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Using QEEG parameters (asymmetry, coherence, and P3a novelty response) to track improvement in depression after choir therapy

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Abstract: *This pilot study reports the findings from a sub-group of nine patients, from a cohort of 32 middle-aged ambulant depressive patients undergoing an intensive 8-week choral singing programme, who received 'before' and 'after' quantitative electroencephalography (QEEG) (resting state and the WinEEG VCPT ERP protocol). 'Before' and 'after' mental state examinations and Beck Depressive Inventory showed significant improvement ($p < 0.001$). Group spectral analysis of resting QEEG showed greater L/R hemispheric symmetry of activity, reduction of right polar pre-frontal hyper activity, and reduction of hypercoherence (all reported depressive parameters). Event related potentials results revealed that an initially heightened P3a novelty cingulate gyrus response reduced significantly over the course of treatment ($p < 0.05$).*

Keywords: QEEG, depression, music therapy, hypercoherence, P3a novelty, right frontal activity

Background

Quantitative electroencephalography

This refers to a range of analytic processes which can be applied to raw EEG signal data to extract patterns that are often not obvious to the naked eye. Though anatomical resolution is poor compared with other brain functional techniques, temporal resolution is in milliseconds, and the low cost and portability of the equipment makes it an attractive research tool. A detailed overview of the subject can be found in Kropotov's text on the subject (Kropotov, 2009).

Depression and the brain

A range of research observations across several domains supports the view that left and right hemispheric functional differences are closely involved in the affective disorders. But in what ways? We know that left anterior lesions are associated with depression, and right anterior lesions can produce states of fatuous cheerfulness. We also know there is an antero-posterior component. The more anterior the left hemispheric lesion, and the more caudal the right hemispheric lesion, the greater the chance of depression. There is a large (and sometimes conflicting) literature on the emotional properties of the hemispheres. However, a useful and comprehensive review can be found in McGilchrist (2010, especially pp. 63–64), who writes: 'the right frontal pole has a depressive stance compared with the left frontal pole *or its own* parieto-occipital cortex' (p. 63) (Our italics) … and furthermore: 'depression *per se* is probably associated with reduced right posterior activity in addition to increased right frontal activity' (p. 63). … and 'severe posterior right hemisphere hypo-activity is associated with withdrawal and apathy' (McGilchrist, 2010, pp. 63–64).

The vertical (cortico-bulbar) axis is also implicated, but this too has a 'lateralisation' component. We know that myelinated vagus (ventral nucleus and nucleus ambiguous) connections interact principally with right brain functional sites to do with eye-contact, facial expression, prosody, social interaction (See Porges, 2011). This in turn impacts on affective states.

Quantitative electroencephalography (QEEG) findings in depression are compatible with this broad view, and suggest that EEG indices of increased right frontal (beta activity) and decreased left frontal function (EEG power, preponderance of alpha waves) correlate well with depressive states. More recently, researchers

(Leuchter, Cook, Hunter, Cai, & Horvath, 2012) have also reported hypercoherence in depressive conditions. McGilchrist reminds us that an intricate relational dynamic between the hemispheres (their 'dance' or 'dialogue'), rather than a simplistic predominance of one hemisphere over the other, may be a better model for the way the brain manages mood and affect.

Choral singing involves both music and interrelations between the group members. The caudal right hemisphere subserves both functions, and in turn engages left hemispheric function. We might therefore expect it to enhance interhemispheric 'dialogue' and in turn have a powerful positive effect on mood states.

Confounding variables

There is a good deal of individual variation in EEG patterns in a normal population. This also applies to the QEEG patterns in depression we see from one person to the next. To make matters even more complex, brain functional changes that occur as depression lifts can sometimes depend on the kind of treatment used. For instance, Mayberg (2006) found that fMRI scans showed *reduced* activity in the frontal cortex when patients were treated with CBT, and *heightened* activity in the same areas when they were treated with paroxetine, a Selective Serotonin Reuptake Inhibitor (SSRI).

Pooling QEEG data, and compare 'before' and 'after' group results, allows us to extract common factors which might be obscured by a range of individual variations.

A brief history of research in QEEG and depression

A range of studies across several disciplines over the last 20 years suggest that cerebral hemispheric imbalances are associated with affective disorders. Work by Australian visual neuroscientist Jack Pettigrew (Pettigrew, 2001; Pettigrew & Miller, 1998) supports the view that excessive left hemispheric activity may be associated with hypomanic and manic states, whereas excess right hemispheric activity goes with depression.

In the US, Davidson et al. (1991) found that anterior cerebral alpha asymmetry reflected relative differences in activity between the right and left hemispheres. This in turn reflected trait-like tendencies of either excitement/approach (left hemisphere) or avoidance/fearfulness (right hemisphere). Since alpha states are so-called 'idling' states, high left frontal alpha would be associated with a depressive attitude, and high right frontal alpha with a hypomanic one. There was some suggestion that this pattern of asymmetry emerged early in life and could therefore be an 'endophenotype' of proneness to depression.

The situation is actually more complicated than this, because as we noted earlier, there is also an antero-posterior gradient for each hemisphere. We know that left anterior strokes are associated with depression, and the more anterior the stroke, the greater the depression. We also know that right anterior strokes can produce inappropriate cheerfulness. Moreover, the more posterior the lesion in the right hemisphere, the greater the chance of depression.

Leuchter and Cook (See Cook, O'Hara, Uitdehaage, Mandelkern, & Leuchter, 1998) began to use 'cordance' (a QEEG value derived from an addition of absolute and relative EEG power values at any one location) as a measure of regional brain activity because it correlated strongly with regional blood flow. They reported cordance asymmetry (power imbalance) in the frontal hemispheres in depressed patients. Left frontal brain power was less than right frontal brain power.

This fitted in with Davidson's earlier findings that there was more alpha (resting) activity in the left brain in the depressed. Leuchter (See Cook et al., 1999) took this work further to use cordance to predict which depressed patients might respond best to fluoxetine (another SSRI). Prefrontal theta cordance (probably reflecting cingulate gyrus activity) decreased early in patients who would later respond to antidepressants, but remained steady in those who responded to placebos.

Music therapy, depression and QEEG

Two background EEG 'music therapy for depression' studies claim to have found QEEG changes in response to treatment. In one (Jones & Field,

1999), patients with major depressive disorder (MDD) listened to their choice of music for 2 weeks, with reduction of depression and reduction of right prefrontal beta activity. In the other (Sung-Jin & Chul-Jin, 2011), women with post-partum depression were given a single session of music therapy. Before and after background QEEGs showed reduced prefrontal alpha asymmetry.

Depression and EEG hypercoherence

More recently Leuchter et al. (2012) has proposed the theory that brain EEG hyper-coherence (a rigidity of functional interaction) underlies depressive conditions. He and his colleagues report research which examined resting state functional connectivity as measured by QEEG coherence. They found that subjects with MDD had significantly higher overall coherence as compared to controls.

Event related potentials and depression

The only published group studies available (Sumich, Kumari, Heasman, Gordon, & Brammer, 2006) report that normal subjects show R > L asymmetry of amplitude in the N200 response (auditory oddball task), whereas mildly depressed subjects showed more symmetry on this measure.

Kropotov (2009, p. 456) describes a depressed patient whose NoGo responses were suppressed (in comparison with normals) at the left site (F7; corresponding to left medial and ventro-lateral hypoactivity), but not on the right (F8). The paucity of work done on ERPs and depression makes the group ERP findings in our study especially interesting.

Aims

We wanted to test the null hypothesis that QEEG testing *would not* demonstrate any changes in brain wave frequencies as the result of choir therapy for our nine subjects. And if there *were* changes, we were interested to see what kind.

Method

The project involved community dwelling volunteers (N = 32), living in the Blue Mountains, west of Sydney, with an age range of 48–73 years. They were recruited through newspaper advertisements in the region.

The choir group (N = 21) was compared to a control group (N = 11). The 8-week choir programme included weekly meetings for singing exercises and learning new songs. Choir members were given a practice CD of the physical and singing exercises, the meditation dialogue and accompaniments to the songs in the songbook. They were all expected to practise between the weekly sessions. The control group lived their lives as normal between the pre and post testings.

T-tests were carried out to ascertain any significant demographic differences between the two groups. Both groups were also assessed for depression (Beck depression inventory), post-traumatic stress, wellbeing and quality of life (SIWB/spiritual index of well-being score) before and after the choral programme. An ANCOVA was conducted, with Beck post intervention as the dependent variable group as the fixed factor and Beck at pre-intervention as the covariate.

'Before' and 'after' background/resting state QEEGs

A small sample (N = 9), selected at random from the choir group (N = 21) was tested using QEEG to monitor changes in brain wave patterns before and after the choir intervention using the Mitsar/WinEEG system (See Kropotov, 2009).

'Before' and 'after' event related potentials: The visual continuous performance task

As well as collecting 3-minute 'eyes open' and 'eyes closed' background EEGs from each subject, we also gave them the WinEEG VCPT, to elicit a range of ERPs. The VCPT testing protocol elicits a comprehensive range of ERP responses, across some 600 ms post-stimulus, in responses to a range of computer-presented tasks and stimuli. Every 3 seconds, the subject is presented with a picture followed 500 ms later by another picture. If an animal comes up first, and is followed by an animal, the subject presses a response key (This is the so-called GO condition). For any other combination, the response key is NOT pressed (See picture). Up to 400 pairs can be presented, but

100 are sufficient for a reliable result. The 500 ms interval is long enough for the subject to generate a preparatory response (whether to press the button or not). Thus when an animal is followed by a plant, the subject needs to inhibit their tendency to press the mouse button (this is the NoGo condition). Picture pairs are presented randomly (See Figure 1).

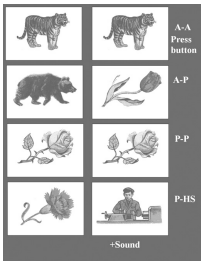

Figure 1: Example of picture pairs used in this study

Of particular significance to this study is the presentation at the bottom of the picture, when a plant is followed by a human, and accompanied by a beeping sound, is the so-called 'novelty' stimulus, which, because it is so unlike the other presentations, elicits its own specific response pattern, the so-called P3a or P3 novelty response (Kropotov, 2009). This was the ERP response that proved to change significantly in our choir participants.

Results

Demographics

T-tests were carried out to ascertain any significant demographic differences (age, gender, employment, single versus partnered, education level) between the two groups. The choir and control groups showed no statistically significant differences on all the main indicators except education which was a confounding factor.

Depression scores – BDI II

Depression scores were measured by the Beck Depression Inventory (BDI II) developed by Beck, Steer, & Brown, 1996. An ANCOVA was conducted, controlling for education. The results showed a significant drop in depression ($F(1,28) = 17.29$, $p < 0.001$) with a power of 98%, indicating less severe depressive symptoms (Figure 2).

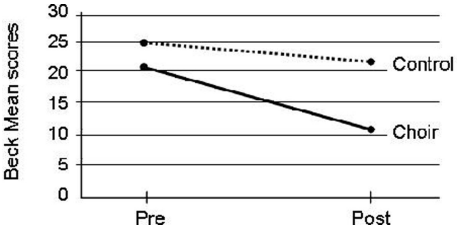

Figure 2: Drop in depression measured by the Beck Depression Inventory (BDI-II)

Neither the quality of life scale or the post traumatic stress disorder inventory pre-versus post-score differences were found to be statistically significant.

Wellbeing scores – Spirituality Index of Wellbeing (SIWB)

Wellbeing was measured using the Spirituality Index of Wellbeing developed by Daaleman & Frey, 2004. An ANCOVA analysis was conducted controlling for education. It showed a significant difference between the groups in post intervention total scores ($F(1,28) = 7.04$, $p < 0.013$) power 72.6%. This showed an overall improvement in wellbeing. The self-efficacy sub-scale of the SIWB showed statistical significance between groups at post intervention. This indicated that proactive wellbeing increased. The life scheme sub-scale was not statistically significant.

Weekly choir surveys

Weekly choir surveys showed significant results in two areas: Increased comfort with singing ($p < 0.008$), and enjoyment of social interactions ($p < 0.004$).

Pre-and post clinical interviews

A psychiatrist performed a brief mental state examination with a special focus on mood with each subject before and after treatment. These clinical observations also confirmed that subjects' moods had improved considerably.

Background or resting EEGs; group findings

Proviso

We remind the reader that even though in our findings, pre- and post-changes in background activity were especially marked in the delta and

high beta and theta ranges, these are also the frequencies most subject to artefacts.

The **international 10–20 system** of electrode placement was used in this study. Each site has a letter to identify the lobe and a number to identify the hemisphere location (See Figure 3). The letters F, T, C, P and O stand for frontal, temporal, central, parietal, and occipital lobes, respectively. A 'z' refers to an electrode placed on the midline. Even numbers (2, 4, 6, 8) refer to electrode positions on the right hemisphere, whereas odd numbers (1, 3, 5, 7) refer to those on the left hemisphere. See diagram below.

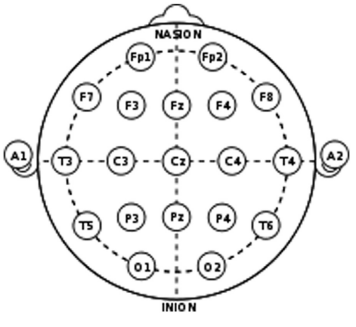

Figure 3: International 10–20 electrode placement

There is a colour bar at the top right hand corner of each coloured brain map diagram. It is calibrated in microvolts (or percentages if a comparison is being made).

Figure 4 Spectra and maps show heightened activity at Fp2 in the beta 2 and gamma frequencies. Delta is also prominent at F8. Excessive right polar pre-frontal activity in depression is consistent with a range of research findings described earlier (McGilchrist, 2010), especially in the higher frequencies; the sort of pattern to be expected in states of anxious or agitated depression.

Figure 5 shows that right polar prefrontal activity is greater than left, across every frequency except the alpha (idling) range. Though lower frequencies like delta correlate with reduced levels of consciousness, they may also have a 'binding' or integrative function. Furthermore, delta is often seen in the orbital pre-frontal cortex, and may in fact correlate with increased integrative activity in that region (See Sherlin, in Budzinski, Budzinski, Evans, & Ababarnel, 2009; pp. 86–94). Thus excessive right prefrontal delta may be, paradoxically, be associated with heightened activity. Again, this right to left asymmetry favouring the right hemisphere is consistent with other research findings in depression (Henriques & Davidson, 1991).

Post-choir, the left/right differences seen in the earlier resting EEG are reduced (Figure 6).

The interhemispheric asymmetry maps now show much less difference between left and right hemispheres across all frequencies, with a reduction in left polar power in the higher frequencies (Figure 7). There is still some excessive activity in the right frontal region but it has shifted back from the Fp2 to the F8 position. Again, this is consistent with previous research findings (McGilchrist, 2010).

Comparisons with norms

Before: Comparison with norms. Age averaged across the entire sample to 12-12-1965; i.e., 45 years.

In Figure 8, we can see that, compared to the normative data base, beta 1 beta 2 and gamma in the right frontal hemisphere is excessive (C4 beta 2 $p < 0.0090$, C4 gamma $p < 0.0163$), as might be expected from previous research findings (Cook et al., 1998).

There is also excessive alpha parietally (P3 lead $p < 0.0313$; P4 lead $p < 0.0163$). While we could not find any research reports of increased parietal alpha in depression, we are reminded by McGilchrist (2010, p. 63) that the antero-posterior gradient in the right hemisphere is an important factor, the more disabled (or in this case, 'idling') the posterior region, the more depressed the subject.

Post-choir comparison with normative database; average age taken as 45

Graphs of EEG power spectra fragment: grand average, offset: 0.00 s, length: 138.79 s, number of epochs 1.

Alpha is more widespread frontally, especially to the right side (Fp1, 7.81 Hz, $p < 0.0039$), possibly consistent with more relaxed, less hyperaroused individuals (Figure 9).

The left/right asymmetry noted in the 'before' spectra and maps with heightened right hemispheric activity in the higher frequencies is gone.

Contrasting after versus before EEG spectra and maps

Fragment: grand average, offset: 0.00 s, length: 138.79 s, number of epochs 9.

Two main findings emerge (Figure 10).

1. The amount of delta activity in the left prefrontal area (Fp1) has increased (probability range of $p < 0.0234$ to 0.0288 across 1.22–3.24 Hz). We are reminded that delta is often seen in the orbital pre-frontal cortex, and may in fact correlate with increased integrative activity in that region (See Sherlin, in Budzinski et al., 2009; pp. 86–94). This could be consistent with the lifting of depression.
2. We also note a reduction of beta 2 activity (most marked at 20.75 Hz at C4, $p < 0.324$) suggesting that excessive right polar pre-frontal activity associated with depression has normalised in the post-choir group resting EEGs.

Our overall findings are also consistent with findings in a range of other studies looking at 'resting EEG' changes after music therapy for depression (See Jones & Field, 1999), and a Korean study (Sung-Jin & Chul-Jin, 2011).

Coherence

Coherence is the correlation between activity in two different brain regions, in terms of EEG power in any particular frequency. It can vary from zero to one. The signals in the two areas will usually have a time difference, but the *phase* in one area will be locked to the phase in the other area (completely, if coherence is one, imperfectly, if less than one, and not at all, if zero).

The significance of EEG coherence is still an area of considerable controversy, but one possible way of looking at it is in terms of an index of goodness of integration of brain function, but integration in a special sense as defined by researchers like Siegel (2007). Siegel uses the term 'integration' to describe optimal flexible states of mind that are neither locked in rigidity nor fragmented by chaos (the 'Goldilocks' spot if you like, neither hypercoherent nor hypocoherent, but 'just right').

The WinEEG software allows the mapped computation of 'average coherence' across a range of frequencies across the brain, and gives us a window onto 'integration' of function in that range.

Leuchter et al. (2012) reports hypercoherence in the QEEGs of depressive patients (especially marked in the alpha range).

Statistical analysis of coherence is problematic. These parameters are not normally distributed, therefore non-parametric statistics are required, and the 'selection' issue (what kind of coherence to look at; left right, antero-posterior, etc) is also problematic. A measure of 'global' coherence depends on how that is defined.

We have come to no satisfactory resolutions for these issues, nor can we apply Leuchter's analytic method (Leuchter et al., 2012) to our data because of differences in methodology. We have therefore omitted a statistical analysis.

Nevertheless, we present the pre- and post-coherence diagrams above (Figures 11 and 12), because the graphics are highly suggestive of diminution of coherence in association with the choir experience.

In the field of QEEG correlates of depression, Leuchter and colleagues at UCLA, have been some of the world's leading researchers. As we mentioned in the **brief history** section earlier, Leuchter's most recent formulation is that depression is a state of *hypercoherence* in the brain. Brain functions are locked too tightly, into dysfunctional patterns.

Leuchter's most recent publication on this subject (Leuchter et al., 2012) reports research which examined resting state functional connectivity as measured by quantitative electroencephalographic (QEEG) coherence. They found that subjects with MDD had significantly higher overall coherence as compared to controls. Coherence also seemed most marked in the alpha range and frontal areas.

The findings in our study are in accordance with this. While we could not put statistical probability

figure to 'average coherence' graphics generated by the WinEEG programme, the pre-choir WinEEG Coherence maps above clearly suggest increased coherence in frontal and occipito-parietal regions across all frequencies (orange areas), whereas the post-choir maps show markedly reduced coherence (many blue and dark blue areas), everywhere except in three more localised areas: (i) the occipital area, where coherence is confined to the alpha band; and (ii) Fp1 beta 2; and (iii) T3 beta 2.

In summary, one possible hermeneutic is that the depressive state involves a kind of brain-lock or brain-network rigidity, which QEEG hyper-coherence could reflect, and that as depression clears, the hemispheres, and sub-hemispheric regions, gain more 'independence' and hence a greater flexibility in communication ('talk' with each other in a freer way).

Event related potentials results

We grouped all our subjects' VCPT results as 'before' and 'after', and used the WinEEG programme to average the 'before' and 'after' VCPT results and compare them. The P3 novelty response differences stood out. The presentation at the bottom of the picture, when a plant is followed by a human, and accompanied by a beeping sound, is the so-called 'novelty' stimulus, which, because it is so unlike the other presentations, elicits its own specific response pattern, the so-called P3a or P3 novelty (Nov) response (Kropotov, 2009). See Figure 13(a) P3 Nov pre and post.

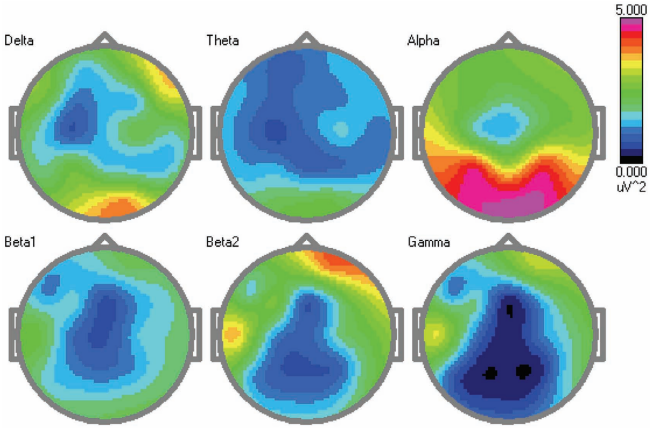

Figure 4: Average eyes open pre-choirr; all 9Ss

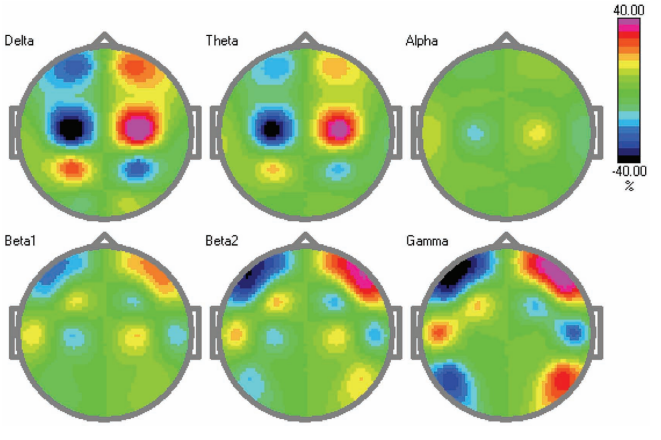

Figure 5: Interhemispheric asymmetry maps

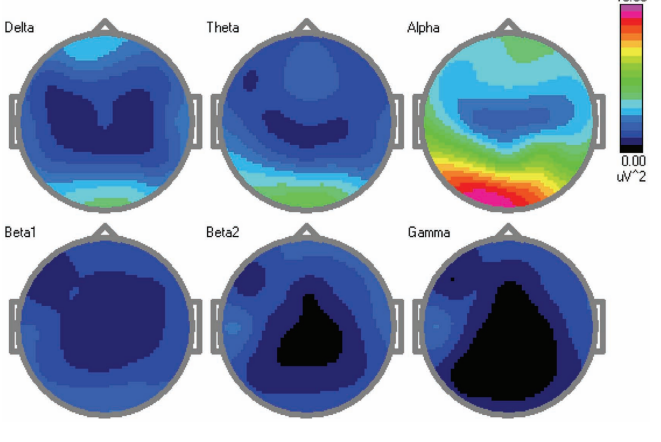

Figure 6: Average eyes open to post-choir; all 9Ss

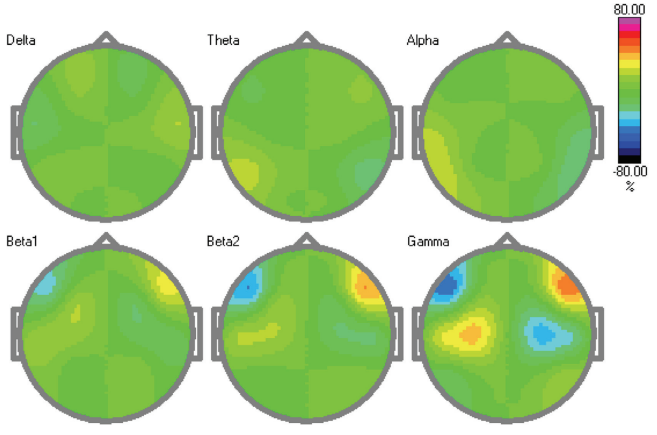

Figure 7: Interhemispheric asymmetry maps

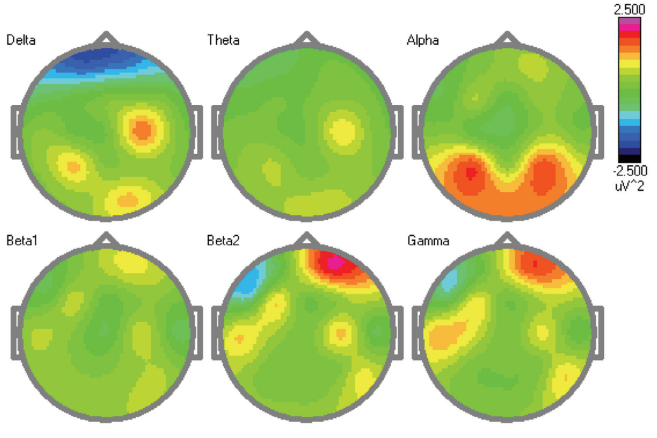

Figure 8: Pre-choir comparison with norms

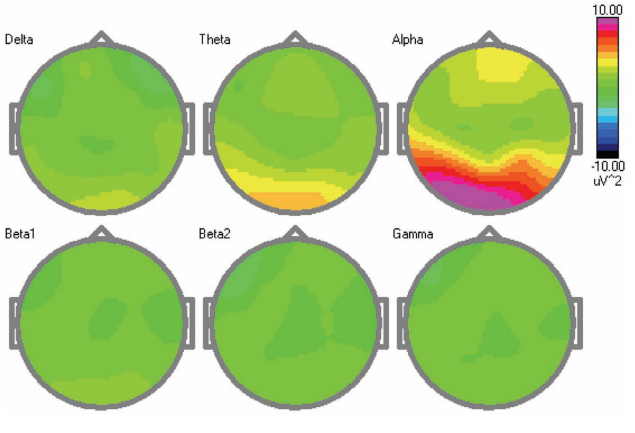

Figure 9: Post-choir comparison with norms

Figure 13 captures the changes in P3 nov from several perspectives.

The subjects had a heightened P3 Nov response before the choral work. Afterwards, this response was much lower. The difference was significant at the $p < 0.05$ level. See (a) pre and post P3 Nov response, and (b) P3 Nov differences.

An S-Loreta localisation showed that the region involved was the dorsal cingulum. See (c) top right: Loreta image.

Brain 2D maps (d) bottom right also show differences between pre and post cingulate activity. This is much reduced after the choir experience (in the Cz region).

Finally, when we compare the 'before' choir practice P3 Nov wave with the P3 Nov in the WinEEG normative data base, it is excessive.

Discussion

What are we to make of this? The depressed state is accompanied by anxiety symptoms. There is debate about whether this is co-morbid or simply part of the depressive syndrome (See Andrescu & Lenze, 2012; Coryell et al., 2012). Our view is that part of the depressive syndrome is a chronic state of negatively affect-loaded hyper-responsiveness to new stimuli. This is seen in children with depression, whose late P3a responses are enhanced (See Lepisto et al., 2004). This hyper-reactivity is also a characteristic of PTSD and PTSD-like syndromes, though when depression is so severe that retarded and blunted-affect symptoms pre-dominate (this would be found in hospitalised depressive patients, not in our ambulant group) P3a also becomes blunted (possibly because there is insufficient right anterior prefrontal modulation of the middle cingulum). As Partiot et al. (1993) put it; 'This

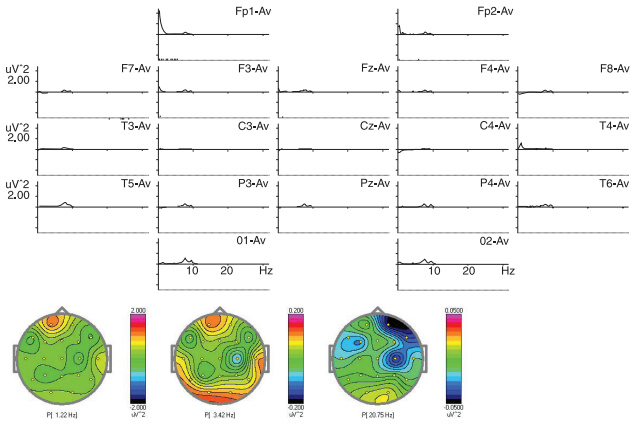

Figure 10: Spectra and maps

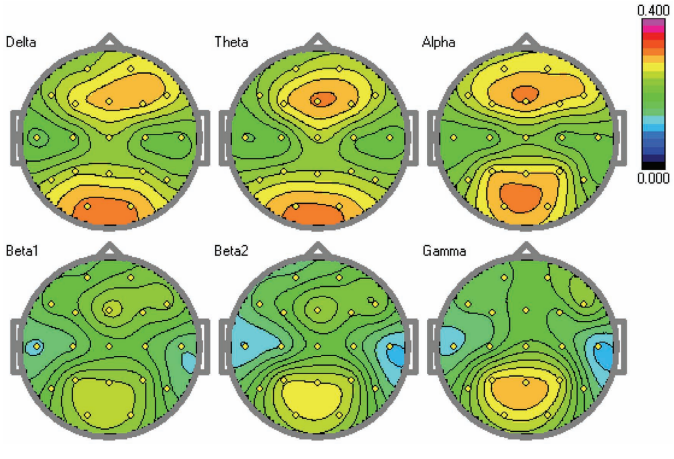

Figure 11: Pre-choir coherence

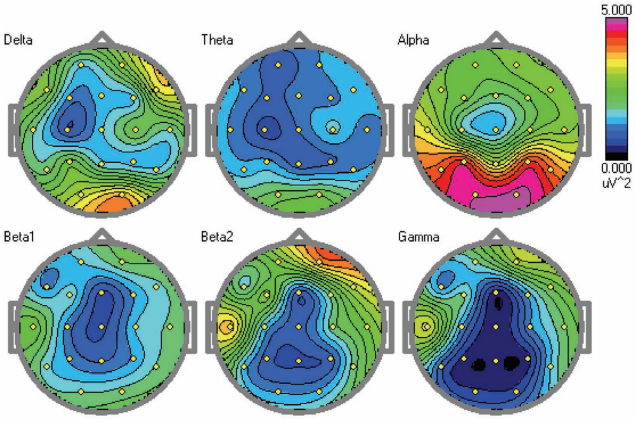

Figure 12: Post-choir coherence

suggests that this special type of cognitive dysfunction in depression is rather related to negative symptoms than to depression itself'.

Models of hyper or hypo function of brain regions are over-simplistic. Researchers like Tolin et al. (2012) are using the term 'apparent biphasic pattern' to refer to regional activity that is *both* hypo and hyper functional. They describe, in a functional imaging study of anterior cingulate cortex (ACC) and insula activity in patients with hoarding disorder, hypofunction in response to items that did not belong to them and hyperfunction to items that did belong to them. We suspect that something similar is occurring in the neural circuit setting of the ACC of our depressed patients.

We think that our depressed subjects were also chronically hyperaroused at the beginning, and became easier in their responses to unexpected stimuli after they had completed the choral work.

Interestingly, recent work by one of our colleagues (Saunders, 2013) parallels these findings. Saunders is completing a Doctorate at Bond University Queensland, which looks at the effects of transcranial direct current stimulation (tDCS) and cogmed (a cognitive enhancement programme) on patients with PTSD. The combined tDCS and cogmed protocol thus far seems to have a strong anti-depressant effect, and her patients also show a reduction in P3a activity post-treatment. Thus two completely different treatment paradigms both result in symptoms reduction and P3a reduction.

Conclusion

Comparing group findings for before and after QEEGs, changes in various QEEG parameters were

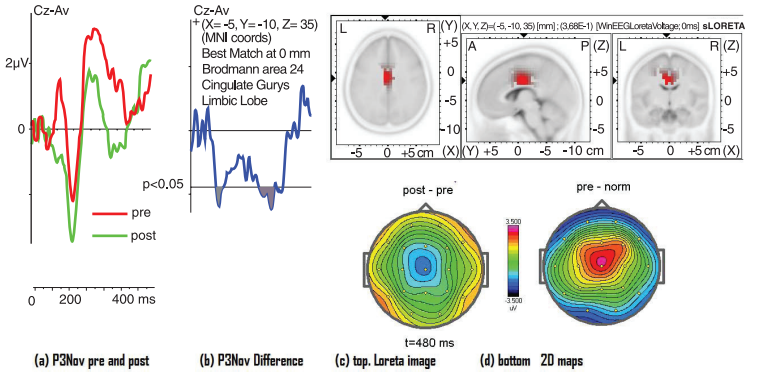

Figure 13: Composite P3 Novelty, Loreta and QEEG scans

found at the $p < 0.05$ level or better; thus challenging the null hypothesis that a choir programme would be ineffectual. The changes are all in step with a range of earlier research findings (as described earlier) in QEEG changes as depression improves. The ERP changes in this study are a novel finding.

Our after choir findings show;

1. A more symmetrical balance between left and right hemispheric activity
2. A better balance between anterior and posterior right hemispheric activity
3. A reduction of hypercoherence
4. An improvement in the ERP P3a novelty component (and hence ACC function).

The 'power' issue (only nine subjects for the QEEG component of the study) makes this a pilot study only. It needs replication. However, our findings are promising. Not only were there 'background' QEEG changes in parallel with clinical improvement (similar to some found in similar research) but ERP changes were detected as well. This suggests that the pattern of: (i) reduced right prefrontal activity; (ii) increased interhemispheric symmetry; (iii) decreased hyper-coherence; (iv) reduced P3a novelty ERP, may be a useful way of tracking improvement in a range of treatments for depression.

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