EEG correlates of moderate Intermittent Explosive Disorder

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Abstract

Objective: We investigated electroencephalographic (EEG) correlates of moderate Intermittent Explosive Disorder (mIED), which is characterized by uncontrollable, impulsive attacks that either manifest in aggressive outbursts of temper, or in implosive, auto-aggressive behaviour.

Methods: In two Experiments, EEG data were recorded during rest conditions, and while subjects were presented with auditory and visual stimuli. Additionally, scores of the I_7 impulsivity scale (designed to capture acting on impulse) were obtained.

Results: In Experiment 1, individuals with mIED showed a stronger increase in the power of oscillatory activity in the beta band, along with a stronger power decrease in the theta band in response to both visual and auditory stimuli. Based on discriminant function analysis, a model of discriminant functions was derived that clearly separated the mIED group from the control group. In Experiment 2, subjects were categorized into either of two groups (supposedly without mIED, with mIED) based on this model of discriminant functions. Results showed that I_7 impulsivity scores clearly differed between groups.

Conclusion: The present data show a relation between oscillatory brain activity and mIED. They indicate that this brain activity is related to the impulsivity facet of impulsive action, and suggest that mIED can be assessed based on the analysis of electrophysiological data.

Significance: To our knowledge, this is the first study on EEG correlates of (m)IED. Results open up new perspectives for future investigations on disorders characterized by substantial impulsivity.

Keywords: Intermittent Explosive Disorder, Impulsivity, Aggression, EEG, beta activity

1. Introduction

Intermittent Explosive Disorder (IED), as defined in DSM-IV, is a disorder characterized by discrete episodes of aggressive impulses that result in serious assaultive acts or destruction of property. The degree of aggression expressed during an episode is grossly out of proportion to any precipitating psychosocial stressors, and the explosive episodes are not better accounted for by another mental disorder or due to the direct physiologic effects of a substance or a general medical condition (for overviews see McElroy, 1999; Olvera, 2002). It is assumed that IED is probably more common than realized and may be an important cause of violent behaviour (e.g., McElroy, 1999; Coccaro et al., 1998, Kessler et al., 2006; Coccaro et al., 2005). Moderate forms of IED (here referred to as mIED) are usually not diagnosed, possibly due to the lack of appropriate diagnostic instruments (see also Coccaro et al., 1998).

Similarly to IED, individuals with mIED typically produce impulsive outbursts of temper which are out of proportion to a precipitating event. In contrast to IED, however, individuals with mIED act less intensely during an episode, and in a fashion which is usually socially tolerated (e.g., slamming doors, smashing dishes or loud angry shouting during rage attacks). Nevertheless, these outbursts often have a disadvantageous impact on individuals, their families, and their occupational career. Individuals with mIED typically report that they cannot control these attacks, and that they view the

actions performed during these episodes as alien, often embarrassing, and distasteful. They regret violent acts performed during their outburst immediately after the attack is over, although they agree that this regret does not help to avert such episodes in the future. In contrast to IED, which is considered exclusively as an aggression disorder, some individuals with mIED may not show aggressive outbursts, but rather implosive, auto-aggressive behaviour (such as strong inner rage, or in extreme cases self-injuring behaviour). Impulsive aggression (whether explosive or implosive) is, thus, also an important aspect of this phenomenon (see also Siebel, 1994).

Literature on neurophysiological correlates of (m)IED is relatively scant. A number of studies has reported reduced serotonin levels in personality disordered individuals with IED (for an overview see Olvera, 2002), and previous literature has linked the abrupt outbursts typical for individuals with (m)IED to an accumulation of stress hormones which are suddenly released when serotonin levels are low (this phenomenology was described as a "Cerebro-Physiological Switch"; Siebel, 1994; Siebel & Winkler, 1996). Electrophysiological correlates of (m)IED have, to our knowledge, not been reported so far.

2. Experiment 1

In Experiment 1, we examined oscillatory brain activity in individuals with and without mIED. Participants' EEGs were measured during rest conditions, as well as during the presentation of auditory, and visual stimuli (an excerpt from the first movement of Beethoven's 5th symphony, and sentences describing mIED). These stimuli were chosen to agitate the mIED subjects, with the idea that this agitation leads to mIED-specific alterations of oscillatory brain activity which can be detected using spectral analysis of the EEG.

Regarding the hypotheses, no previous (m)IED study has been available to predict specific effects. However, possible effects could be expected based on investigations of children with attention deficit/hyperactivity disorder (AD/HD). Clarke et al. (2001a) reported that a subgroup of AD/HD children with increased temper tantrums had increased relative beta, along with decreased relative alpha, and a decreased theta/beta ratio (for an overview see also Barry et al., 2003). Similar findings were reported in another study from Clarke et al. (2001b), in which a group with excessive beta showed less absolute theta and less relative theta power than a typical AD/HD group. Again, this group was more prone to temper tantrums and mood swings. The increased beta, and decreased theta as well as alpha power values in these impulsive groups had been linked to cortical hyperarousal (Clarke et al., 2001a,b), and the results of these studies suggest that elevated beta activity (and decreased theta as well as alpha activity) might be indicative for increased impulsiveness (particularly with regards to the impulsivity facet impulsive action / behavioural disinhibition), probably also in individuals without AD/HD. Consistent with these findings, Houston & Stanford (2005) reported lower delta and theta activity in a non-clinical group scoring high on the Barratt Impulsiveness Scale (BIS-11).

Based on these studies, we hypothesized that alterations in the spectral power of the EEG during the presentation of auditory and visual stimuli compared to the rest conditions would differ between individuals with and without mIED. We analyzed power values in theta, alpha, and beta frequency bands, and tested possible differences between groups in each of the three frequency bands. According to the mentioned results from Clarke et al. (2001a,b), increased beta activity, along with decreased theta and alpha activity was to be expected.

In addition to the EEG measurements, we obtained scores of the impulsivity scale of the I$_7$ impulsivity questionnaire (Eysenck et al., 1990) from each subject. This scale captures acting on impulse, sometimes despite the probability for negative consequences. Because mIED is also characterized by impulsive actions that often have disadvantageous outcomes, it was hypothesized that subjects with mIED score higher on the I$_7$ impulsivity scale than subjects without mIED.

2.1. Methods

2.1.1. Participants

54 subjects were included in the study, 28 without mIED (mean age = 26;7 years, range 18 – 55 years; 14 females), and 26 with mIED (mean age = 28;4 years, range 18 – 54 years; 14 females). Subjects did not take medication, and reported to have normal hearing and normal (or corrected to normal) vision.

2.1.2. Participant selection

Subjects underwent an unstructured narrative interview in which they were asked about experiences typical for mIED: They were asked whether they sometimes produce outbursts of temper, and – if so – whether these outbursts are often in excess of what other individuals might consider as appropriate with respect to the precipitating event. Furthermore, they were

asked if they are able to control these attacks, and if they regret violent acts performed during an outburst immediately after the attack is over. They were also asked if they viewed the actions performed during these episodes as foreign and distasteful, and if they agreed that such regret had not been helpful in averting such episodes. As mentioned in the Introduction, some individuals with mIED may show autoaggresive attacks, rather than outbursts. Thus, subjects were also asked if they frequently had experiences of inner rage in which they direct their aggression inwards, rather than outwards. Typically, such individuals reported that they feel almost paralyzed, and are hardly able to speak during such episodes of inner rage (one individual reported that she performed self-injuring behaviour).

In each group, half of the subjects underwent the interview before, and half of the subjects underwent the interview after the EEG measurements to exclude the possibility that the interviews had any influence on the subjects' performance, or mood (and, thus, probably on the subjects' brain activity) during the EEG measurements. All subjects were categorized to either group only on the basis of the interviews, i.e., subjects who underwent the interview after the EEG measurement were categorized to a group without prior knowledge of their EEG. Subjects were not informed that the interview and the EEG-session were part of the same study. Cases in which subjects could not clearly be assigned to either group (n = 21) were excluded from the study.

2.1.3. Stimulus materials

Two musical excerpts were used: four minutes from the first movement of L. v. Beethoven's 5th symphony (Teldec, ASIN: B000095IUM), and four minutes from F. Handel's Watermusic (Universal, Archive Production, ASIN: B000001G4Q). The Beethoven piece was chosen because it has musicologically been described as particularly impulsive, e.g. due to frequent abrupt fortissimo passages, and due to frequent changes from calm passages to highly agitated passages (Schleuning, 1978). In addition, a subgroup of 32 participants was presented with the excerpt from Handel: This was, in contrast to the Beethoven excerpt, a calm piece with virtually no abrupt changes in loudness. Both pieces had the same RMS power (i.e., on average comparable loudness). The tempo of the Beethoven excerpt was around 90, of the Handel excerpt around 60 beats per minute.

The questionnaire presented during the EEG session (referred to here as *EEG-questionnaire*) consisted of 25 items. Items were chosen to describe aspects of mIED (such as "Sometimes I have outbursts of temper that I cannot control", or "Sometimes I have attacks that are like switched on – and then like switched off"). To match the approximate length of the EEG-questionnaire with the music conditions, we also added items which we assumed to describe further characteristics of individuals with mIED (e.g., "I am afraid of peace and quiet", "I am bored when quiet and harmony last too long", see also Siebel, 1994).

2.1.4. Procedure and experimental design

The experimental session started with filling out the I$_7$ questionnaire (Eysenck et al., 1990). For 24 participants (12 with, and 12 without mIED, 6 females in each group), the EEG recording session began with a 2 min eyes-closed rest condition (referred to as *initial rest*) which was followed by the 4 min excerpt from Beethoven's 5th symphony. During the presentation of the music, subjects were instructed to look at a fixation cross and to judge if they sometimes felt how the music sounded. The music condition was followed by another 2 min eyes-closed rest condition (referred to as *intermediate rest*) which was followed by the EEG-questionnaire. Items of this questionnaire were presented visually on a computer monitor. Presentation of items was self-paced: Each item was presented until subjects pressed response buttons to rate how accurately this statement applied to their personality. After such a response, the screen went blank for 3000 ms, and then the next item was presented on the screen. Responses were made on a scale ranging from 1 ("highly applicable") to 6 ("not applicable at all"). The EEG-questionnaire was followed by a 2 min eyes-closed rest condition (referred to as *final rest*).

The effects observed after the measurement of the first 24 participants raised the question if the effects elicited by the Beethoven music were specifically due to the impulsive character of this music, or if similar effects would also be observed when listening to non-impulsive music. Therefore, the experimental procedure for the remaining 30 participants (16 without, and 14 with mIED) was identical to that of the first 24 participants, except that the EEG session started with a "pre-Handel" rest condition (2 min, with eyes closed) which was followed by a 4 min excerpt from Handel's *Watermusic*. As for the condition in which music from Beethoven was presented, subjects were instructed to look at a fixation cross during the presentation of the Handel excerpt, and to judge during the music if they sometimes felt like the music sounded. The experimental procedure following the music from Handel was identical to the procedure of the other 24 participants.

Note that the application of rest conditions enabled us to normalize the data by calculating contrasts between experimental conditions and rest conditions. Furthermore, the use of eyes-closed rest conditions allows a comparison to previous studies also using eyes-closed rest conditions.

2.1.5. EEG recordings and Data analysis.

EEG data were measured with Ag-AgCl electrodes, digitized with a sampling rate of 500 Hz using the following 37 electrode positions of the international 10 - 20 system: FP1, FPZ, FP2, AF7, AF3, AFZ, AF4, AF8, F7, F5, F3, FZ, F4, F6, F8, FT7, FC5, FC3, FCZ, FC4, FC6, FT8, T7, C3, CZ, C4, T8, CP5, CP6, P7, P3, PZ, P4, P8, POZ, O1, O2. Additional electrodes were placed on the left (M1) and right (M2) mastoids, as well as on the nose tip. M1 served as reference, the ground-electrode was located on the chest. To control for artefacts caused by eye movements, vertical and horizontal electro-oculograms were recorded bipolarly.

After the measurements, raw data were filtered using first a 3 Hz high-pass filter (5917 points, Blackman window, finite impulse response) to reduce artefacts in frequency ranges below 3 Hz. Then, EEG data were re-referenced offline to the algebraic mean of both mastoid electrodes to obtain a symmetric reference. For artefact rejection, each sampling point was centred in a gliding window, and rejected if the standard deviation exceeded 50 microvolt either within a 200 ms, or an 800 ms gliding window (this procedure was applied for each channel, as well as for vertical and horizontal EOGs).

A power spectrum analysis was performed using Welchs' method of spectral averaging. Artefact free EEG epochs, lasting 2.048 seconds each, were selected and divided into three segments with a length of 1.024 seconds and an overlap of 50%. For each condition, single segment power spectra were computed via Fast Fourier Transform (FFT) and then averaged to yield the mean power spectrum. Before FFT calculation, data segments were windowed using a Hamming function in order to reduce spectral leakage, and zero padded to obtain a spectral resolution of 0.448 Hz. Mean band power values were calculated at subject level for each condition (initial rest, music, intermediate rest, EEG-questionnaire, final rest) by averaging power values across frequency bins. Subsequently, mean band power values were logarithmized (log10) for each subject, each condition and each frequency band separately. Normalization of the music and the EEG-questionnaire condition was achieved by calculating the contrasts (a) music

minus the rest directly preceding the music condition, and (b) EEG-questionnaire minus the rest directly preceding the EEG-questionnaire.

If not indicated otherwise, statistical analyses were conducted for each frequency band (upper theta: 6-8 Hz; alpha: 8-12 Hz; beta: 15-30 Hz) by computing repeated measures ANOVAs on the logarithmic FFT data with factors *stimulation* (stimulation vs. rest with two levels: (1) music and EEG questionnaire, (2) rests preceding the music and the EEG questionnaire), *type* (two levels: (1) music and preceding rest, (2) EEG questionnaire and preceding rest), *anterior-posterior* (two levels), *hemisphere* (two levels), and *group* (two levels: (1) without mIED, (2) with mIED).

2.1.6. Discriminant function analysis

To discriminate participants based on their EEG characteristics, the following statistical values were obtained from the EEG data of each subject, and entered into a discriminant function analysis. First, seven regions of interest (ROIs) were calculated for each subject by averaging the FFT-waveforms for each subject across the electrodes of each ROI: anterior midline (FPZ, AFZ, FZ), left anterior (FP1, AF3, AF7), right anterior (FP2, AF4, AF8), left fronto-central (F5, F3, FC3), right fronto-central (F6, F4, FC4), left fronto-temporal (F7, FT7, FC5), and right fronto-temporal (F8, FT8, FC6). ROIs were computed to obtain more representative power values from the respective scalp regions. Subsequently, the following parameters were computed for each ROI:

(1) The mean spectral power in the upper theta (6-8 Hz), alpha (8-12 Hz), and beta (20-30 Hz) band for the music condition, as well as for the EEG questionnaire.

(2) The spectral power of the music contrast (initial rest subtracted from music), and of the EEG questionnaire contrast (intermediate rest subtracted from EEG questionnaire), again for the theta, alpha, and beta band.

As results will show, the mIED group showed strong beta activity with a scalp distribution typical for muscular activity. Gasser et al. (2005) suggested that the amount of muscle activity can roughly be estimated from the power values of oscillations in frequency ranges well above around 30 Hz. Therefore, Gasser et al. (2005) proposed to estimate the EMG power in lower frequency ranges (around 20-30 Hz) by computing a linear regression of log FFT data in higher frequency ranges, and subtracting the values on the regression line from the log EEG data in lower frequency ranges. To capture brain activity in the beta

range superimposed on muscular activity, we thus also calculated for each subject:

(1) Linear regressions on the logarithmic FFT-data for the frequency range of 20 - 30 Hz, and 20 - 86 Hz (data of the 48 – 52 Hz frequency range were excluded because of the electric noise occurring in this frequency band). The following values entered the discriminant analysis for each regression: (a) the two beta values (intercept, linear trend), and (b) goodness of fit (explained variance, r^2). In subjects without mIED, but with strong oscillatory activity due to muscle artefacts, the regression of the logarithmic data should result in a high goodness of fit in the frequency range between 20 and 86 Hz (Gasser et al., 2005). Lower values are to be expected in the 20-30 Hz range for subjects with mIED (due to a possible overlap of oscillatory activity originating from muscular activity with activity originating from the brain, see also Results).

(2) For the beta band (20-30 Hz), a polynomial curve fitting was performed for the music condition, as well as for the EEG questionnaire to find the coefficients of a polynomial of degree 2 that fitted the (non-logarithmic) FFT data in a least squares sense. The following values of this fit entered the discriminant function analysis: (a) the 3 polynomial coefficients (intercept, linear trend, quadratic trend), and (b) goodness of fit (norm of the residuals). This computation was performed because power peaks in subjects with mIED in the frequency range between 20 - 30 Hz should be reflected in higher values of the coefficient of the second exponent (quadratic).

(3) Finally, the frequency with the maximal spectral power value within the 20 - 45 Hz range was obtained, as well as the mean of the spectral power in the 20 - 86 Hz range, and the variance of the normalized FFT data between channels in the 20 - 30 Hz range.[1]

2.2. Results

2.2.1. Scores of the I_7 impulsivity inventory.

As expected, subjects with mIED scored higher on the impulsivity scale of the I_7 than subjects without mIED (without mIED: M = 30.5, SD = 14.9; with mIED: M = 41.4, SD = 19.7), the group difference being significant (t(52) = 2.3, p < .05).

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[1] A Matlab-script (MathWorks, Natick, MA, USA) extracting and calculating these values from single subject averages is provided on request by S.K.
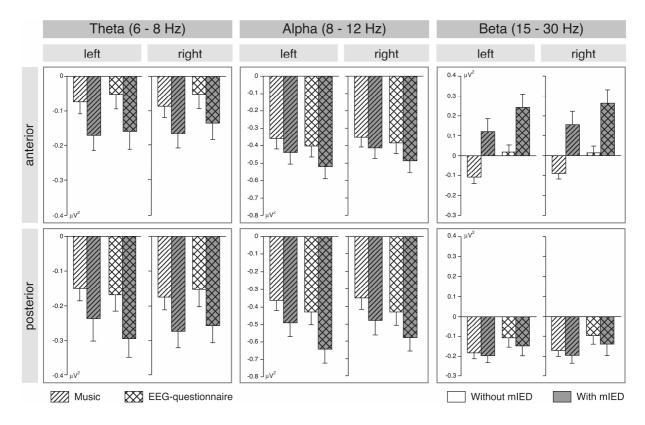
2.2.2. FFT-data

Figure 1 shows normalized logarithmic FFT-data of the contrasts (a) Beethoven music minus initial rest, and (b) EEG-questionnaire minus intermediate rest, calculated separately for both groups (with mIED, without mIED) for four ROIs: left anterior (FP1, AF3, AF7, F5), right anterior (FP2, AF4, AF8, F6), left posterior (O1, P3, P7, CP5), and right posterior (O2, P4, P8, CP6). In both the upper theta (6-8 Hz) and the alpha band (8-12 Hz), power values decreased during the stimulus conditions compared to the rest conditions. In both frequency bands, this decrease was stronger in the group with mIED than in the group without mIED (at all ROIs, and during both stimulus conditions). In the beta band (15-30 Hz), power values increased significantly during stimulus conditions at frontal ROIs in the mIED group, but not in the group without mIED. That is, the following differences were observed between groups: The mIED group showed lower power values in both the (upper) theta and the alpha band, and a stronger increase of power values in the beta band (particularly at frontal ROIs).

Figure 2 shows the scalp distribution of the normalized grand-averaged (non-logarithmic) power elicited by the EEG questionnaire (contrasted to the preceding rest), separately for the two groups and the three analyzed frequency bands. The theta effect had a fronto-central maximum at FCZ, the alpha effect was maximal over parietal sites, and effects in the beta range were most prominent at anterior frontal, and fronto-temporal electrode sites (i.e., over electrodes situated over the frontalis and temporalis muscle). The following three sections provide detailed statistical analyses of these findings.

2.2.2.1. Theta band.

An ANOVA on the logarithmic FFT data of the 6 - 8 Hz range with factors stimulation (stimulus, rest), type (music, EEG questionnaire), anterior-posterior, hemisphere, and group indicated an effect of stimulation (p < .0001), reflecting that the theta power decreased during the stimulus conditions compared to the rest conditions. Moreover, a marginally significant interaction between factors stimulus and group was found (p < .07), reflecting that the decrease of theta power during stimulus conditions was stronger in the mIED group (see Table 1 for results of ANOVAs, see *Methods* for explanation of ANOVA model). When tested one-sided (justified by the hypothesis of a decrease of theta oscillations, see Introduction),

Figure 1. Normalized logarithmic power values (means, error bars indicate SEM) of the contrasts *music minus initial rest* (striped bars), and *EEG-questionnaire minus intermediate rest* (squared bars). Power values are given separately for each ROI, and for each of the three analyzed frequency bands (see text for details). White bars represent data measured from subjects without mIED, grey bars data from subjects with mIED. In both the theta and the alpha band, power values decreased during stimulation more strongly in subjects with mIED. In the beta band, considerable differences between groups were measured at anterior ROIs: During both music and EEG questionnaire, stronger power values were observed in subjects with mIED than in subjects without mIED.

the stronger decrease of theta power in the mIED group is statistically significant (p < .05).

An ANOVA with theta power values (averaged across the four ROIs) of the music condition as dependent variable, group as fixed factor, and theta power values of the initial rest as covariate indicated a marginal effect of group ($F(1,52) = 3.0$, $p < .09$, reflecting that power values differed between groups during the music condition), and a significant covariation of the power values of the music condition with the power values of the initial rest ($F(1,52) = 93.9$, $p < .0001$, reflecting that the theta power values at rest across all subjects predicted the theta power values during the music condition). Comparable results were indicated by the analogous ANOVA with power values of the EEG questionnaire as dependent variable, group as fixed factor, and theta power values of the initial rest as covariate (effect of group: $F(1,52) = 3.0$, $p < .09$; covariation of the power values of the EEG questionnaire with the power values of the initial rest: $F(1,52) = 68.2$,

$p < .0001$). However, no significant differences were indicated between groups for the rest conditions (rest preceding music condition: p > .7; rest preceding EEG questionnaire: p > .3). These results indicate that theta power values did not differ between groups at rest, whereas group differences emerged during the music condition and the EEG questionnaire. *2.2.2.2. Alpha band.*

An ANOVA on the logarithmic FFT data of the 8 - 12 Hz range with factors stimulation, type, anterior-posterior, hemisphere, and group indicated an effect of stimulation (p < .0001), but no interaction between factors stimulation and group (p = .18). However, power values decreased more strongly in response to both stimulus conditions in the group of mIED, at all four ROIs. The probability of this constellation is $p < .005$ according to a binomial distribution, rendering it unlikely that the consistently stronger power decrease in the mIED group in response to the stimuli was merely due to chance.
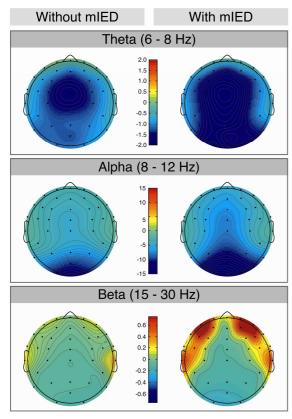
Figure 2. Scalp distribution of the normalized logarithmic power values of the contrast *EEG-questionnaire minus intermediate rest* (red: power increase relative to rest; blue: power decrease relative to rest), separately for the group without (left column), and with mIED (right column). The power decrease in the theta band had a fronto-central, and in the alpha band a parietal maximum. In the beta band, effects were strongest over anterior frontal and temporal electrodes covering the frontalis and the temporalis muscles. Effects in all three frequency bands were stronger for the mIED group (see text for details).

2.2.2.3. Beta band.

For the beta band, the ANOVA with factors stimulation, type, anterior-posterior, hemisphere, and group indicated an interaction between stimulation, anterior-posterior, and group (p < .0001), reflecting that increased power values in response to the stimulus conditions differed between groups particularly at anterior electrodes. An ANOVA computed for the frontal ROIs only (with factors type, condition, hemisphere, and group) indicated an interaction between factors condition and group (p < .0001).

An ANOVA with beta power values (averaged across the two frontal ROIs) of the music condition as dependent variable, group as fixed factor, and beta power values of the initial rest as covariate indicated a clear effect of group ($F(1,51) = 22.5$, $p < .0001$), and a significant covariation of the power values of the music condition with the power values of the initial rest ($F(1,51) = 11.5$, $p < .002$). Comparable results were indicated by the analogous ANOVA with power values of the EEG questionnaire as dependent variable, group as fixed factor, and beta power values of the intermediate rest as covariate (effect of group: $F(1,51) = 18.5$, $p < .0001$; covariation of the power values of the EEG questionnaire with the power values of the initial rest: $F(1,51) = 8.3$, $p < .007$). Similarly to the results of the analysis of the theta power values, no significant differences were indicated between groups for the rest conditions (rest preceding music condition: $p > .1$; rest preceding EEG questionnaire: $p > .1$). These results indicate that beta power values did not significantly differ between groups at rest, whereas clear group differences were measured during the music condition and the EEG questionnaire.

	Significance-values	
	$F(1,52)$	*p*-value
Theta (6-8 Hz)		
stim	39.8	.0001
stim x group	3.6	.07
antpost	14.8	.0005
stim x antpost	19.2	.0001
Alpha (8 – 12 Hz)		
stim	100.3	.0001
antpost	60.2	.0001
hem	6.3	.05
stim x type	7.7	.01
stim x antpost	4.0	.05
stim x hem	6.9	.05
type x antpost	7.2	.01
type x hem	4.7	.05
Beta (15 – 30 Hz)		
type	18.0	.0001
stim x group	4.3	.05
antpost	15.5	.0005
antpost x group	18.1	.0001
stim x type	10.7	.005
stim x antpost	106.3	.0001
stim x antpost x group	35.3	.0001

Table 1. Summary of ANOVAs. ANOVAs were conducted with four regions of interest on the logarithmic FFT data with factors stimulation (stimulus, rest), type (music, EEG questionnaire), anterior-posterior, hemisphere, and group (without mIED, with mIED).

2.2.3. Discriminant function analysis

For the development of techniques suitable for the assessment of mIED it is vital to make statements on the basis of individual data sets. The clearest difference between groups was observed in the beta band, but it is important to note that the distribution of the elevated beta power in the mIED group indicates that this effect was largely due to muscular activity (c.f. Goncharova et al., 2003). Although muscular activity clearly differed between groups, this activity nevertheless did not clearly differentiate both groups (e.g., because some subjects without mIED also showed muscular artefacts, while some subjects with mIED did not). It is possible, however, that the increased beta power values in the mIED group did not originate entirely from muscular activity, but at least partly from brain activity, which overlapped with the oscillations in the beta range caused by muscular activity. To capture such brain activity we computed several measures from the EEG data (see *Methods*) for each subject and for all ROIs, and subjected these data to a stepwise DFA (in addition to power values in the theta, alpha, and beta band, see *Methods*), probability for entry was $p = .05$, for removal $p = .10$. Eight variables were selected by the discriminant analysis, the canonical discriminant function was significant (Wilks' Lambda = .016, $\chi^2_8 = 87.7$, $p < .0001$), and 96.3% of cross-validated grouped cases were correctly classified.

2.2.3. Scores of the EEG-questionnaire.

Mean scores of the EEG-questionnaire were calculated for each subject, and then grand-averaged per group. The mean scores were identical for both groups (4.2 on a scale ranging from 1 to 6). That is, in contrast to the scores of the impulsiveness scale of the I_7 inventory, the behavioural data collected during the EEG questionnaire did not differ between groups.

2.2.4. Difference between music from Beethoven and from Handel

To test if the effects in the beta range observed in the mIED-group were due to the impulsive character of the Beethoven music, or if such effects would also be elicited by non-impulsive music, a subset of 30 participants was also presented with a piece of Handel music (see *Methods*). Again, for each subject contrast values were calculated for (a) Handel music minus the rest directly preceding the Handel music, and (b) Beethoven music minus the rest directly preceding the Beethoven music for the four ROIs also used in the previous analyses.

Contrary to our hypothesis, the Handel music elicited virtually the same effects in all three frequency bands (see Table 2).

	without mIED		with mIED	
	Beethoven	Handel	Beethoven	Handel
Theta[1]	-.13 (.04)	-.16 (.03)	-.23 (.05)	-.27 (.06)
Alpha[1]	-.41 (.06)	-.43 (.05)	-.42 (.07)	-.40 (.08)
Beta[2]	-.08 (.04)	-.10 (.03)	.15 (.09)	.14 (.08)

[1] Frontal and parietal ROIs
[2] Frontal ROIs

Table 2. Power values of the two music contrasts (Beethoven music minus preceding rest, and Handel music minus preceding rest), separately for each group and each analyzed frequency band. Contrast values did not differ between the two music conditions, in neither of the two groups.

2.2.5. Predictive Validity

One major purpose to which discriminant function analysis (DFA) is applied is that the model of the discriminant functions provided by the DFA can also be used to predict the group membership of new data sets. To assess the predictive validity of the classification functions provided by the DFA, 25 participants (9 with mIED, 16 without mIED) were measured in a re-test session (time between the two measurements ranged from two weeks to three months). EEG-data of the re-test sessions were entered into the discriminant function analysis, but unlike the first measurement (where subjects were classified to either of the two groups before performing the DFA), the DFA was now used to classify the data sets into either of the two groups. Results showed that 23 of the 25 subjects (i.e., 92 percent) were classified by the DFA to the same group as in the initial measurement (test/retest cross-tabulation: Pearson $\chi^2_1 = 14.31$, $p < .0001$).

Because a discriminant function is more stable the more cases are included, a DFA including the data sets of all first measurements (except those of the two subjects who were not correctly classified in the re-test analysis), as well as the 23 correctly classified data sets from the re-test sessions was performed. This DFA resulted in a correct classification of 100% of cross-validated grouped cases (Wilks' Lambda = .07, $\chi^2_{23} = 189.38$, $p < .0001$). Group centroid of the group without mIED was -2.49, and 5.30 for the group with mIED, respectively. The standardized canonical discriminant function

coefficients of this analysis are provided in Table 3. These coefficients can be used in further studies by other investigators to calculate the discriminant scores of single subject data sets [1]. Probability for membership in the group without mIED is > .99 for scores below 0, and > .99 for scores above 2 in the group with mIED.

2.3. Discussion

The purpose of Experiment 1 was to identify EEG correlates of mIED. Subjects with mIED showed during both the music condition and the EEG-questionnaire an increase of beta power, along with a decrease of theta and alpha power. The increased power in the beta range was to a considerable amount due to muscle activity. However, it is likely that oscillations in the beta range did not entirely originate from muscular activity, but also at least partly from brain activity. This assumption is supported by two observations: First, the contribution of brain activity to the increased beta power values in the mIED group is reflected in the decrease of theta (and alpha) power, which is known to decrease with increasing beta power (associated with an increase in cortical arousal, Steriade, 1999; Barry et al., 2004). Second, in the model of the discriminant functions seven coefficients were derived from midline electrodes over which muscle artefacts are rather minor (Goncharova et al., 2003; see also Figure 2). Future studies should bear in mind that research on electrophysiological correlates of mIED is faced with the inherent problem that individuals with mIED are often more tense, leading to stronger muscular artefacts, and thus to a systematic bias of spectral power values, especially in the beta band.

The model of discriminant functions classified the majority of subjects (> 90%) correctly, and the predictive validity of this model was high. This shows that the DFA model is capable of discriminating between subjects with and without mIED, suggesting that this method could be developed for the identification of mIED in future studies (but see also General Discussion). As mentioned above, some coefficients of the DFA model were derived from midline electrodes (over which muscle artefacts are rather minor), and two other coefficients were derived from power values in the theta range. This indicates that the DFA model did not discriminate data sets only on the basis of muscular activity.

The data obtained with the I_7 impulsivity scale showed that subjects with mIED scored significantly higher on this scale than control subjects. This provides some external validation of our classification of subjects, because mIED represents an impulsivity facet characterized by impulsive action (or behavioural disinhibition), and this facet is at least partly captured by the I_7. Note that impulsivity is a heterogeneous phenomenon which can be subdivided into at least two, perhaps more different aspects (Moeller et al., 2001; Winstanley et al., 2004; Lansbergen et al., 2007). Winstanley et al. (2004), for example, suggested to distinguish between impulsive decision making (or impulsive choice), and behavioural disinhibition (or impulsive action), Moeller et al. (2001) also mention perseverance of a response that is punished or unrewarded (see Whiteside & Lynman for an overview about different conceptualizations of impulsivity). Thus - although individuals with mIED show increased impulsivity with respect to the impulsivity facet "impulsive action" – not all impulsive individuals (particularly those scoring high on other impulsivity facets such as impulsive choice) have mIED.

Contrary to our hypothesis, the Handel music elicited virtually the same effects in all three frequency bands. That is, the Handel condition shows that it is not the impulsive nature of the Beethoven music which led to the effect of strong oscillations in the beta band in subjects with mIED (because power values did not differ between both music conditions). It is, thus, probable that also items other than those of the EEG-questionnaire would have led to similar effects; this issue remains to be specified further.

The behavioural data collected during the EEG questionnaire did not differ between groups, probably due to the rather personal character of the questions of the EEG questionnaire (such as "I remain closed to others"). It is likely that such questions provoke responses influenced by social desirability, as compared to the questions of the I_7 inventory, which rather refer to questions about behaviour with no particular social value (such as "Sometimes I buy things on impulse"). The data indicate that the questions of the EEG-questionnaire are not suited to assess mIED behaviourally (note that this was not the purpose of the EEG-questionnaire, and that the questionnaire form was used only to control if participants actually read the text presented on the computer screen).

Condition	Parameter	Freq. Range	ROI	Function
music	LR, intercept	20-86	FP2, AF4, AF8	2,054
music	LR, intercept	20-86	FPZ, AFZ, FZ	-,979
music	LR, r^2	20-86	FP2, AF4, AF8	,358
music	LR, r^2	20-86	FPZ, AFZ, FZ	-,663
music	LR, r^2	20-30	FP2, AF4, AF8	-1,022
music	PF, quadr. Trend	20-30	F5, FC3, F3	1,067
music	PF, quadr. Trend	20-30	FPZ, AFZ, FZ	-,404
music	PF, quadr. Trend	20-30	F7, FT7, FC5	-1,514
music	PF, linear trend	20-30	F6, FC4, F4	,744
music	VNC	20-30		,534
Music minus rest	MSP	20-30	FPZ, AFZ, FZ	-,487
EEG-questionnaire	LR, intercept	20-86	FP1, AF3, AF7	1,203
EEG-questionnaire	LR, intercept	20-86	FPZ, AFZ, FZ	-1,107
EEG-questionnaire	LR, intercept	20-86	F8, FT8, FC6	,423
EEG-questionnaire	LR, r^2	20-30	FP2, AF4, AF8	,863
EEG-questionnaire	LR, r^2	20-30	FPZ, AFZ, FZ	-,653
EEG-questionnaire	LR, r^2	20-30	F8, FT8, FC6	,463
EEG-questionnaire	PF, linear trend	20-30	F7, FT7, FC5	-,665
EEG-questionnaire	PF, intercept	20-30	F7, FT7, FC5	,725
EEG-questionnaire	FMP	20-45	FPZ, AFZ, FZ	-,434
EEG-questionnaire	MSP	20-86	FP1, AF3, AF7	-,805
EEG-questionnaire	MSP	6-8	FP1, AF3, AF7	,321
EEG-quest.minus rest	MSP	6-8	F8, FT8, FC6	,695

Table 3. Standardized canonical discriminant function coefficients. LR: linear regression, PF: polynomial fit, MSP: mean of spectral power, FMP: frequency with maximal spectral power. VNC: variance of normalized FFT data between channels

3. Experiment 2: Test of the DFA model

As mentioned earlier, mIED is characterized by impulsive action (or behavioural disinhibition). The relation between mIED and this impulsivity facet is also reflected in the data of Experiment 1, where subjects with mIED scored higher than control subjects on the impulsivity-scale of the I_7 inventory. Thus, the model of discriminant functions, which discriminated between individuals with and without mIED in Experiment 1, should also discriminate between individuals with higher and lower impulsivity. To test this, Experiment 2 was conducted with an independent group of subjects who filled out the I_7 questionnaire, and were measured with EEG as in Experiment 1. Participants were assigned to either of two groups (supposedly with, and without mIED) solely based on the classification functions provided by the DFA (as derived in Experiment 1), with the hypothesis that I_7 scores would differ between the two groups.

It was hypothesized that if I_7 scores do not differ between groups, it is unlikely that the DFA model is capable of identifying mIED. If, on the other hand, I_7 scores differ between groups, the DFA differentiates between subjects with high and low impulsive action (or

behavioural disinhibition); this would support the assumption that the DFA model tends to differentiate between subjects with and without mIED.

3.1. Methods

3.1.1. Participants.

45 females (age range 22 – 39 years, mean age 27.8 years) without psychiatric disorders participated in the experiment, none of which had participated in Experiment 1.

3.1.2. Stimuli and Procedures.

Stimuli and Procedures were identical to those of Experiment 1, except that no condition with Handel music was employed. That is, the experimental session started with filling out the I_7 questionnaire followed by the EEG recordings. EEG recordings and Data analysis were identical to Experiment 1.

3.2. Results and Discussion.

The classification functions provided by the DFA in Experiment 1 assigned 21 subjects to

the group with and 24 subjects to the group without mIED. The I_7 impulsivity scores clearly differed between groups: the mean of the I_7 scores was 29.7 (*SEM* = 4.0) in the non-mIED group, and 45.6 (*SEM* = 5.4) in the mIED group, the difference between groups being significant ($t(43)$ = 2.4, p < .05, two-sided, independent samples t-test).

These results show that the DFA model discriminates between individuals with higher and lower impulsivity (the impulsivity being characterized by impulsive action, or behavioural disinhibition). This replicates the relation between mIED and impulsivity reported in Experiment 1, and provides further support for the assumption that the DFA model is capable of discriminating between subjects with and without mIED.

4. General Discussion

The present study investigated electrophysiological correlates of mIED. Subjects with mIED showed during both stimulus conditions an increase of beta power, and a decrease of theta and alpha power. This finding is in accordance with previous studies reporting that children with AD/HD who show increased temper tantrums have increased beta, along with decreased alpha, and decreased theta activity (Clarke et al., 2001a, b). Our results show that this EEG pattern is not confined to individuals with AD/HD, and they suggest that this pattern is, on a more general level, related to an increased tendency for impulsive action and behavioural disinhibition. This interpretation is supported by the finding that individuals with mIED scored higher on the impulsivity scale of the I_7, which captures this impulsivity facet at least partly.

Another aim of this study was to discriminate between subjects with and without mIED on the basis of their EEGs. Therefore, we performed a discriminant function analysis (DFA), which provided a model of discriminant functions that had a high statistical power, and proved to be reliable. This model was tested in Experiment 2 in which subjects were assigned to either of two groups (supposedly with and without mIED) solely by the classification functions provided by the DFA. The I_7 impulsivity scores differed between groups, showing that the DFA model is capable of discriminating between individuals with high and low impulsivity (as measured with the I_7 inventory). Because impulsivity, as captured with the I_7 inventory, is characteristic for mIED, this finding provides some external validation of the DFA model. The statistical power and the reliability of the model provided by the DFA make it

promising to develop tools for the assessment of mIED using neurophysiological measures. With regards to impulsivity research, the assessment of mIED using such measures, perhaps in conjunction with standardized subjective measures, would have the advantage of being less dependent on measures that introduce subjective bias inherent to subjects and investigators.

As mentioned in the Discussion of Experiment 1, the increased beta activity in individuals with mIED was presumably largely due to muscular activity. However, it is likely that the group difference in beta activity was not entirely due to muscular, but at least partly due to brain activity. This assumption is supported by the observation that the increased beta activity in the mIED group was accompanied by a decrease of theta (and alpha) activity: theta and alpha activity is inversely related to beta activity, and the reduction of theta and alpha activity cannot be explained by muscular activity (Goncharova et al., 2003). It is also important to note that the model of discriminant functions did not discriminate data sets only on the basis of muscular activity, because this model was partly based on coefficients derived from power values in the theta range, and from beta activity measured at midline electrodes (over which muscle artefacts are rather minor).

EEG beta activity is thought to be paced by the thalamus, modulated by brainstem neurons, and generated by cortical neurons in response to cognitive processes and attention requirements (Steriade, 1999). EEG activity in the beta range is considered to be an index of the level of cerebral activation (also sometimes denoted as *arousal*), because increased alertness has been shown to be associated with increased power values in the beta band (Steriade, 1999). E.g., during non-REM sleep power values in the beta band decrease, being inversely related to the power spectral density in the delta and theta band that characterizes cerebral deactivation (Steriade, 1999). Chapotot et al. (1998) reported a temporal coupling between EEG beta activity and cortisol secretion, indicating a correlation between secretion of hypothalamus-pituitary-adrenal (HPA) axis hormones and brain activation level as reflected in the beta band. Chapotot et al. (1998) suggested that HPA axis activity is correlated with the central alertness level of which EEG beta activity is an indicator, and that HPA axis activity and EEG beta activity represent two elements of an arousal system through which a psychoneuroendocrine regulation of alertness is organized. The increased beta power in the subjects with mIED in response to the EEG-questionnaire, the impulsive music from Beethoven, and the non-impulsive music from

Handel suggests that subjects with mIED generally respond more alertly to sensory stimuli, and show greater stress responses to such stimuli. Notably, the I_7 scores show that the heightened arousal in the mIED group (as reflected in the increased beta activity) is tightly related to increased impulsivity (particularly with regards to impulsive action and behavioural disinhibition), a relation which also becomes apparent in the restlessness and hyperactivity of some disorders characterized by substantial impulsivity (such as AD/HD).

Correspondingly, aberrant beta power has been reported in several clinical populations: With respect to impulsivity, previous studies investigating children suffering from attention deficit/hyperactivity disorder (ADHD) showed strongly increased power values in the beta range (Clarke et al., 2001a,b). This effect had been related to impulsivity, rather than to attention deficits, corroborating the findings of increased beta activity in subjects with mIED. Furthermore, increased beta power has been reported for patients with insomnia during both REM and non-REM sleep (e.g., Hall et al., 2000; Merica et al., 1998), for restless patients with major depression during both sleep (Nofzinger et al., 2000; Armitage, 1995) and wakefulness (Kano et al., 1992; Knott et al., 2001), and for combat veterans with post-traumatic stress disorder (PTSD; Begic et al., 2001; Jokic-Begic, 2003). The authors of the latter two studies cautiously attributed the increased beta activity to the hyperexcitability in PTSD patients, to their hyperarousal and restlessness, and possibly also to a greater anxiety and impulsiveness of the patients. However, it is important to note that, although mIED might be found in other disorders characterized by substantial impulsivity (particularly when impulsivity is characterized by impulsive action and behavioural disinhibition) it is unlikely that all impulsive individuals also exhibit mIED (particularly when increased impulsivity is characterized by impulsive decision making or impulsive choice).

With respect to its origins, ventromedial prefrontal cortex (vmPFC which is part of the orbitofrontal cortex, OFC), possibly along with the (right) inferior occipital cortex, has been reported to be involved in the generation of scalp-recorded beta activity (Nofzinger et al., 2000). Involvement of the OFC has also been reported in association with impulsive behaviour by a number of studies (e.g., Horn et al., 2003; Soloff et al., 2003; Berlin et al., 2004; Best et al., 2002; Berlin, et al., 2005), especially with respect to the role of the OFC for the control of affective behaviour and for the inhibition of socially inappropriate impulsive actions. The increased power in the beta band in sub-

jects with mIED might, thus, at least partly be related to a greater effort to control impulsive actions during the experimental session. However, the topological origins of the EEG effects observed in this study remain to be specified.

The notion that individuals with mIED show greater behavioural disinhibition, increased arousal, and greater HPA axis activity in response to sensory stimuli is in agreement with previous studies that suggest an association between IED and decreased serotonin (5-HT) activity (see Olvera, 2002, for an overview; for further associations between impulsivity and 5-HT see, e.g., Clark et al., 2005). Ascending 5-HT fibers are in close contact with the HPA axis through both direct and indirect pathways. Especially 5-HT has been implicated in an inhibitory function on the secretion of stress hormones. It is, thus, conceivable that individuals with mIED have lower serotonin levels, which lead to stronger HPA axis activity, and thus to higher oscillatory activity in the beta band. It has previously been suggested that lower 5-HT levels, and stronger HPA axis activity (particularly abrupt changes of HPA axis hormones) are related to the sudden outbursts of temper typical for individuals with (m)IED (this phenomenology was conceived of as a "Cerebro-Physiological Switch", Siebel, 1994; Siebel & Winkler, 1996). Testing the hypothesis of lower 5-HT levels, as well as increased levels of stress hormones (such as corticotropin releasing hormone and arginine vasopressin) in individuals with mIED in future studies would provide important insights into the neurochemical correlates of mIED.

In conclusion, the present data show electrophysiological correlates of mIED. The increased beta activity, along with decreased theta and alpha activity in response to auditory and visual stimuli in individuals with mIED is taken to reflect that these individuals are more aroused by, and show greater stress-related responses to sensory stimuli than control subjects. The method for the assessment of mIED by means of analyzing the EEG data with the DFA model showed to be highly replicable. Thus, this method represents a step towards the assessment of impulsivity facets using physiological measures. The combination of such measures with standardized subjective measures would have the advantage of being less dependent on subjective bias introduced by subjects or investigators. Notably, the impulsive aggressive and auto-aggressive behaviour characteristic for individuals with mIED can also be found in individuals with other disorders characterized by substantial impulsivity such as AD/HD (at least the impulsive type), borderline and antisocial personality disorder, bulimia nervosa, trichotillomania, self-

injurious behaviour, and sexual compulsions. Our methods might thus motivate future research to investigate the presence of mIED in such disorders.

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