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# EEG and eyeblink response to different acupuncture modalities: some preliminary results from four exploratory pilot studies

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> "I think you'll find it's the actual point that's causing me to blink – every time it fires off in Colon 4"
>
> "I felt the blinking started when the electrical stimulation started"
>
> (Study participants)

## INTRODUCTION

Encephalography (EEG) records electrical activity on the scalp, and is a useful low-cost tool for investigating rapidly changing cortical brain states. Eyeblink (bilateral, symmetrical and synchronous [1]) may be spontaneous, reflex or voluntary. Blinking maintains corneal moistness [2], but also allows attention to be released for internal processing [3-6]. Spontaneous eyeblink rate (EBR) is a marker for central (striatal) dopamine function [7-9], and is also inversely correlated with parasympathetic activity [10,11]. After adolescence, spontaneous EBR remains quite constant for the healthy individual under controlled conditions [12-14], although it may be affected by many factors (e.g. drowsiness [15], direction of gaze [16], time of day [17] and ambient lighting [18]). **Table 1** shows some correlations from the literature.

**Table 1.** Some correlations from the literature.

| **Increased EBR** | **Decreased EBR** |
|---|---|
| STATE | |
| Corneal dryness [19] | Downward gaze |
| Drowsiness [22], sleep deprivation [20,21] | Visual attention [22] |
| Higher baseline arousal [23,24] | Following stress [25] |
| TRAIT | |
| Anxiety [26] | |
| Cognitive flexibility [27,28] | Convergent thinking [29] |
| Neuroticism, introversion? | |
| PATHOLOGY | |
| Panic disorder [10] | |
| Schizophrenia (positive symptoms) [8,30,31] | Schizophrenia (negative symptoms) [32] |
| Other psychiatric disorders | |
| Huntington's disease [26] | Repetitive behaviour disorder [33] |
| Focal dystonia [26] | Parkinsonism [34-36] |
| Autism [26], Fragile X syndrome [37] | |
| MEDICATION | |
| Oral contraception [38] | Cocaine dependence [39] |

## RESEARCH QUESTIONS

- How do the EEG and EBR respond to different modalities of acupuncture?

  [manual acupuncture (MA), electroacupuncture (EA), transcutaneous electrical acupoint stimulation (TEAS)]

- How do the EEG and EBR respond to stimulation at different acupoints?
- How do the EEG and EBR respond to electrical stimulation at different frequencies?
- In particular, does stimulation 'drive' the EEG or blinking?

## METHODOLOGY

EC = Eyes closed, EO = Eyes open (both monitoring with no intervention); MA = Manual acupuncture; EA = Electroacupuncture; TEAS = Transcutaneous electrical acupoint stimulation

*Protocols*

Four small pilot studies were conducted. All intervention and EEG monitoring 'slots' lasted for 5 minutes, except in **Pilot 4**, in which the last two slots in each session were for 10 minutes, and all monitoring after baseline EO was also for 10 minutes. In **Pilot 1**, 5-minute EEG monitoring *followed* each intervention slot. In **Pilots 2 & 3**, 5-minute monitoring and stimulation were *concurrent*.

In **Pilots 1-3**, only 2.5 Hz or 10 Hz stimulation was used throughout each session. In **Pilot 4**, 'simultaneous' stimulation was also used, 2.5 Hz on one ear and 10 Hz on the other.

The following point combinations were used, in balanced order:

**Pilot 1.** LI4[2], ST36[2], LI4[2] & ST36[2]; Left LI4 & ST36, Right LI4 & ST36, Bilateral LI4 & ST36 (all six in each session). Five participants attended for two sessions (2.5 Hz or 10 Hz TEAS), two for only one session each.

**Pilots 2 & 3.** LI4[2], ST36[2]; Left LI4 & ST36, Right LI4 & ST36
(in Pilot 2, one combination per session; in Pilot 3, two combinations per session). In Pilot 2, 12 participants attended for four sessions, and in Pilot 3, four participants from Pilot 1 (a year before) also attended for four sessions, each experiencing four of a possible eight interventions.

**Pilot 4.** *shenmen* & concha ear points – Left, Right, Bilateral or 'Simultaneous' (e.g. 2.5 Hz Left, 10 Hz Right). Single case study.

Order of 'slots' in each Pilot:

**Pilot 1** (9 slots, all EC except for EO1 and EO2)

| EC | EO1 | TEAS1 | TEAS2 | TEAS3 | TEAS4 | TEAS5 | TEAS6 | EO2 |
|---|---|---|---|---|---|---|---|---|

**Pilot 2** (8 slots, all EO)

| EO1 | MA1 | EA1 | EA2 | EA3 | EA4 | MA2 | EO2 |
|---|---|---|---|---|---|---|---|

**Pilot 3** (11 slots, all EO)

| EO1 | MA1 | EA1 | EO2 | MA2 | EA2 | EO3 | TEAS1 | EO4 | TEAS2 | EO5 |
|---|---|---|---|---|---|---|---|---|---|---|

Or

| EO1 | TEAS1 | EO2 | TEAS2 | EO3 | MA1 | EA1 | EO4 | MA2 | EA2 | EO5 |
|---|---|---|---|---|---|---|---|---|---|---|

**Pilot 4** (5 slots, all EO)

| EO1 | TEAS1 | TEAS2 | TEAS3 | TEAS4 |
|---|---|---|---|---|

*Monitoring and analysis*

EEG was monitored following standard procedures (frequency bands and filtering, average reference montage), using the 10/20 system of electrode location (19 electrodes with linked ears as reference) [**Figures 1-2, Table 2**]. The Mitsar EEG-202 amplifier and WinEEG software (v2.91.54) were used (Mitsar Ltd, St Petersburg). Following artefact processing, relative power data was exported and means and differences calculated in Excel. Statistical computation (Bootstrap, ICC, Pearson's r, Friedman, Wilcoxon signed-ranks, Binomial and Independent-samples T tests) was carried out in SPSS (v 20).

EBR was not part of our original EEG protocol, so participants were not informed that we were observing their blinks [16]. With eyes open, they were asked to focus gently on an object in front of them. Blinking was permitted, but constrained in that they were occasionally asked to reduce blinking if it became too frequent (which would have invalidated the EEG record).

The cornea is positively charged relative to the retina. During blinking, the eye rotates, and the resulting vertical movement of the cornea-retina dipole makes the blinks visible in the EEG trace [1,40,41] (movement of the lid relative to the eye can also be seen [42]). EBR was thus assessed either from raw EEG records by directly counting the blink artefacts from one frontal EEG electrode (Fp1) or following processing for artefacts and 'inverting' those for eyeblink obtained from independent component analysis (ICA) of the whole EEG record [**Figure 3**]. EBR was averaged for each slot, and the averages compared for the different slots.

To assess the likelihood of stimulation triggering blinks, the time between the peak of the last stimulation artefact before a subsequent blink and the onset (zero crossing) of the blink itself

was calculated using the cursor and precise coordinates provided by WinEEG for the first 22 blinks in nine different data samples (five from the same participant).

The distribution of these times was then plotted, dividing the times by the period of the applied stimulation and multiplying by 100 to give a percentage of the period for each time, enabling a comparison between the results for 2.5 Hz and 10 Hz stimulation.

**Fig 1.**

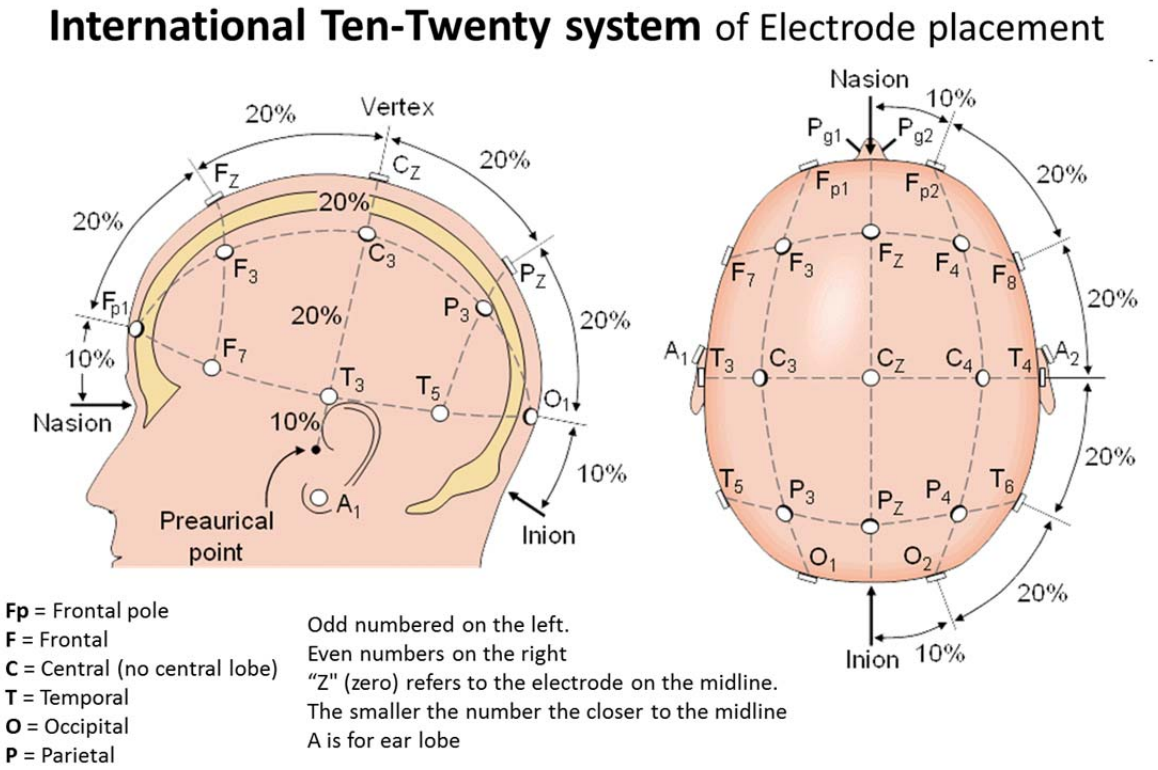



**Fig 2. Experimental set-up**

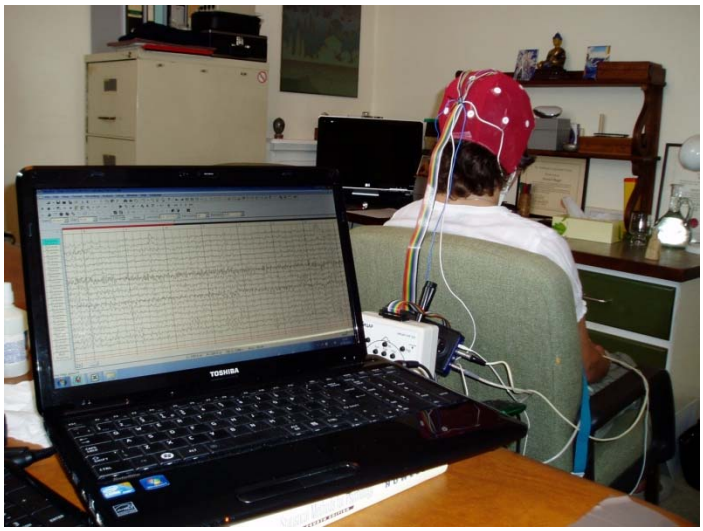
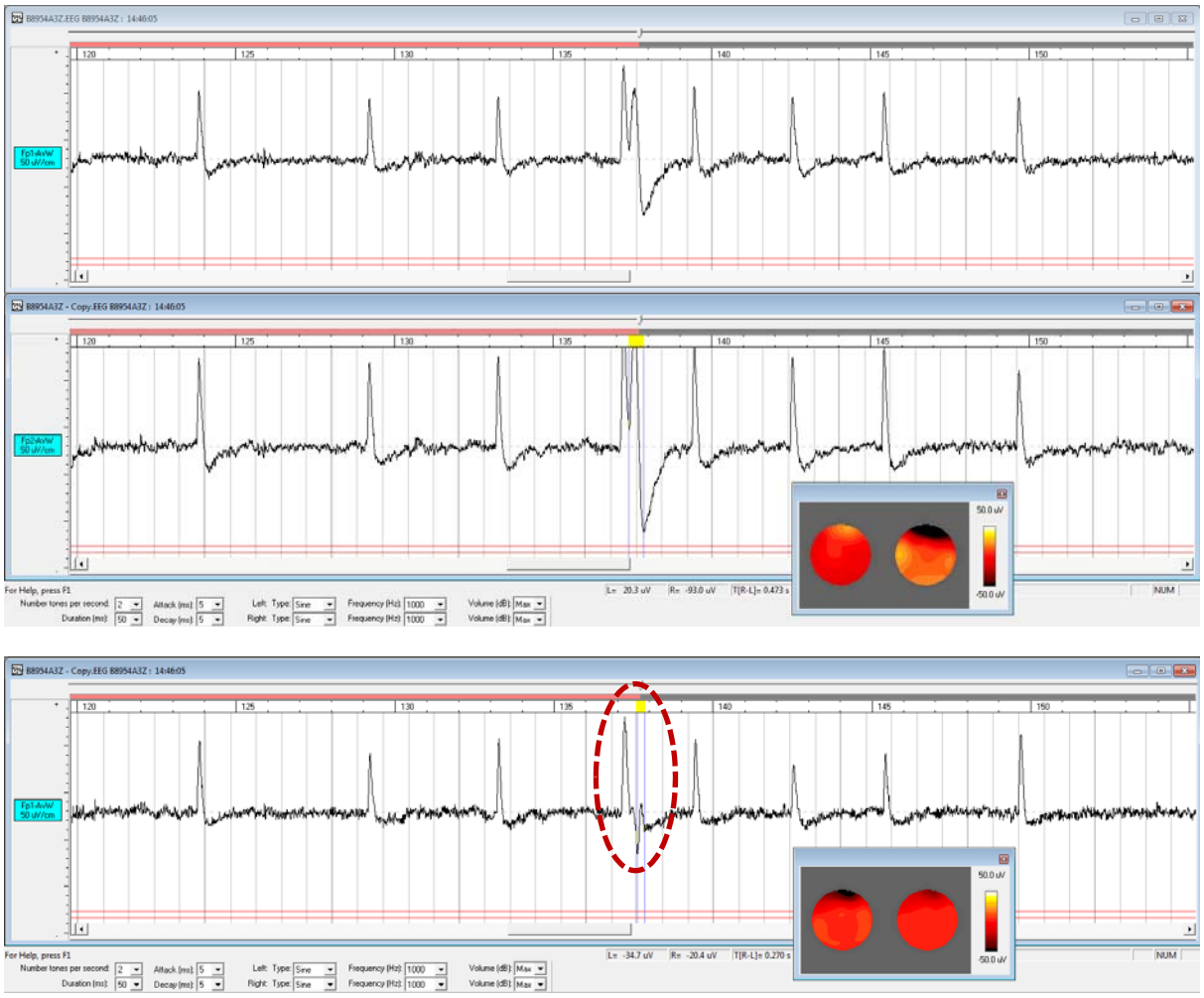


**Table 2. EEG frequency bandranges used in this study**

| Name | Frequency range |
|---|---|
| Delta | 1.5-4 Hz |
| Theta | 4-8 Hz |
| Alpha1 | 8-10 Hz |
| Alpha2 | 10-12 Hz |
| Alpha (All) | 8-12 Hz |
| SMR (sensorimotor rhythm) | 12-15 Hz |
| Beta1 | 15-18 Hz |
| Beta2 | 19-25 Hz |
| Beta3 | 25-35 Hz |
| Beta ('All') | 13-21 Hz |
| Gamma | 35-45 Hz |

**Fig 3.** Eyeblinks visible in the EEG: (a) in the raw EEG, comparing traces for electrodes Fp1 and Fp2; (b) as 'inverted' ICA artefacts (showing apparent blink as another type of artefact)



For further details on methodology, please contact the authors.

## SALIENT RESULTS

1. EEG

Only results from **Pilot 1** have been analysed, and to date no marked difference in response to TEAS at 2/5 Hz and 10 Hz has been found.

In contrast, stimulation at different locations gave some unexpected and highly significant results:

Stimulation on the **Right** results in **greater** relative spectral power than stimulation on the **Left** (at all EEG electrodes,[a] and in all bandranges used[b])

Stimulation of **ST36**[2] results in **greater** relative spectral power than stimulation at **LI4**[2] (at all 19 EEG electrodes except Fp2,[a] and in all of the 11 bandranges used[a]).

Thus, stimulation on the **Left** results almost always in **decreased** relative spectral power, and stimulation on the **Right** in **increased** spectral power, *relative to the previous intervention*[a]

Similarly, stimulation of **LI4**[2] results almost always in **decreased** relative spectral power, and stimulation at **ST36**[2] in **increased** spectral power, *relative to the previous intervention*.[a]

However, stimulation amplitude may be a confounding factor in these results,[c] and this needs to be investigated further.

2. EBR

Results from **Pilots 1-4** have been analysed. A possible difference in response to TEAS at 2.5 Hz and 10 Hz in **Pilot 1** was found, but this was not supported by results from Pilots 2-4 [**Table 5**].

In contrast, stimulation at different locations and for the three different modalities used gave some unexpected and sometimes significant results:

A. Comparison between stimulation locations

EBR was more often **higher** during stimulation on the **Left** than on the Right, and at **ST36**[2] than at LI4[2].

**Pilot 2**

Mean EBR was **higher** during stimulation on the **Left** than on the Right, but only after 10 minutes of stimulation. Mean EBR also increased **more** over the course of stimulation with **Left** stimulation[d] [**Figure 4a**].

Mean EBR was **higher** during **ST36**[2] than LI4[2] stimulation (for all MA and EA 'slots'[e]). Mean EBR also increased more over the course of stimulation with **ST36**[2] stimulation[d] [**Figure 4b**].

**Pilot 3**

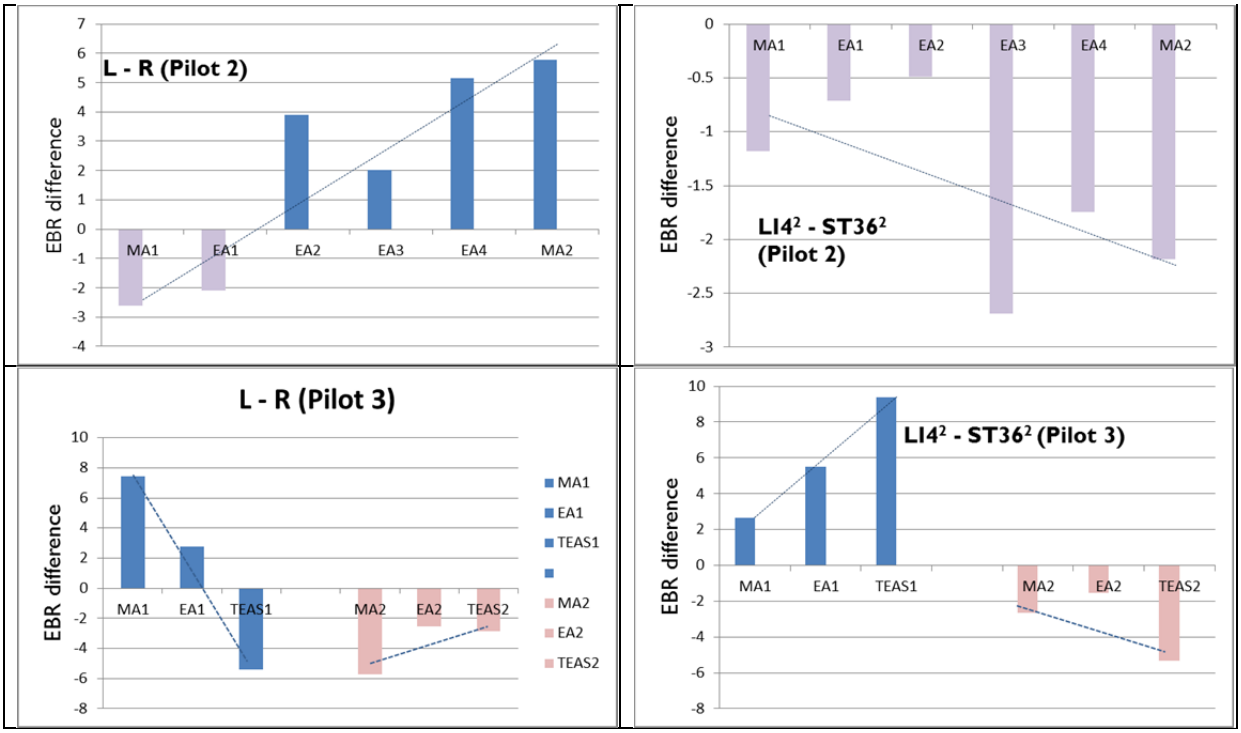
Mean EBR was **higher** during stimulation on the **Left** than on the Right during MA1 and EA1, but **lower** during MA2, EA2, TEAS2 and TEAS1[f] [**Figure 4c**]

Mean EBR was **higher** during **LI4**$^{2}$ than ST36$^{2}$ stimulation when these were *first* stimulated during each session (MA1, EA1, TEAS1), but **lower** during *second* stimulation (MA2, EA2, TEAS2)[f] [**Figure 4d**]

**Pilot 4**

Mean EBR was **higher** during TEAS on the **Left** than on the Right ear.[g]

**Fig 4.** Differences in mean EBR between: (a) Left and Right, and (b) LI4$^{2}$ and ST36$^{2}$ stimulation (**Pilot 2**); (c) Left and Right, and (d) LI4$^{2}$ and ST36$^{2}$ stimulation (**Pilot 3**).




B. Comparison between modalities

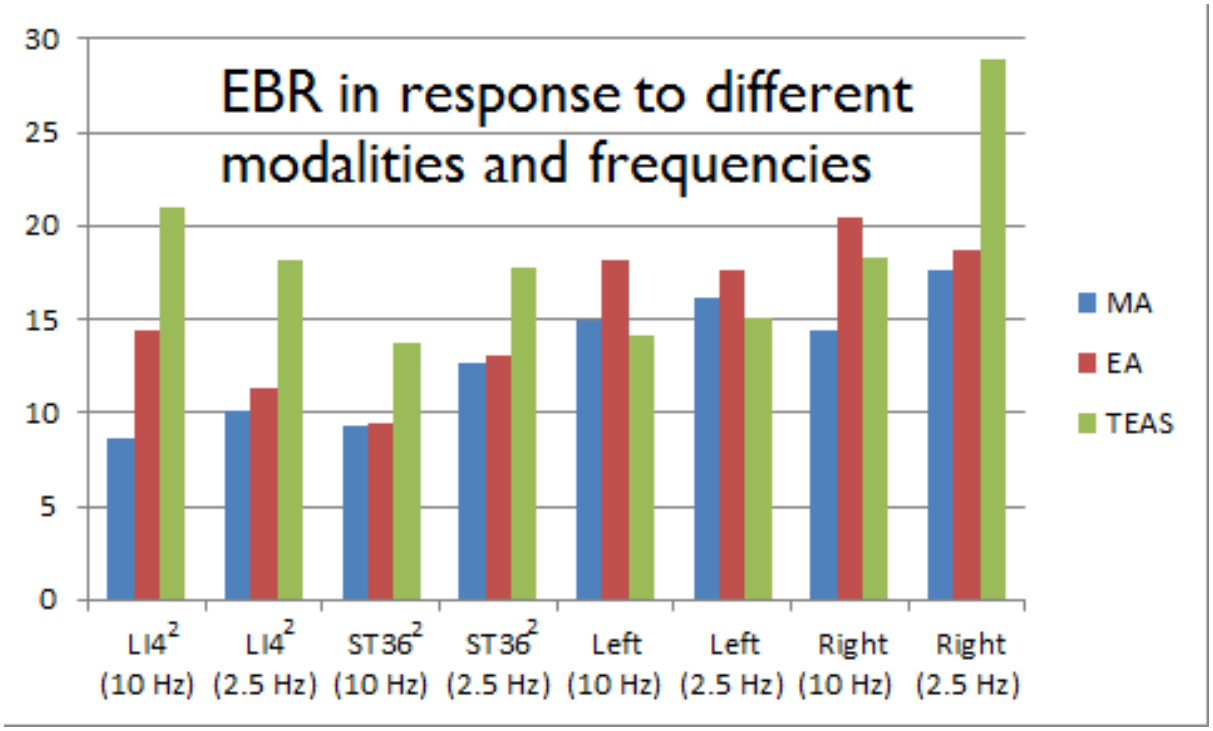
In **Pilot 2**, most increases in EBR occurred **between MA1 and EA1**, and **between EA1 and EA4**, suggesting greater activation with EA than MA, and with 20 minutes of EA rather than 5 minutes. In **Pilot 3**, EBR during EA usually increased compared to during prior MA,[h] decreasing again in the subsequent EO slot.[i] At all locations, EBR during MA was less than during EA, but during TEAS was sometimes more and sometimes less than during EA or MA [**Table 3, Figure 5**].

**Table 3.** Numbers of EBR increases and decreases between successive interventions

| **Pilot 2** | EO1 to MA1 | MA1 to EA1 | EA1 to EA4 | EA4 to MA2 | MA2 to EO2 |
|---|---|---|---|---|---|
| Increases | 25 | 29[j] | 30[k] | 22 | 19 |
| Decreases | 18 | 15 | 11 | 23 | 23 |
| **Pilot 3** | EO to MA | MA to EA | EA to EO | MA to TEAS | EA to TEAS |
| Increases | 11 | 24[l] | 4[l] | 10 [7] | 7 [4] |
| Decreases | 14 | 3 | 24 | 3 [5] | 4 [10] |

Square brackets indicate results for reverse order (e.g. TEAS to MA, rather than MA to TEAS).

**Figure 5.** Mean EBR (**Pilot 3**) is consistently greater for EA than MA, and usually greater for TEAS than MA (except at Left); for TEAS it is greater with 2.5 Hz (except at LI4[2]), and for EA with 10 Hz (except at ST36[2]).[m]



C. Delay time between blinks and preceding stimulation EEG spike artefacts

In **Pilot 3**, spike artefacts from TEAS at LI4[2], Left and Right were clearly visible in the EEG, provided that the current applied is sufficiently strong [**Fig 6**]. They were less frequently observed with EA, and not at all from ST36[2] stimulation.

**Fig 6.** EEG traces showing stimulation artefacts, associated blinks (single blue lines) and unrelated blinks (double blue lines). (a) 10 Hz; (b) 2.5 Hz.

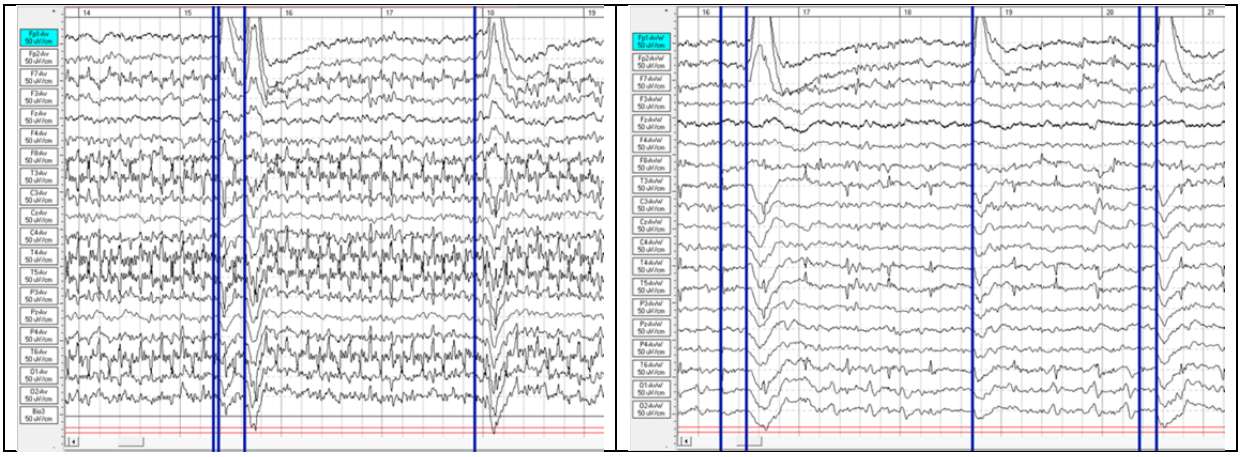
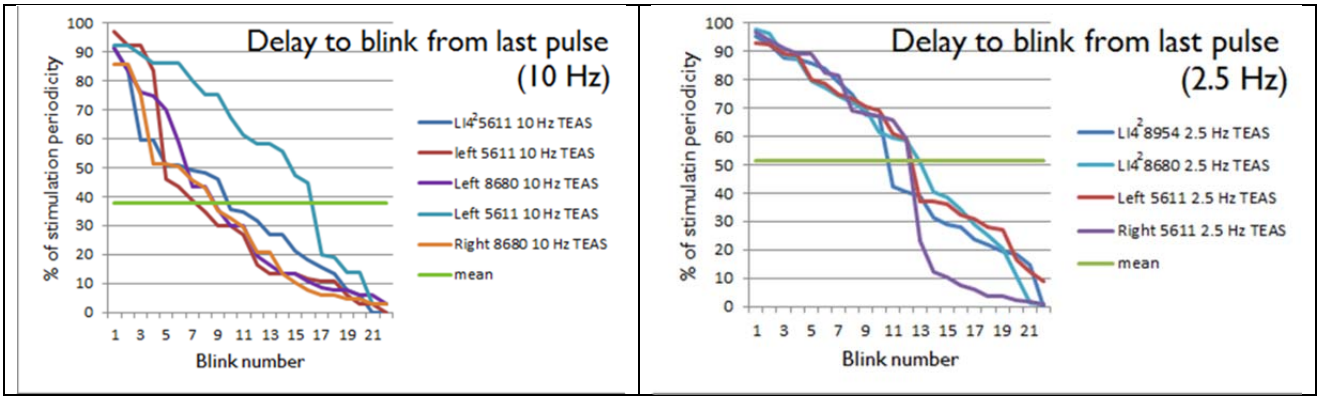


**Figure 7** shows the distribution of normalised delay times between blinks and preceding stimulation spike EEG artefacts.

**Fig 7.** Distribution of normalised delay times between 22 blinks and preceding stimulation spike EEG artefacts: (a) for 2.5 Hz stimulation; (b) for 10 Hz stimulation.

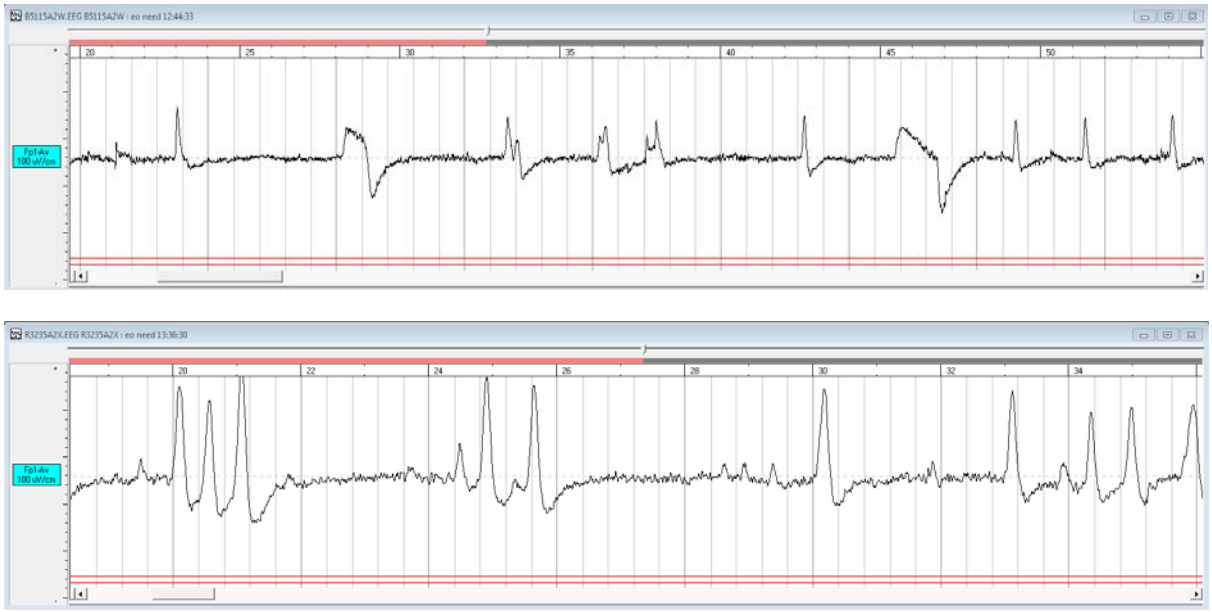



Note that blinks occur with less delay following pulses during 10 Hz than 2.5 Hz TEAS (timescales normalised),[n] suggesting greater EBR facilitation, and possibly even that blinks are more likely to be associated by the participant with the sensation of stimulation at 10 Hz than at 2.5 Hz. Applied current does not appear to affect delay as a confounding factor (the greatest mean delay for 10 Hz occurred with a current close to the median, and the lowest mean delay for 2.5 Hz with the maximum current in the range)

D. Other findings

Agreement between the count methods used (Fp1, Fp2, ICA inversion) was good[o] although not perfect, usually because of difficulties in interpreting whether an artefact represented one or more blinks (or not a blink) in the manual count. **Figure 3**, for example, shows an apparent double blink (a) that following ICA inversion is seen as a single blink plus another type of artefact (b); **Figure 6** shows other blink variants that appeared in both the raw and inverted ICA Fp1 trace.

**Fig 6.** Blink variants in the EEG trace: (a) partial blinks and saccade; (b) multiple and 'mini' blinks.



Inter-individual EBR varied widely, as did EBR for the same individual in different sessions, even at baseline [**Table 4**]. Thus most consistent patterns of change were *within* particular sessions, with parallel changes across sessions dependent on baseline and to some extent regardless of intervention [**Figure 7**]. Pre-Post EBR differences could be increases or decreases [**Table 4**], and there was no cumulative effect over repeated sessions. Differences in EBR with 2.5 Hz and 10 Hz stimulation were not consistent across the four Pilots, with a trend to more or greater increases with 2.5 Hz than 10 Hz in Pilots 2 and 3, respectively.

**Table 4.** Baseline values for Pilots 1 & 3, showing intra- and inter-individual variability.

| | **Pilot 1** | | | **Pilot 3** |
|---|---|---|---|---|
| **Case** | Session 1 | Session 2 | Mean (sessions 1&2) | Mean (sessions 1-4) |
| 2185 | 18.4 | 9.6 | 14 | 22.0 |
| 5611 | 13.2 | 13.4 | 13.3 | 49.0 |
| 7032 | 0.4 | | 0.4 | |
| 8311 | 26.2 | | 26.2 | |
| 8680 | 5.8 | 11.6 | 8.7 | 13.8 |
| 8875 | 8.0 | 15.2 | 11.6 | |
| 8954 | 1.6 | 2.2 | 1.9 | 23.3 |

**Fig 7.** Patterns of EBR change in four different sessions for one participant in Pilot 2.

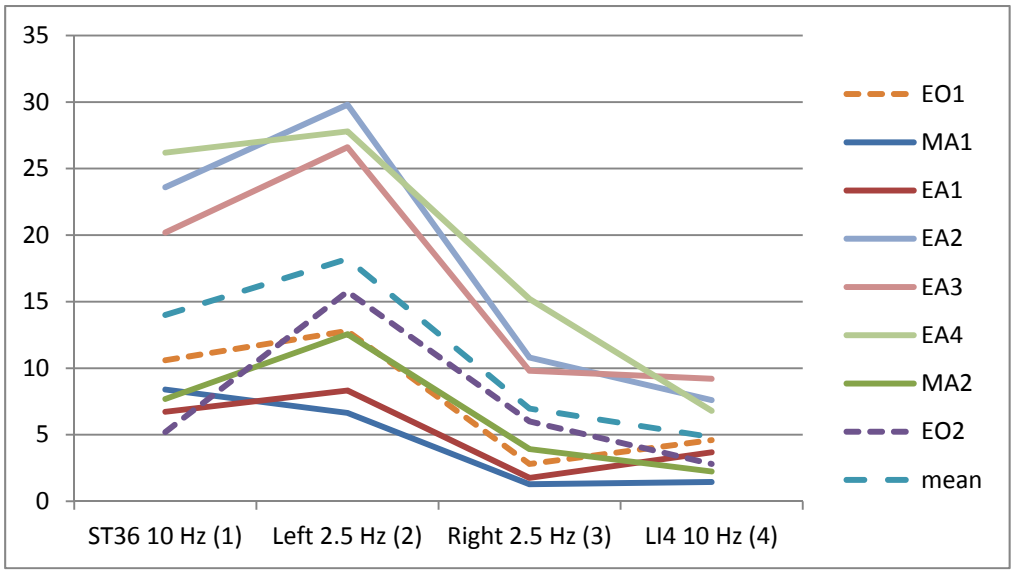



**Table 5.** Changes in EBR (beats/min)over sessions in the four Pilot studies

| | Mean change over session | Number of increases | Number of decreases | Mean change (2.5 vs 10 Hz) |
|---|---|---|---|---|
| **Pilot 1** | +0.3 | 5 (all at 2.5 Hz) | 7 (6 at 10 Hz) | +4.7 vs -4.1 (6-) |
| **Pilot 2** | +4.2 | 32 | 16 | +4.1 vs +4.3 |
| **Pilot 3** | +8.2 | 13 | 3 | +3.8 vs +4.4 |
| **Pilot 4** | -1.2 | 3 | 3 | -2.1 vs -0.2 |

## DISCUSSION

"I shut my eyes and all the world drops dead; I lift my lids and all is born again."

Sylvia Plath (Mad Girl's Love Song, 1951)

The most significant findings are those relating to differences in EEG relative power in response to Left vs Right and LI4[2] vs ST36[2] stimulation. Although the corresponding EBR changes were not found to be significant, these EEG and EBR effects may be related – some authors have suggested an association between reduced alpha power and increased EBR [21,22].

Also significant are the differences in EBR between MA, EA and TEAS, suggesting possible 'dosage' or order effects, with EA perhaps having a greater effect on dopaminergic function or arousal than MA. This may have implications when selecting modality for the treatment of conditions characterised by low or high autonomic or cortical arousal, or for conditions such as schizophrenia or Parkinson's disease.

Increases in EBR over the course of sessions (**Pilots 1-3**) may suggest arousal rather than relaxation, but could merely be a concomitant of drowsiness. The EBR results from **Pilot 1** might indicate that 10 Hz is experienced as more relaxing than 2.5 Hz, but this is not supported by the results of **Pilots 2-4**.

However, 10 Hz stimulation does appear to facilitate blinks more than 2.5 Hz, and so is perhaps more likely to be interpreted by participants as triggering those blinks.

**Study limitations.** We did not appreciate how widely baseline EBR can vary, nor the possible impact of partially constraining blinking or the importance of a consistent protocol (gaze direction, ambient lighting, minimal interaction). Furthermore, sample numbers are small (too small in some cases for the Wilcoxon test), and although this shortcoming has been remedied to some extent by using Bootstrap resampling of the EEG data, our EBR results should be treated cautiously.

**Further research** is required to clarify these findings and to explore questions such as whether baseline EBR correlates with responsiveness to acupuncture (as it may for hypnosis), whether acupuncture has a 'normalising' or 'balancing' effect on EBR, what the effects are of related interventions such as laser acupuncture, and whether stimulation at other acupoints has outcomes similar to or quite different from that at the points used here.

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**Statistics footnotes**

a. Binomial, $p<0.001$

b. Binomial, $p=0.012$

c. Pearson's *r* not significant for correlations between applied amplitude and relative spectral power except for $ST36^2$ stimulation, when correlations were found between amplitude and power summed over all bands at T3, T4, T5 and T6, and between amplitude and power summed over all electrodes in Band D (Alpha2, 10-12 Hz). Furthermore, no consistent significant differences in applied amplitude were found between the various interventions (Left vs Right, $LI4^2$ vs $ST36^2$, etc.) when using the Wilcoxon signed-ranks test.

However, if the differences in applied current amplitude between the various interventions are simply counted, case by case, then it does seem that greater amplitudes are associated with higher EEG spectral power, in that the amplitude differences tend more often than not to be in the same direction as those in spectral power:

| Amplitude differences (Binomial significance) | Agreement with main direction of EEG relative power change (in parentheses) | Disagreement with main direction of EEG relative power change (in parentheses) |
|---|---|---|
| Left/Right (p=0.039) | 8 (209) | 1 (0) |
| $ST36^2/LI4^2$ (p=0.006) | 11 (208) | 1 (1) |

Further comparative results not included here support this finding.

d. With 2.5 Hz but not 10 Hz EA; b. with 10 Hz but not 2.5 Hz EA

e. But difference possibly significant only for EA1, EA2 and EA4 at 10 Hz (Wilcoxon, Sample 11, $p<0.05$)

f. Differences not significant (Wilcoxon and Binomial, $p>0.05$)

g. Wilcoxon (sample 6), $p<0.001$; in only one session out of six did Right TEAS result in higher EBR than Left TEAS

h. Wilcoxon (sample 32), $p<0.001$; 24 increases, 4 decreases, Binomial $p<0.001$ (4 negligible changes)

i. Wilcoxon (sample 32), $p<0.001$; 25 decreases, 5 increases, Binomial $p<0.001$ (2 negligible changes)

j. Binomial, $p=0.049$

k. Binomial, $p=0.004$

l. Binomial, $p<0.001$

m. Differences not significant (Friedman, $p>0.05$)

n. Independent-samples T-test, $p=0.013$ (2-tailed, unequal variances)

o. ICC for single measures 0.930, $p<0.001$ (95% CI, one-way random effects model)

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