EEG anomalies in Attention-Deficit/Hyperactivity disorder: linking brain and behaviour.

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EEG in Children with ADHD

Studies have typically found:

- Increased levels of theta activity primarily in the frontal regions.

- Increased posterior delta, and decreased posterior alpha and beta activity.
CNS Models of ADHD

Maturational Lag

or

Developmental deviation in CNS functioning.

or

Hypoarousal
Aims Study 1

- To determine whether the EEGs of children with ADHD differ from normal children.

- To investigate whether children with inattentive and combined subtypes of ADHD are electrophysiologically independent.
Subjects

- Three groups of 20 children.
- Groups consisted of an ADHD Combined type, ADHD Inattentive type and a Control group.
- Age range was 8 to 12 years.
- Each group was matched on age and sex.
ADHD Subjects

- Drawn from new patients at a paediatric practice
- Assessed using DSM-IV criteria for the Combined or Inattentive subtypes of ADHD
- IQ >85
- Right handed and footed
Control Subjects

- Acquired from schools and community groups
- Assessed using parent interview and Connors Rating Scale
- IQ > 85
- Average range for reading and spelling
Procedure for EEG

- Eyes closed, resting condition.
- 24, 2.5 second epochs were recorded for analysis.
- EEG was Fourier transformed and values calculated for absolute and relative power in the delta (0.5-2.5 Hz), theta (2.5-7.5 Hz), alpha (7.5-13.5 Hz) and beta (13.5-20.5 Hz) bands.
Electrode Placement
Discussion Study 1

- The EEG can be used to differentiate children with ADHD from normal children.

- EEG differences exist between subtypes of the disorder.

- The differences between subtypes appear to be one of degree of severity rather than the groups being neurologically independent.

- The data supported a maturational lag model of ADHD.
Aims Study 2

1. To replicate the results of Study 1 in a larger independent sample.

2. To further investigate the nature of the EEG abnormality in ADHD using calculations of ratio coefficients between bands.
Subjects & Procedure

- Three independent groups of 40 children.
- The same inclusion criteria and procedure was used as in Study 1.
- Mean frequency was calculated for the delta, theta, alpha, beta and total power.
- Ratio coefficients were calculated between all permutations of the 4 frequency bands.
All significant relative power effects in study 1 were replicated in this study.

Results in absolute power were less stable with group differences in the theta, alpha and beta bands becoming significant.
Theta Band

 абсолютная мощность

Регион

Мощность

front cent post

Region

Power

Controls ADHDin ADHDcom
Discussion Study 2

- ADHD is a developmental deviation in CNS functioning, not a maturational lag.

- The ADHD Combined type group had frontal differences in their EEG which were indicative of a different type of CNS dysfunction to that found in the Inattentive group.
EEG Outliers

- In the first two studies (Clarke et al., 1998, 2001) found approximately 20% of ADHD Combined type subjects had elevated levels of beta activity.

- Chabot & Serfontein (1996) found 13% of children in their sample has excess beta.
Beta in Normal Children

- Not common in normal children.
- Not normally above $20 \, \mu V$ in amplitude.
Aims Study 3

1. Ascertain the percentage of children with ADHD who have excess beta activity in their EEG.

2. Determine if ADHD children with excess beta activity have behavioural profiles different from other children with ADHD.
Subjects

- 208 children with ADHD Combined type (ADHDcom).
- 90 children with ADHD Inattentive type (ADHDIn).
- 80 normal children.
- Age range was 8 to 12 years.
Data Analysis Aim 1.

- Means and SD were calculated for male and female controls for relative power.

- ADHD subjects were deemed to have an excess or deficiency of power if there EEG was more than 2 SD above or below the mean.
## Results (Aim 1)

<table>
<thead>
<tr>
<th>Group</th>
<th>Total Sample</th>
<th>Male Subjects</th>
<th>Female Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ADHDcom (N=208)</td>
<td>ADHDcom (N=159)</td>
<td>ADHDcom (N=49)</td>
</tr>
<tr>
<td>ADHD</td>
<td>84.6%</td>
<td>81.2%</td>
<td>96.0%</td>
</tr>
<tr>
<td></td>
<td>ADHDDin (N=90)</td>
<td>ADHDin (N=51)</td>
<td>ADHDin (N=39)</td>
</tr>
<tr>
<td>Excess beta</td>
<td>15.4%</td>
<td>18.8%</td>
<td>4.0%</td>
</tr>
<tr>
<td></td>
<td>2.2%</td>
<td>3.9%</td>
<td>0.0%</td>
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</tbody>
</table>
Results (Aim 1 continued)

- Beta was in the 16 Hz to 19 Hz range.
- Mean amplitude was from 5.8 μV in the frontal regions and 4.7 μV in posterior regions.
- 10% of subjects had high amplitude beta spindles.
Data Analysis Aim 2.

- Only ADHDcom subjects were used.

- The behavioural profile used in the diagnosis was compared between the typical and excess beta groups.
Results

Behavioural Profiles

- No Significant differences between the ADHD groups’ symptoms on DSM-IV behaviours.

- Within both groups, 5 behaviours were noted which were not part of DSM criteria.

- Moody and prone to temper tantrums were more common among the excess beta group.
ADHD with excess beta is a valid independent group.

The excess beta group has a distinct behavioural profile which is not common in “typical” profile children with ADHD.
Study 4

To investigate the number of groups with distinct EEG profiles that exist among children with the Combined type of ADHD.
Subjects

- 184 boys with ADHD Combined type.
- 40 normal children.
- Age range was 8 to 12 years.
Data Analysis

- Factor analysis was used to reduce the number of variables.
Data Analysis (cont.)

- Cluster analysis was performed on the three regions for each frequency band.

- The identified clusters were then compared to the control group.
Results

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Total Sample</th>
<th>Cluster 1</th>
<th>Cluster 2</th>
<th>Cluster 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Power</td>
<td><img src="image1.png" alt="Image" /></td>
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<tr>
<td>Relative Delta</td>
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<tr>
<td>Relative Theta</td>
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<tr>
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</table>
Conclusions

- ADHD is a highly heterogeneous.

- A number of different causes can result in similar behavioural profiles, which indicates that behavioural descriptions of a disorder are of limited value.
Study 5

- Aimed to investigate whether different profiles could be found in a sample of children with the Inattentive type of ADHD.
- Subjects were 100 ADHD boys and 40 Control subjects.
- Age between 8 and 13 years.
- Same procedure as Study 4.
Results

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
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<th>Cluster 1</th>
<th>Cluster 2</th>
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<tr>
<td>Total Power</td>
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<tr>
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<tr>
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</table>
Results

Comparison of diagnostic groups within Clusters

- Combined Hypoaroused group are more hypoaroused than the Inattentive Hypoaroused group.

- No significant differences were found between the two Maturational lag groups.
Conclusions

- There are two types of CNS dysfunction that result in ADHD, Hypoarousal and Maturational Lag, and these are independent of the present diagnostic criteria.

- A third group (Hyperaroused), is primarily found in hyperactive children.
Conclusions (cont.)

- These groups allow certain predictions to be made about the developmental time course of the disorder and treatment outcomes.
Problems with Models

- Not been empirically validated – they remain largely hypothetical.
- Hyperarousal – Pure speculation.
- Hypoarousal – link between EEG and SCL is not well developed.
- Mat Lag – EEG of ADHD children have not been compared to younger normal children.
The Problem with Arousal

- Poorly defined within the psychophysiology literature.
- Systematically interchanged with activation, activity and processing, although it has long been recognised that this is inaccurate (Lacey, 1959).
Study 6
EEG differences due to differences in arousal, in normal children

- Aim: To determine the EEG components which are associated with different levels of arousal.
Subjects

- 24 normal boys

- Standard EEG procedure, eyes-closed resting condition (limited processing condition).

- SCL recorded using Ag/AgCl electrodes on the medial phalanges of the second and third digits of the non-preferred hand, with 0.05 M NaCl in an inert viscous ointment.
Statistics

- Subjects were split into high and low SCL groups (12 in each).
- EEG in each frequency bands were compared between groups.
Conclusions

- Changes in arousal are primarily associated with changes in the alpha band.
This study examined the use of caffeine to manipulate arousal level without the confounds associated with task-related activation.
Subjects & Method

- 18 healthy university students.
- 2 counterbalanced recording sessions.
- Eyes-closed EEG and SCL were recorded 30 minutes after ingesting 250 mg of caffeine and a placebo.
Conclusions

- Changes in arousal are primarily associated with changes in alpha activity.
Aim. To examine Arousal differences between EEG defined subtypes of children with AD/HD.

- 141 Boys with AD/HD Combined type.
- Eyes-closed resting EEG and SCL.
- Cluster analyzed as per study 1.
SCL in EEG-defined types of AD/HD

![Graph showing SCL (µS) for different groups: Control Group, Hypoaroused Group, Mat Lag Group, Hyperaroused Group. The x-axis represents the groups, and the y-axis represents SCL in microsiemens (µS). The graph shows a decrease in SCL from the Control Group to the Hypoaroused Group, with a slight increase in the Mat Lag Group and Hyperaroused Group.]
Conclusions

- Hypo-arousal is a core deficit in ALL children with AD/HD.

- Increased beta activity found in some AD/HD children is not associated with an increase in arousal and hyper-arousal does not appear to be a factor in AD/HD.
Conclusions

- Our current EEG based models of AD/HD are too simplistic, with a number of different CNS abnormalities producing the disorder profile.
**Study 9. Effects of caffeine on the EEG of children with AD/HD**

- **Aim.** To investigate the role of arousal in children with AD/HD.

- **18 children with AD/HD.**

- **SCL recorded at baseline and 30 minutes after ingesting 80 mg of caffeine.**
Results

- Controls
  - Linear dose dependent effect.

- AD/HD
  - Non-linear dose effect. The more under-awroused a subject, the greater the change to normality.
Results

- AD/HD
  - Change in SCL positively correlated with the hyperactivity/impulsivity score from the Conners’ Parent Rating Scale ($r= .41$).
Conclusions

- This suggests that, in addition to the anomalous arousal levels in AD/HD, there is an anomalous arousal mechanism underlying impairment in that symptom dimension.
Mislabelled

Control

Hypoarousal

Hyperarousal

Total Power

Relative Delta

Relative Theta

Relative Alpha

Relative Beta
Anomalous Results

Reduced arousal increases Alpha

AD/HD associated with reduced arousal AND reduced Alpha

Must be another anomaly acting to reduce Alpha
Theta/Beta Ratio

- Not a marker of arousal
- Is it a marker of a processing deficit?
# Anomalous Results

| Paper | D1A | D1B | D2A | D2B | D3 | D4 | D5 | T1A | T1B | T2 | T2B | T3 | T4 | T5 | A1A | A1B | A2 | A3 | A4 | A5 | B1A | B1B | B2 | B3 | B4 | B5 |
|-------|-----|-----|-----|-----|----|----|----|-----|-----|----|-----|----|----|----|-----|-----|----|----|----|----|-----|-----|----|----|----|----|----|----|
| 1 u   | u   | u   | u   | u   | d  | u  | u  | d   | d   | d  | d   | u  | u  | d  | u   | u   | u  | d  | d  | d  | u   | u   | u  | d  | d  | d  | u  |
| 3 d   | u   | d   | d   | d   | u  | d  | d  | d   | d   | d  | d   | d  | d  | d  | u   | u   | u  | d  | d  | d  | d   | d   | d  | d  | d  | d  | u  |
| 4 d   | u   | d   | u   | u   | d  | d  | d  | d   | d   | d  | d   | d  | d  | d  | u   | u   | u  | d  | d  | d  | d   | d   | d  | d  | d  | d  | u  |
| 5 u   | u   | u   | u   | u   | u  | u  | u  | u   | u   | u  | u   | u  | u  | u  | u   | u   | u  | u  | u  | u  | u   | u   | u  | u  | u  | u  | u  |
| 6 u   | u   | u   | u   | u   | u  | u  | u  | u   | u   | u  | u   | u  | u  | u  | u   | u   | u  | u  | u  | u  | u   | u   | u  | u  | u  | u  | u  |
| 7 u   | u   | u   | u   | u   | u  | u  | u  | u   | u   | u  | u   | u  | u  | u  | u   | u   | u  | u  | u  | u  | u   | u   | u  | u  | u  | u  | u  |
| 8 d   | u   | d   | d   | d   | u  | d  | d  | u   | u   | u  | u   | u  | u  | u  | u   | u   | u  | u  | u  | u  | u   | u   | u  | u  | u  | u  | u  |
| 9 u   | u   | u   | u   | u   | u  | u  | u  | u   | u   | u  | u   | u  | u  | u  | u   | u   | u  | u  | u  | u  | u   | u   | u  | u  | u  | u  | u  |
| 10 d  | u   | u   | u   | d   | d  | d  | d  | d   | d   | d  | d   | d  | d  | d  | u   | u   | u  | d  | d  | d  | d   | d   | d  | d  | d  | d  | u  |
Study 10. Coherence differences between AD/HD children + or – Autistic features.

- Aim. To investigate EEG coherence differences between children with or without Autistic features.
- 120 boys with AD/HD, 60 Control subjects.
Results
ADHD- VS Control

- Reduced frontal and central delta coherence.
- Increased short/medium intrahemispheric theta coherence.
- Reduced Long intrahemispheric alpha coherence.
- Increased short/medium intrahemispheric, frontal, temporal & central/parietal/occipital beta coherence.
Results

ADHD+ VS ADHD-

- Reduced short/medium intrahemispheric, frontal, temporal & central/parietal/ occipital beta coherence in the ADHD+ group.
Conclusions

- In ADHD, beta coherence results are affected by levels of autistic features in the sample.

- Differences in studies are not random noise but factors not measured in the study.
Study 11

- To test the hypothesis that the theta beta/ratio is a measure of processing by investigating the relationship between the P300 and the theta/beta ratio.
The P300 wave is an event related potential (ERP) component elicited in the process of decision making.

More specifically, the P300 is thought to reflect processes involved in stimulus evaluation or categorization.
Subjects

- of 47 normal adults
- Used an auditory/auditory paradigm.
- The P300 and theta/beta ratio measured at Fz and correlated.
Results

- No correlation between P300 amplitude and theta/beta ratio.

- Significant correlation ($r = .295, p < .05$) between P300 latency and theta/beta ratio.
Results

- Significant correlation ($r = .295$, $p < .05$) between P300 latency and theta/beta ratio.
Conclusions

- These data support the hypothesis that the theta/beta ratio is a marker of cognitive processing.
Study 12. Behavioural Differences in EEG-Defined Subtypes of AD/HD.

- Aim. To investigate behavioural differences in EEG-defined subtypes of children with AD/HD.

- 155 boys with AD/HD Combined type.
Method

- Eyes closed resting EEG.
- Assessed using the CBCL, DBC, Conners’ and DAYS.
- Behavioural scores for each cluster compared to the remaining sample.
<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Excess Beta</th>
<th>Theta/beta ↑</th>
<th>Mat Lag</th>
<th>Theta/beta ↑</th>
<th>Excess Alpha</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Relative Delta</strong></td>
<td><img src="image1" alt="Image" /></td>
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<td><img src="image14" alt="Image" /></td>
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<td><img src="image16" alt="Image" /></td>
<td><img src="image17" alt="Image" /></td>
<td><img src="image18" alt="Image" /></td>
</tr>
<tr>
<td><strong>Relative Beta</strong></td>
<td><img src="image19" alt="Image" /></td>
<td><img src="image20" alt="Image" /></td>
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<td><img src="image22" alt="Image" /></td>
<td><img src="image23" alt="Image" /></td>
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</tbody>
</table>
Behavioural Results

- Increased delinquent behaviour
- Reduced signs of guilt
- Reduced scores on measures of inattention, self-harming/suicidal ideation, strange ideas, and physical problems
**Behavioural Results**

- Substantially fewer problems across most scales
- Reduced symptoms of AD/HD
- Happier than the remaining group
Behavioural Results

- greater levels of impulsivity and inattention

- preference for the company of younger children

- fewer problems in relation to jealousy, perfectionism, need for sleep, and ritualistic behaviours
**Behavioural Results**

- substantial similarities to the remaining sample

- less nervous and frightened (reduced anxiety)

- enjoy themselves (reduced depression)
Behavioural Results

- increased hyperactivity
- increase in ritualistic behaviours
- set high standards for themselves
- disliking for school
- often seemed confused or in a fog
Conclusions

- Each EEG cluster presents with a different behavioural profile.
- Further evidence for the maturational lag model.
Study 13. Behavioural correlates of EEG bands in AD/HD.

- Aim. determine whether any of the commonly found EEG abnormalities correlate with the core symptoms of this disorder.

- 60 boys with AD/HD Combined type.
Method

- Eyes closed resting EEG.
- Assessed using the Conners’ Rating Scale
- Z-transformed relative power in each band correlated with the inattention and hyperactivity-impulsivity indexes of the Conners’.
Results

- Frontal theta significantly correlated with the Inattentive (r = 0.246) and Total (r = 0.243) subscales

- Frontal theta/beta ratio correlated with the Hyperactivity-Impulsive (r = 0.219) and Total (r = 0.241) subscales
Conclusions

- Results indicate the role of frontal lobe deficits in AD/HD.

- Frontal theta may be a specific marker of inattention in a number of disorders.

- Theta/beta ratio may be the most sensitive marker of hyperactivity-impulsivity.
Study 14. Behavioural correlates of Gamma activity in AD/HD.

- **Aim.** Investigate gamma band abnormalities in children with AD/HD.
- **50 children with AD/HD.**
- **Assessed using the CBCL, DBC, Conners’ and DAYS**
Gamma band.
Results

**Absolute Power**

<table>
<thead>
<tr>
<th></th>
<th>DELTA</th>
<th>THETA</th>
<th>ALPHA</th>
<th>BETA</th>
<th>GAMMA</th>
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<tr>
<td>CONTROL</td>
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<td><img src="image2" alt="Control Theta" /></td>
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<td>UNMEDICATED AD/HD</td>
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<td><img src="image9" alt="Unmedicated Beta" /></td>
<td><img src="image10" alt="Unmedicated Gamma" /></td>
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</tbody>
</table>
Results

- Absolute gamma negatively correlated with Connors’ DSM Inattention scale (r = -0.24), and the CBCL scale for Attention Problems (r = -0.28).
Conclusions

- Reduced gamma is associated with the core symptoms of AD/HD and need further investigation.
Major Conclusions

- Hypo-arousal is a core deficit in ALL children with AD/HD.

- Our current EEG based models of AD/HD are too simplistic, with a number of different CNS abnormalities producing the disorder profile.
Major Conclusions

- Alpha activity associated with arousal.

- Frontal theta and gamma may be a specific marker of inattention.

- Theta/beta ratio may be the most sensitive marker of hyperactivity-impulsivity.
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