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EEG coherence adjusted for inter-electrode distance in children with attention-deficit/hyperactivity disorder

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Abstract

Cognition and behaviour depend on the integration of activity in different brain regions, and hence study of the coupling between regions is useful in understanding dysfunctional processes involved in disorders such as attention-deficit/hyperactivity disorder (AD/HD). Such coupling can be estimated by the electroencephalographic (EEG) coherence between scalp electrodes. However, EEG coherence between two points is strongly affected by the distance between them, being inflated by volume conduction effects at short distances and reduced by signal phase differences at larger distances. These distance effects preclude simple comparison of coherence estimates involving different inter-electrode distances. Our group recently introduced a procedure for adjusting coherence measures to remove such distance effects, and explored its potential using normal children. In this study we applied that coherence adjustment procedure to groups of children with AD/HD of the combined (AD/HDcom) and predominantly inattentive (AD/HDin) subtypes, and compared them with a control group. All groups were age- and gender-matched. AD/HD children were found to have a reciprocal pattern of coherence disturbance in the cortico-cortical circuits involved in slow and fast wave activity—elevated slow-wave coherences and reduced fast-wave coherences. This disturbance was larger for inter-hemispheric than intra-hemispheric coherences, and varied markedly with region, suggesting a complex pattern of coherence anomalies with a substantial frontal focus. This complex pattern differed little between subtypes, suggesting that it may constitute the fundamental dysfunction underlying the inattention common to both groups. In contrast, coherence was globally elevated in children with AD/HDcom compared with both AD/HDin and control children. This elevation in coherence may be directly related to the hyperactivity and impulsivity unique to that subtype. Further research using the coherence adjustment procedure appears useful in elucidating the electrophysiological anomalies underlying AD/HD and other disorders.

Keywords: Coherence; EEG; Inter-electrode distance; Attention-deficit/hyperactivity disorder; Adjustment; Children

1. Introduction

The integration of activity in different brain regions is important in determining both cognition and behaviour. Such coupling of brain activity between different recording sites can be measured by the *coherence* between EEG activity at the two sites. This is conceptualised as the correlation in the time domain between two signals in a given frequency band (Shaw, 1981). Hence the study of EEG coherence should be useful in understanding dysfunctional processes involved in disorders such as attention-deficit/hyperactivity disorder (AD/HD).

However, a recurring problem in this field is the contribution of volume conduction to observed coherence (Nunez et al., 1997; Srinivasan et al., 1998)—diffuse random neuronal activity may produce noise contributing to the observed EEG at each of two electrodes, artificially inflating the calculated coherence. A second problem is that coherence decreases with increasing inter-electrode distance (e.g., Thatcher et al., 1986)—the measured coherence between two points is reduced by signal phase differences, which increase with distance. Taken together, these obser-

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vations indicate that the measure of functional linkage between two cortical regions will be (i) inflated by diffuse random neuronal activity, and (ii) underestimated as the measured coherence is reduced by relative phase delays. The first of these effects will be greater at short inter-electrode distances, and the second will predominate at long inter-electrode distances.

Simple analysis of coherences involving different inter-electrode distances is precluded by these distance effects. Hence, most group comparisons of coherence values have tested each electrode pair separately, often without adjusting their alpha levels for the number of tests employed. For example, Marosi et al. (1993) reported 420 unprotected *t*-tests between groups − 105 electrode pairs (15 electrodes) × 4 EEG bands. Such problems may be reduced to some extent by calculating only a subset of the possible coherences. Thus a study by Barry et al. (2002) examined 16 coherence measures in each of the standard EEG frequency bands in two subtypes of AD/HD children, reporting reduced cortical differentiation and specialisation in AD/HD, particularly in cortico-cortical circuits involving theta activity. Their analytic strategy was to separately examine group differences in laterality effects involving longer or shorter inter-electrode distances, and intra-hemispheric coherences averaged within the frontal, temporal and central/parietal/occipital regions, avoiding comparisons differing substantially in inter-electrode distance. Despite a complex analytical strategy involving five regional ANOVAs within each of four frequency bands, Barry et al. (2002) could not statistically explore effects between regions, or between inter-hemispheric and intra-hemispheric coherences, limiting the potential richness of the data.

Subsequently Barry et al. (2005a) investigated ways of overcoming these limitations. As a first step, Nunez et al. (1997) had suggested estimating the inflation produced by *random coherence* due to volume conduction from uncorrelated sources to the electrode pair as

$$\text{Random coherence} = \exp((1 - x)/a) \quad (1)$$

where x is the distance between scalp electrodes (in cm), and a is a constant between 3 and 5. Their Fig. 4 suggested that $a = 3$ was an appropriate value for a linked-ear reference. The *reduced coherence* found by subtracting the estimate of random coherence from the measured coherence should be a more accurate estimate of brain coherence, free of the inflation due to volume-conduction effects.

From that starting point, Barry et al. (2005a) further adjusted coherences to remove systematic effects of inter-electrode distance. Gasser et al. (1988a) had previously reported that coherence from 10 electrode pairs in the frontal, central, parietal and occipital regions varied markedly with inter-electrode distance (measured from a hairdresser's plastic head). They calculated residual coherence at each site after removing their systematic distance effect by linear regression. Barry et al. (2005a) followed their general approach, except that they first subtracted estimated random coherence following Nunez et al. (1997), then used exponential rather than linear regression (a better empirical fit) to remove the systematic distance effects. Further, rather than examining the residual coherences, these were adjusted by adding the value expected at the mean inter-electrode distance, preserving the mean level of reduced coherence, and avoiding potential confusion with negative coherence values (as occurred in the Gasser et al., 1988a residuals). Finally, rather than using a model head, Barry et al. (2005a) measured inter-electrode distances from 10 children aged 8–13 years. These highly consistent values were used as the estimated inter-electrode distances in a study of EEG coherence in a larger group of normal children of that age-range.

Their mean coherences for each frequency band and electrode pair are shown as a function of inter-electrode distance in the top panel of Fig. 1. Coherence showed a strong monotonic decrease with increasing inter-electrode distance—the fitted black exponential trend line represented approximately 75% of the variance in the coherence data. Also plotted in this panel is Nunez et al.'s (1997) estimate of random coherence due to distributed uncorrelated brain sources (Eq. (1) above—grey line). Nunez et al.'s (1997) reduced coherence, obtained by subtracting the estimate of random coherence at each inter-electrode distance, is shown in the middle panel of Fig. 1. A strong dependence on inter-electrode distance remained—the fitted exponential trend line in the middle panel represents some 51% of the variability in the reduced coherence means. Deviations from this regression line may be considered as residual coherence values, corrected for the remaining systematic effects of inter-electrode distance. These corrected coherences were then adjusted to reflect the value expected at the mean inter-electrode distance. The bottom panel of Fig. 1 shows the 64 adjusted residual coherences, together with a black line representing the value which had been added. For these data, the mean *adjusted coherence* equals the mean *reduced coherence*, but there is no systematic dependence on inter-electrode distance remaining (the horizontal black line is also the fitted regression line).

Comparison of the data points plotted in each panel in Fig. 1 shows how the transformation from *raw* to *reduced* to *adjusted* coherence is marked by two effects: a systematic reduction in coherence at short inter-electrode distance (reflecting removal of coherence inflation produced by volume conduction), and a lesser increase in coherence at long inter-electrode distance (reflecting adjustment for coherence underestimated because of signal phase differences). Clarification of the variable effects obtained in that exploratory study suggested the potential value of the adjustment procedure in investigating coherence anomalies in AD/HD.

Hence the adjustment procedure of Barry et al. (2005a) was used in the present study to explore coherence in age- and gender-matched groups of children with the two