essential to increase speed and accuracy of BCI systems. Nonetheless, for the technology to be useful to people with severe communication disorders, it must be tested, and validated, by end-users.

The paper published by Lulé et al. (2013) examines BCI use in 16 control subjects and 18 disabled subjects, two with locked-in syndrome (LIS) and 16 with disorders of consciousness (DOC; i.e., unresponsive wakefulness syndrome or minimally conscious state). Extending BCI use to patients with DOC may eventually allow these patients to regain rudimentary communication. In addition, this line of research may provide insight into why people with complete locked-in syndrome (CLIS) are unable to communicate with a BCI, a question that has eluded BCI research from inception (Birbaumer, 2006; Kübler and Birbaumer, 2008; Sellers and Donchin, 2006). DOC render people immobile, possibly affecting motor pathways over time, and is potentially the most similar population to that of CLIS. Kübler and Birbaumer (2008) tested seven CLIS patients, none of whom were able to communicate with a BCI; aside from this study very few CLIS patients have been tested and these data remain unpublished. In contrast to CLIS, people with LIS retain some rudimentary ability to communicate through eye movement, or subtle muscle movements. In LIS populations, studies have shown effective communication with visual implementations of the P300 BCI paradigm (Kübler and Birbaumer, 2008; Sellers et al., 2010). Conflicting results have been shown regarding whether the severity of neuromuscular disability affects BCI performance. Kübler and Birbaumer (2008) found that remaining neuromuscular function is not related to BCI performance. Contrary to these results, Piccione et al. (2006) found that BCI performance deteriorates with greater neuromuscular disability. The differing results may be attributed to small sample size and/or individual differences. Thus, studies with much larger sample sizes are needed to begin to disambiguate this important issue.

1.1. Auditory P300 brain-computer interfaces and their limitations

Lulé et al. (2013) have extended a 4-choice auditory paradigm, which provides basic yes/no communication (Sellers and Donchin, 2006), to a large number of DOC patients. Their results show that all but one DOC and one LIS patient were unable to communicate using an online four-choice auditory BCI. Offline analyses suggested a performance level of 57% for the successful DOC patient, which is not considered sufficient for effective communication. Nonetheless, the study suggests that such communication may be possible. The study also provides a realistic appraisal of the many logistical difficulties encountered when working with such patients.

A number of papers has suggested that an auditory BCI can be a viable option to a visual BCI. This is obviously true if it is not possible to use a visual system. However, there are a number of potential problems associated with auditory P300 BCI paradigms. Auditory ERPs show greater variability than the visual ERPs and accuracy is generally higher for visual paradigms (Furdea et al., 2009; Klobassa et al., 2009; Nijboer et al., 2008; Sellers and Donchin, 2006). Auditory stimuli must be presented in a serial order, whereas multiple visual stimuli can be presented simultaneously. Auditory stimuli also take approximately 10 times longer to present than visual stimuli. For example, spoken stimuli take approximately 500 ms to present and visual stimuli take approximately 50 ms to present. Thus, several more selections per minute are possible in the visual modality. Attention must be paid to every stimulus in an auditory paradigm if more than two stimuli are used. The identity of each stimulus must be verified to determine if it is the desired selection (see Schreuder et al. (2010) for an auditory localization task that avoids this problem), which is not necessary in a visual paradigm. A two-choice auditory P300 BCI is most likely not beneficial. One stimulus must be presented with a much higher probability than the other stimulus in an oddball paradigm, and the less probable stimulus may elicit an unwanted P300 regardless of whether or not it is the desired choice. Setting stimulus probability at 0.5 will also significantly reduce P300 amplitude (Duncan-Johnson and Donchin, 1977). Moreover, in a typical auditory paradigm only two stimuli are presented and the subject is required to monitor for the less probable stimulus and essentially ignore the more probable stimulus. There are also logistical issues with an auditory system. Most importantly the sounds presented by the BCI to the user may be distracting for the people not using the BCI. Having the BCI user wear headphones is an obvious remedy to this problem. However, this may further isolate the patient from interaction with others, compared to a visual BCI. Nonetheless, as we have previously noted, if an auditory system is the only viable communication option, it should be preferred over no communication. However, some people opt for slower communication even though, in some cases, a BCI provides a reliable and faster option. For example, one locked-in individual could communicate using a visual BCI much faster than using eye movements; nonetheless he chose to use the latter.

1.2. Invasive versus non-invasive p300 brain-computer interface

There has been a long standing debate surrounding whether invasive (i.e., electrocorticography (ECoG), cortical neurons, or local field potentials) BCI is superior to non-invasive BCI (e.g., Hochberg et al., 2006; McFarland et al., 2010; Velliste et al., 2008). Krusienski and Shih (2010) used EEG signals before surgery for intractable epilepsy and ECoG signals after surgery. The results showed that the EEG and ECoG signals performed equally well. Moreover, the ECoG and EEG event-related potentials (ERPs) were similar. A second ECoG P300 study showed an information transfer rate of 60.5 bits/min, with approximately 2.4 s between selections (Brunner et al., 2011). A study using EEG reported an information transfer rate of 48.0 bits/min using 3.5 s between selections (unpublished data). Given the modest improvement in performance, non-invasive P300 BCIs accessibility is likely to be preferred over the invasive counterpart. Similar results have been shown when non-invasive sensorimotor rhythm (SMR) cursor control is compared to cortical neuron control. McFarland et al. (2010) showed that manual joystick operation is better than SMR and cortical neuron control, whereas SMR and cortical control are nearly equivalent; although there were task differences (cf. Hochberg et al., 2006; McFarland et al., 2010). As the field progresses, it is most likely that signals best matched to specific applications will be preferred.

1.3. Is the P300-based BCI gaze dependant?

A prominent assumption in the literature is that the visual P300 BCI is dependent on eye gaze (Brunner et al., 2010; Frenzel et al., 2011; Treder and Blankertz, 2010). Inclusion of occipital electrodes for classification is taken as evidence for gaze dependence. However, attention has been shown to modulate ERP morphology at these electrode locations as early as 50 ms post stimulus presentation (Hillyard et al., 1987; Mangun and Hillyard, 1987, 1991). Moreover, auditory oddball paradigms using high density EEG montages have shown that these same electrode locations discriminate target from non-target stimuli (Dien et al., 2003). Thus, while eye gaze may contribute to or bolster classification, the extent of the dependence on eye gaze has not been teased apart from the contribution of attention. Furthermore, it has been shown that very high P300 BCI accuracy can be achieved when gaze is directed at locations not containing the target stimulus (Liu et al., 2011; Treder and Blankertz, 2010). Such papers demonstrate that fixation is not necessary for visual-based BCI use. However, the experimental tasks require fixation of a specific location creating a dual-task situation, which is known to reduce P300 amplitude. Thus, the papers do not address the critical issue: *Can people with somewhat compromised visual ability benefit from a visual BCI*? This is an empirical question that has not been tested in the literature and a patient population will likely be needed to do so.

Curiously, the role of gaze dependence has not been challenged in the context of SMR BCI. A visual SMR BCI requires the subject to track a moving cursor using smooth pursuit eye movements. Thus, one can assume that visual SMR BCI would be more dependent on eye movements than the P300 BCI; however, this issue is yet to be addressed in the literature (Sellers et al., 2012). To the contrary, it is well accepted that SMR BCI is completely independent of motor control.

1.4. The oddball BCI

Brain-computer interface as a modified oddball paradigm was first reported by Donchin (1987) and proof of principle was demonstrated by Farwell and Donchin (1988). Subsequent to these studies some reports have relied exclusively on electrode locations and the canonical P300 component of the ERP (e.g., Donchin et al., 2000; Sellers and Donchin, 2006). Numerous other studies have included features selected from any electrodes that discriminate attended characters from non-attended characters. Thus, there is a subtle, but important, distinction between these classification methods. Whereas, the former rely on the P300 *component* of the ERP, the latter rely on spatiotemporal *features* of the ERP. There are a number of reasons for this. One, whether the P300 component or other ERP features are used for classification is of little concern, as the ultimate goal of BCI is to provide optimal performance. Two, classification methods use all available information that discriminates target from non-target responses. Three, any algorithm may rely more on modeling non-target responses; in large part due to the fact that an oscillatory wave synchronized to the presentation frequency is observed in the non-target waveforms and because the non-target stimuli outnumber the target stimuli by many fold. In light of these reasons, for the most part, the P300 BCI can more accurately be referred to as an oddball BCI.

2. Future directions

The Lulé et al. paper in this issue is a significant step toward expanding the number of people who can benefit from BCI technology. Similar research can help us begin to understand why people in the CLIS state are unable to communicate. Birbaumer et al.

(2008) have hypothesized that once a patient reaches the CLIS goal directed behavior is abolished and BCI communication is no longer possible. To date, no LIS patient has successfully used a BCI and then progressed into CLIS. Similarly, no CLIS patient has successfully used a BCI. Longitudinal study of BCI use in LIS is needed to determine if it is possible to traverse from LIS to CLIS with continued BCI success. On the other hand, it may be the case that BCI use before CLIS staves off CLIS (Birbaumer et al., 2008). The elusive question of why people with CLIS are unable to communicate remains to be answered. To answer this question, more research with additional patients and new populations is needed. Until that time, the ultimate clinical relevance and utility of BCI technology will not be realized.

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