RIJKSUNIVERSITEIT GRONINGEN

VAKGROEP PSYCHOLOGIE

CONSISTENCY OF SEP
AN ANALYSIS OF MULTI-CHANNEL SOMATOSENSORY EVOKED POTENTIALS TO IMPROVE DIFFERENTIAL DIAGNOSIS OF CORTICOBASAL GANGLIONIC DEGENERATION

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Abstract

A new analysis method for multi-channel SEP data is evaluated for its use in making the diagnosis of Corticobasal Ganglionic Degeneration (CBGD) more probable. SEP measures peripheral nerve conduction which is affected in CBGD and other parkinsonian syndromes. A characteristic of this data is that some people show a sharper demarkation between the first cortical components (consistent SEP) than others (inconsistent SEP). The consistency of a SEP is related to the spread of variance of all sample points.

Through the top-centres of a histogram of the variance of SEP data, an exponential and an alpha function are fitted. SEP data from 7 healthy subjects, 5 subjects with other parkinsonian syndromes and 4 patient with probable CBGD is used. Of the resulting parameters the slope of the alpha function seems most useful in separating patients with CBGD from patients with other parkinsonian syndromes and in separating the first affected hemisphere from the other within CBGD patients For separating patient groups, sensitivity is 0.75 and specificity is 0.8. For separating affected hemispheres from unaffected hemispheres within CBGD, sensitivity is 0.75 and specificity is 0.75. Further investigation is necessary, since only a small group of subjects was used and data from affected hemispheres in CBGD patients does not differ from data from other patients. The use of this tool may be improved by focussing on specific parts of SEP data.

1. Introduction

The present study tries to estimate the added value of multi-channel EEG recordings for clinical diagnosis using Somatosensory Evoked Potentials (SEP). Classic SEP measurements will first be explained in short as well as corticobasal ganglionic degeneration (CBGD). SEP can assist in a probable diagnosis of CBGD. Later on a new way to look at SEP-data is introduced and its possible merits for diagnosing CBGD are discussed.

1.1. Classic SEP

SEP tests peripheral nerve conduction and central processing of somatosensory information (figure 1.1). SEP usually involves electrical stimulation of the nervus medianus near the wrist or the nervus tibialis near the ankle. The present study focusses on median nerve stimulation. When this nerve is stimulated a muscle in the hand twitches and simultaneously an electrical signal is sent to the brain. This signal is traditionally measured using four pairs of electrodes: one with an electrode at the sixth vertebra and at the neck. The second pair of electrodes is an electrode at the ipsilateral Erb's point and at location Fz of the international 10-20 system. The third and fourth pair of electrodes are C3' and C4' with a reference at Cz (locations of the international 10-20 system).

If these recordings are averaged over multiple (about 500) trials a healthy subject will show a negativity at C3' or C4' (contralateral to the side of stimulation) after approximately 20 milliseconds, the N20 component, and a positivity after approximately 30 milliseconds, the P30 component. Patients in an early stage of corticobasal degeneration often show a unilateral alteration of the characteristics of one or two of these components (Leenders 2002; Takeda, Tachibana, Okuda, Kawabata & Minoru 1998). In our experience it is usually the N20 amplitude that is decreased.

1.2. Corticobasal Ganglionic Degeneration

CBGD is characterised by a slowly progressing, asymmetric dyspraxia. CBGD shares several characteristics with Progressive Supranuclear Palsy (PSP) and Pick's disease (PD), and other parkinsonian afflictions (Litvan et al., 1997). Onset of the disease usually involves unilateral complaints of clumsiness of a hand or arm. Progress is marked by akinesia and apraxia of the initially afflicted limb, spreading to the contralateral limb. Eventually, one or more limbs will

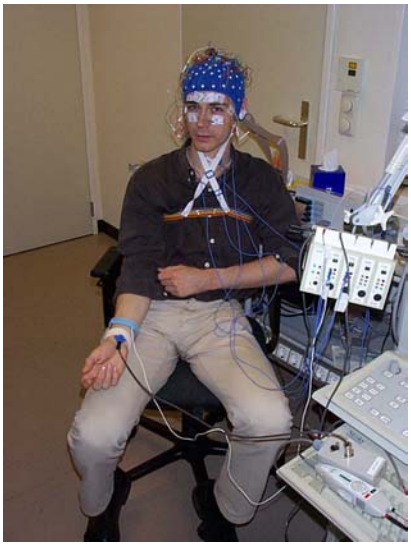


Figure 1.1. SEP and anatomy. Stimulation is performed at the wrist. Locations of interest are the point of Erb, the 5th vertebra (we used the 6th), FZ and C3' and C4' (not depicted). One of our subjects is shown in the upper left.

become dystonic, typically fixed in a wing-like position. Myoclonus may evolve in a later stage, as well as a disability to walk. (Rinne, Lee, Thompson & Marsden, 1994). Alien hands also are a common symptom.

SEP may be a good tool for making the diagnosis of CBGD probable because this disease involves a progressing atrophy of the brain which often starts parietally near the somatosensory cortex. The first cortical components of the SEP are generated in the somatosensory cortex and hence SEP can in principle be used to detect abnormalities in that region of the brain.

1.3. Depression in CBGD and Early Diagnosis

Hargrave (1998) describes the case of a patient with probable CBGD also suffering from a severe depression. Hargrave suggests that this depression may be psychological in nature or that it may be caused by pathophysiological changes inherent to CBGD.

Treatment of CBGD is not yet possible, but if the disease is indeed accompanied by its own kind of depression, psychological guidance to improve the quality of life of the patients will benefit greatly from early diagnosis of the disease. However accurate early diagnosis of CBGD is difficult because of overlap of symptoms with other diseases (Litvan et al, 1997). Therefore it is of paramount importance to find non-invasive measurement parameters that are able to distinguish CBGD from other syndromes in an early stage.

1.4. Problems with classic SEP

As noted by Legatt and Kader (2000) abnormalities of N20 and P30 components in SEP-recordings are sometimes caused by normal variations in the course of the central sulcus and not by dysfunction of the somatosensory cortex. Scalp potentials of N20 and P30 originate postcentrally in area 3b (Valeriani et al, 2001) and area 1 respectively (Buchner et al, 1995) as illustrated in figure 1.2. There is some controversy about the source of the P30 component being located in area 1 (Bötzel, Ecker, Mayer, Schulze & Straube, 1995; Valeriani et al, 2001,).

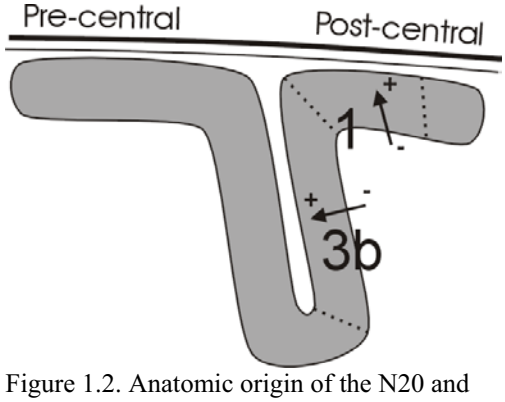


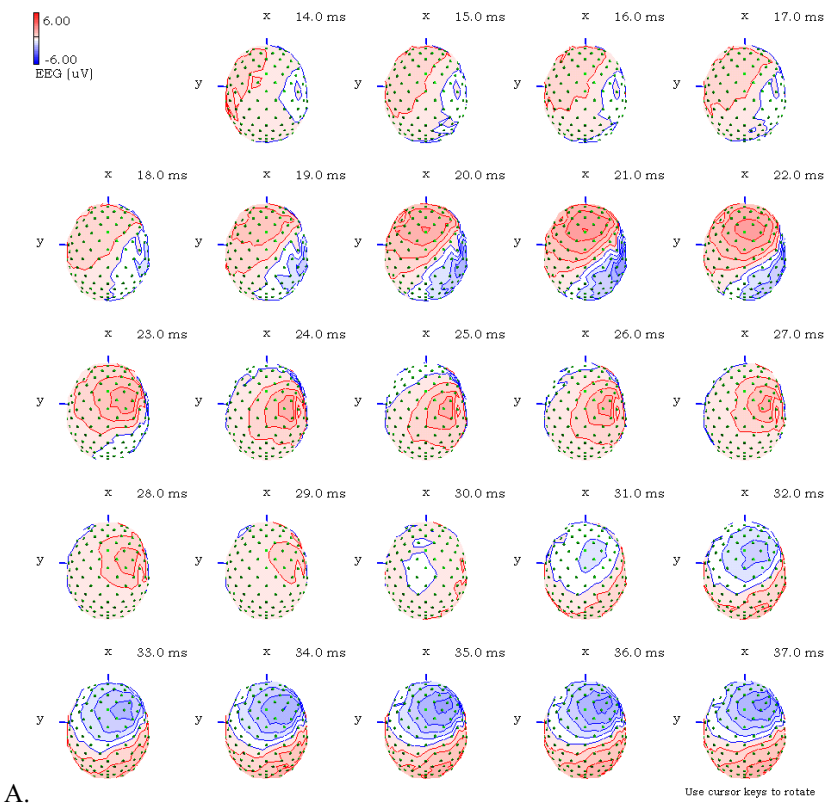
Figure 1.2. Anatomic origin of the N20 and P30 components. The N20 component originates in area 3b and the P30 component originates in area 1.

1.5. Multi-channel recordings

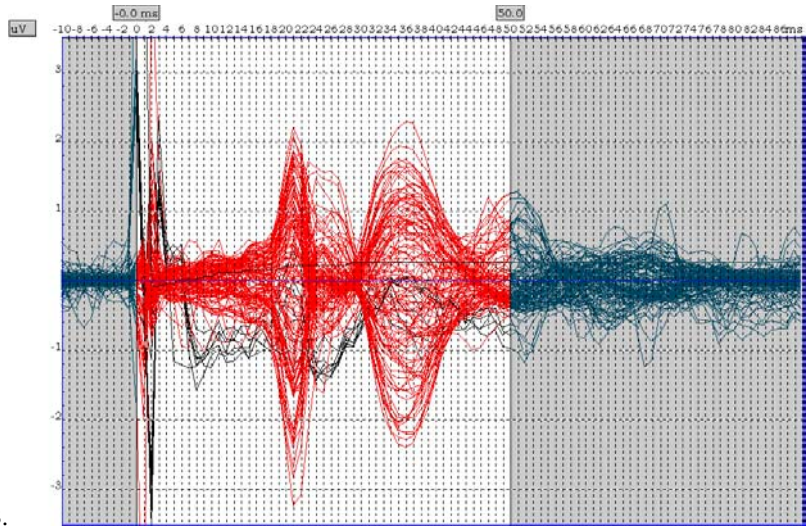
Multi-channel recordings enable distinction between real abnormalities in N20 and P30 components and an atypical course of the central sulcus (Legat & Kader, 2000). This is an enhancement of classic techniques made possible by a larger amount of information. Do multichannel recordings give any information classic SEP doesn't? If a multi-channel recording is combined with MRI it is possible to perform precise source localisation. Even without an accurate head-model, comparison of sources in the left and right hemisphere may indicate a lateralized defect, enabling for example early differential diagnosis of CBGD, because unlike in other Parkinsonian syndromes, symptoms in CBGD show a strong lateralisation (Rinne et al, 1994). Leenders (2002) claims that particularly in the early phase of the disease it is difficult to distinguish CBGD from other diseases with parkinsonism as a symptom. Later on the most important differential diagnosis is PSP and comparison of localized sources may also help to separate one from the other.

1.6. Butterfly plots

SEP data can be represented as a butterfly plot. In a butterfly plot, the EPs of all electrodes are superimposed and this visualises the change of field potentials over time. In figure 1.3 a series of field potentials and the corresponding butterfly plot are given as an example.



A.



B.

Figure 1.3. Butterfly plot. The same SEP data represented as (A) a series of field potentials and (B) as a butterfly plot.

When looking at the butterfly plots of patients (e.g. figure 2.2) we observed that in some people the N20 and P30 component contrast much sharper with the rest of the recording than in others. In other words: before and after the maximum amplitudes of the N20 and P30 some recordings show sharp 'nodes' where the traces of all electrodes switch sign simultaneously. Since the activity during peak amplitudes can be attributed to single sources (more easily) this may be a sign of modular information processing. For the N20 and the P30 this involves areas 3b and 1. As an example, age-related dedifferentiation of dorsal and ventral information streams in visuospatial tasks has been found by Chen, Myerson and Hale (2002). It is possible that 'blurring' of the butterfly plots of SEP measurements is related to dedifferentiation in the somatosensory cortex with age or in patients.

1.7. Hypotheses

If a ‘blurred’ SEP is indeed an indication of dedifferentiation of information processing, the spread of variance per time point over the SEP should change with age and in patients. If this is the case the spread of variance should be able to make a distinction between younger and older people, or between CBGD patients and normal subjects and between the affected and unaffected hemispheres of patients. The present study seeks to find if the spread of variance can indeed make these distinctions. We coin the term ‘consistent’ as an adjective for unblurred SEPs (with sharp nodes) and ‘consistency’ as the characteristic we express as spread of variance over the entire SEP. The hypotheses we are testing are:

1. Consistency can distinguish between age categories.
2. Consistency can distinguish between normal subjects, CBGD patients and patients with other parkinsonian syndromes.
3. Consistency can distinguish between affected and unaffected hemispheres in CBGD patients.

2. Methods

2.1. Experiment

The experiments were conducted at the hospital using standard hospital procedure to ensure that any results would be usable in hospital settings.

2.1.1. Setup

For stimulation and the classic measurements a Nicolet Viking II was used. The EEG-data was collected on a PC using ONYX software. A 128-channel EEG headcap was used with separate electrodes placed at 9 locations: 6 EOG electrodes, 2 electrodes on the earlobes, an electrode at N.Z. and a ground for the EEG. Four electrodes were used for the classic measurements to check for normal peripheral nerve conduction; at the sixth cervical vertebra with a reference at the neck and at the ipsilateral Erb's point with a reference at the sternum. All electrodes were of a tin alloy. Impedances were kept below 20 kΩ. To facilitate contact between the skin and the electrodes an equal mixture of a salt solution and Skinpure was injected in all electrodes.

The median nerve was stimulated at the wrist with a frequency of 2,8 Hz. Each stimulus had a duration of 0,2 milliseconds. Correct stimulation was controlled by stimulating with just enough amperage to elicit a twitch of the thumb.

2.1.2. Subjects

Multi-channel SEPs were recorded from eight healthy, right-handed subjects. Due to a technical problem, the conditions changed during testing of the fourth subject and hence this subject is left out of the analysis. Four patients diagnosed with CBGD are included in the experiment as well as five patients with other parkinsonian syndromes. The healthy subjects and the patients are described in table 2.1.

Subject number	Category	Age	Sex	First Affected Side
1	Normal subject	25	Male	-
2	Normal subject	19	Male	-
3	Normal subject	52	Male	-
4	Normal subject	40	Female	-
5	Normal subject	51	Female	-
6	Normal subject	21	Female	-
7	Normal subject	51	Male	-
8	Normal subject	32	Female	-
9	Other patient	73	Female	-
10	Other patient	73	Female	-
11	Probable CBGD	68	Female	Right
12	Probable CBGD	59	Female	Left
13	Other patient	64	Female	-
14	Probable CBGD	73	Female	Left
15	Other patient	54	Female	-
16	Other patient	68	Female	-
17	Probable CBGD	71	Female	Left

Table 2.1. Subjects.

2.1.3. Measurements

Both the left and the right hand were subject to two runs of at least 500 accepted trials. A trial was rejected by the Viking when the signal was out of bounds. The EEG-data was sampled at 1000 Hz.

2.2. Analysis

A classic analysis was performed on the data of all subjects. Of the classic parameters we have chosen the latencies of the N10 and N13 components to ascertain normal peripheral nerve conduction of the healthy subjects. In clincical practice P13 is used more often. After that the new, experimental parameters will be discussed.

2.2.1. Classic Analysis

The electrodes at Erb's point and the sternum were used to measure the N10 component. This component signals the propagation of the action potential from arm to torso and includes the negativity that travels along the plexus brachialis (Chiappa, 1997). The electrodes at the sixth cervical vertebra and the neck were used to measure the N13 component. The N13 component is reflecting a depolarisation of cell assemblies in central grey matter with a front-to-back

orientation. This means that the electric field is negative in a dorsal direction and positive in a ventral direction. Maximum difference in potential can be measured by comparing the electrode at the sixth cervical vertebra with the electrode at the neck.

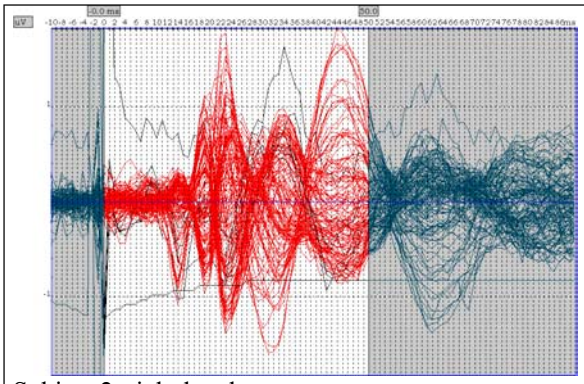
2.2.1.1. Brain Vision Analyser

Brain Vision Analyser software was used for preprocessing of the raw EEG data. After applying a highpass-filter (20 Hz. and 12 dB/oct) the data was segmented based on marker positions. Each segment started 10 msec. prior to stimulation and ended 90 msec. after stimulation. Subsequently, for each channel trials below –100 μV or above 100 μV were rejected as an artifact. An average was computed over the remaining trials of each channel. As a last transformation in Brain Vision Analyser a baseline correction was performed for each channel using the –10 to 0 msec interval as baseline.

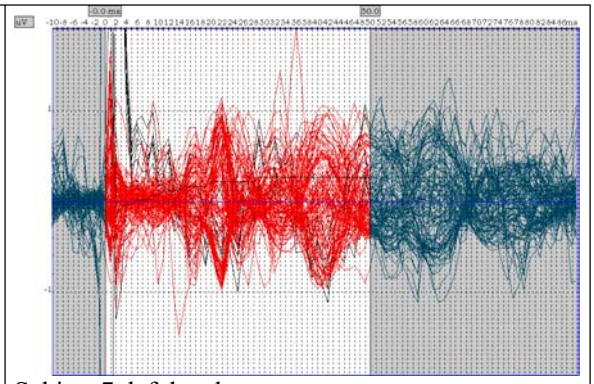
The classic C3' and C4' derivations can now be derived from the SEP data. This provides a first glance at the N20 and P30 components originating in the somatosensory cortex. Usually, physicians inspect the C3' and C4' derivations visually and they will not be discussed any further in this report.

2.2.2. Experimental parameters

Visual inspection of the butterfly-plots of the SEP data (e.g. Figure 2.2.) seems to indicate that some people have a sharp distinction between separate components whereas others do not. A sharp distinction between components can be described as a simultaneous switch of sign of all channels. A SEP with sharper distinctions between components is said to be more consistent than other SEPs. For the present study we try to define a parameter that expresses this consistency and estimate its usefulness.



Subject 2, right hand



Subject 7, left hand

Figure 2.2. Nodes. The components in the multi-channel SEP of subject 2 are more easily identified and separated from each other than the components in the multi-channel SEP of subject 7.

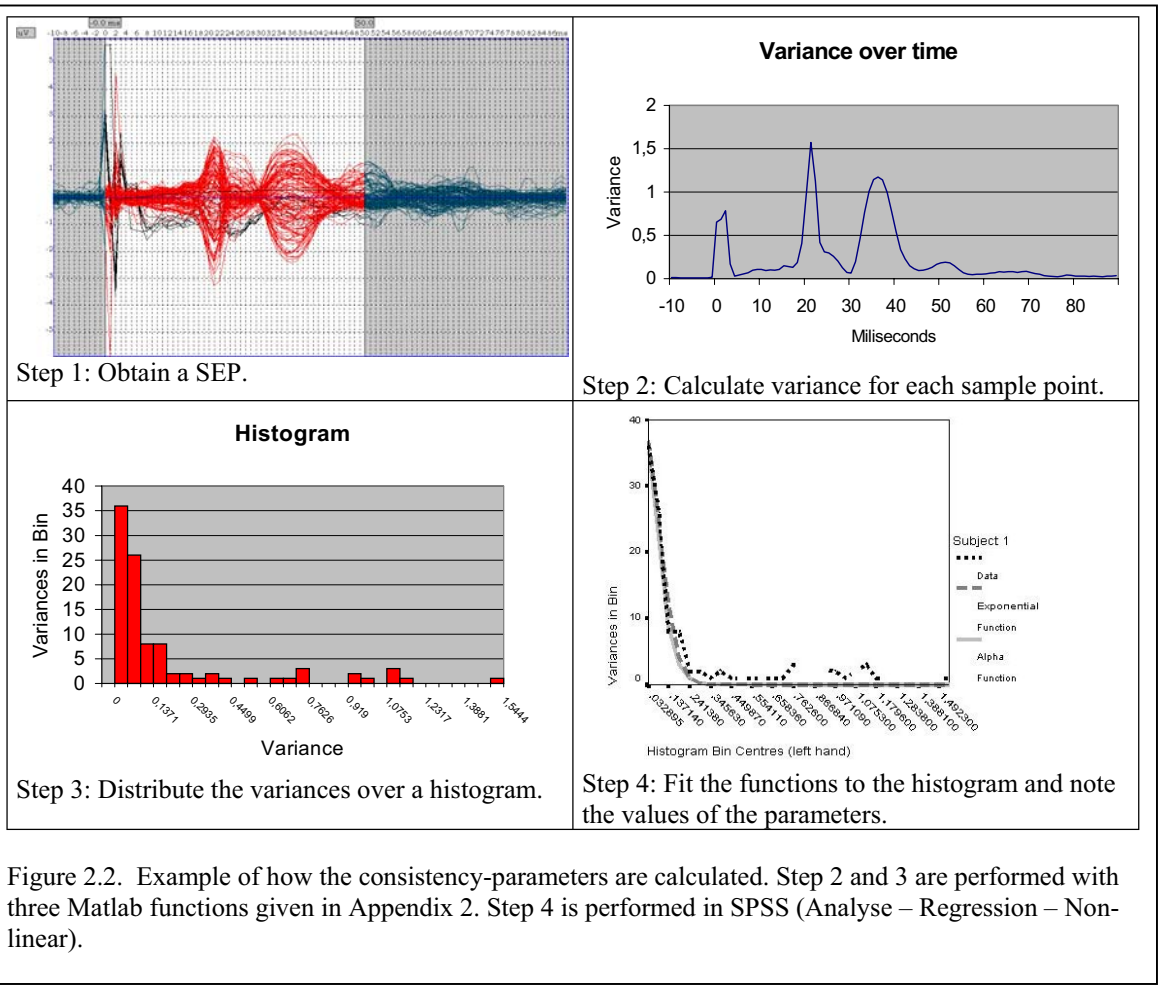
2.2.2.1. Spread of variance as a consistency measure

A consistent SEP differs from less consistent SEPs in the variance over electrodes at each sample point. Consistent SEPs will have relatively low variances at the switchpoints between components and relatively high variances at the peaks of the components. For each SEP the variance at each sample point was calculated and each set of variances was transformed into a histogram with 30 bins. This was done with a few Matlab functions which can be found in Appendix 2. These histograms show the spread of variance. To quantify the spread of variance two functions were fitted through the peaks of the histogram bins; an exponential function and an alpha function. Curve-fitting was performed in SPSS 10 using a 'sequential quadratic programming' goal-function minimalisation algorithm for both functions. A graphic example of the process is given in figure 2.3.

2.2.2.2. Method 1: exponential function fit

The exponential function assumes there is a normal distribution of the variances. It is of the form:

$$p_1 \cdot e^{\left(-\frac{(x-p_3)^2}{2{p_2}^2}\right)}$$



Step 1: Obtain a SEP.

Step 2: Calculate variance for each sample point.

Step 3: Distribute the variances over a histogram.

Step 4: Fit the functions to the histogram and note the values of the parameters.

Figure 2.2. Example of how the consistency-parameters are calculated. Step 2 and 3 are performed with three Matlab functions given in Appendix 2. Step 4 is performed in SPSS (Analyse – Regression – Non-linear).

Parameter P_2 is the standard deviation of the exponential function. Parameters P_1 and P_3 respectively indicate the height of the function at its centre and the location of the centre (see figure 2.3). Because negative variances do not occur and to keep at least half of the function within the range of actually measured data, parameter P_3 was restricted to be 0 or higher.

2.2.2.3. Method 2: alpha function fit

The alpha function assumes that the distribution of the variances approaches the shape of a Poisson distribution. Negative variances can not be fitted by the curve, the curve rises sharply from zero and slowly dies out. It is of the form:

$$p_4 \cdot x \cdot e^{\left(\frac{-x}{p_5}\right)}$$

Parameter P_5 now expresses the location of the function's peak and parameter P_4 indicates the slope of the function (see figure 2.3).

2.2.2.4. Parameters and Consistency

It is hypothesized that the parameters of the functions are largely dependent on the consistency of the SEP they were calculated from. When consistency is high, the number of low variances will be higher and most variances will be concentrated in a limited number of bins at the side of the histogram with low variances. When consistency is low variances will be spread over a larger number of bins. This is reflected in the values of the parameters that fit the functions through the centres of the tops of the bins of the histograms. Specifically, parameter P_2 of the exponential function and parameter P_5 of the alpha function are expected to decrease with consistency and parameter P_1 of the exponential function as well as parameter P_4 of the alpha function are expected to increase with consistency. This is illustrated in figure 2.3.

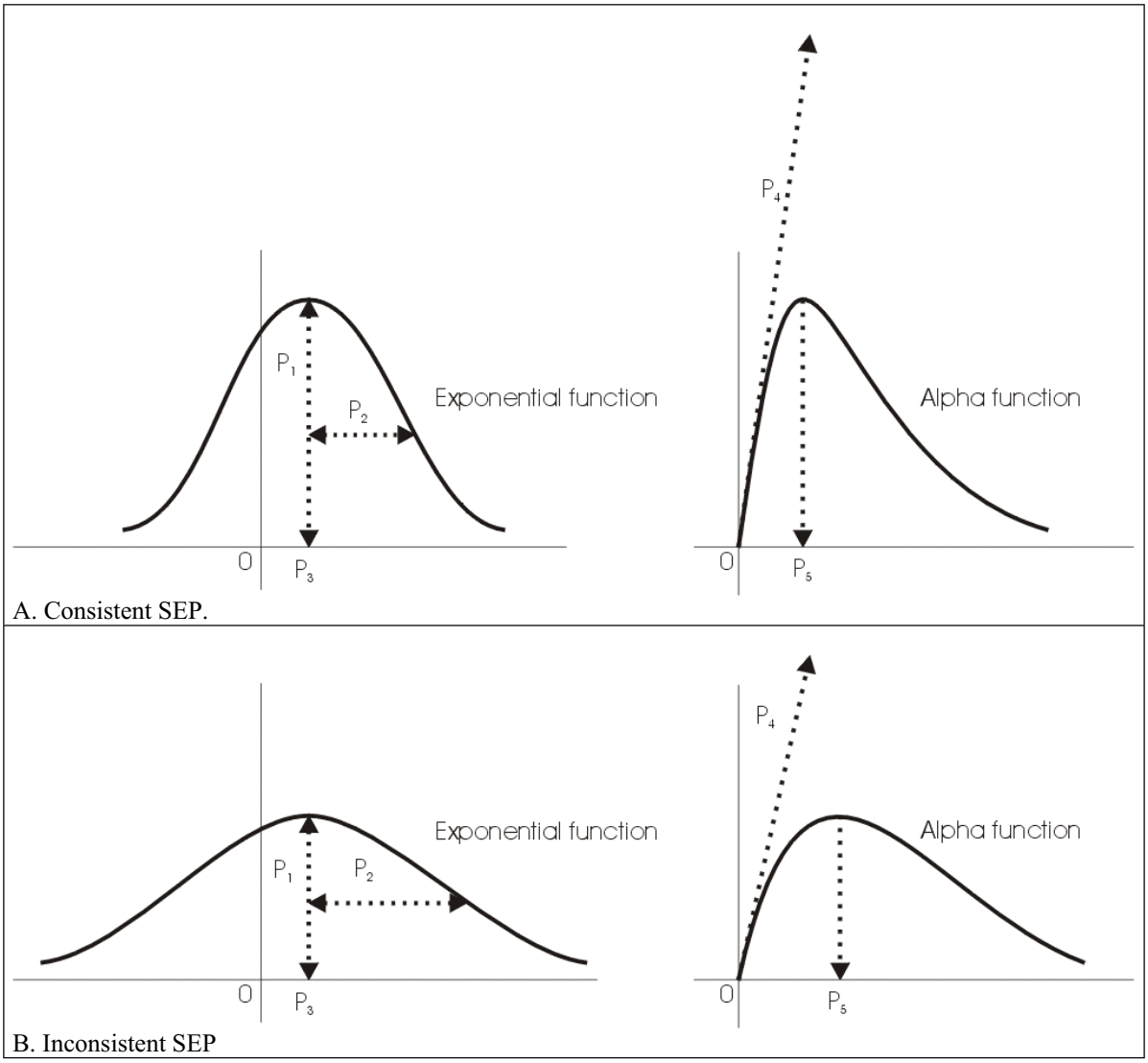


Figure 2.3. Parameters and their relationship with consistency. P1: Height of the exponential function. P2: Standard deviation of the exponential function. P3: Centre of the exponential function. P4: Slope of the alpha function. P5: Peak-location of the alpha function.

3. Results

For most tests mean values of the experimental parameters have been calculated for each hand, except where comparisons with the expert rate are made, as this is a nominal variable. In that case, values were calculated per measurement of about 500 stimulations.

3.1. Classic SEP parameters

For normal subjects the latencies of the N10 and the N13 are analysed to check normal peripheral nerve conduction. Figure 3.1 shows a scatter-plot of the latency of both components. The Kolmogorov-Smirnov test for normal distribution indicates the group of normal subjects has a normal distribution for both the N10 ($p = .718$) and the N13 ($p = .817$).

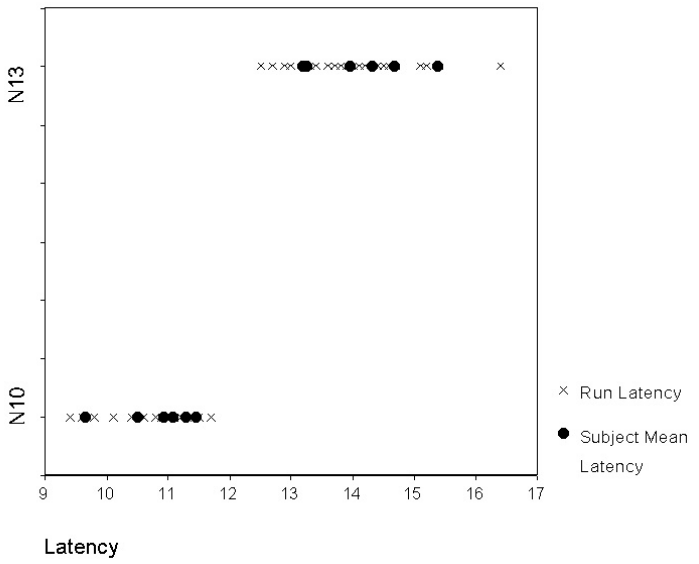
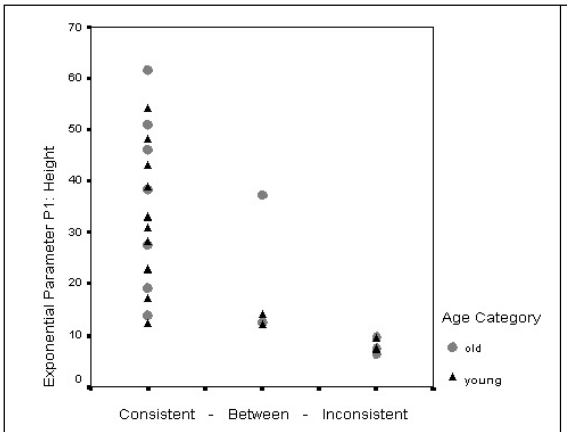
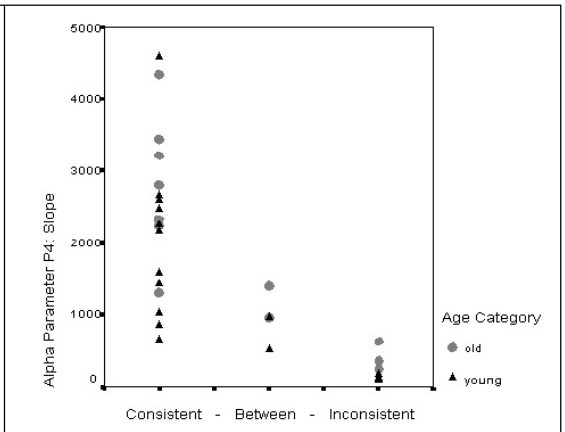


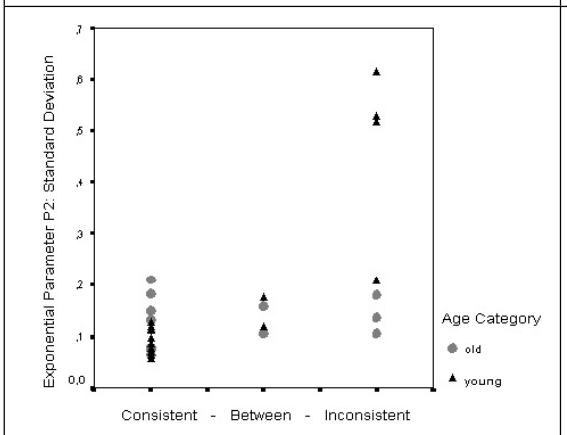
Figure 3.1. Latency of N10 and N13. Both the latencies of individual runs are shown as well as the mean latency for each subject.

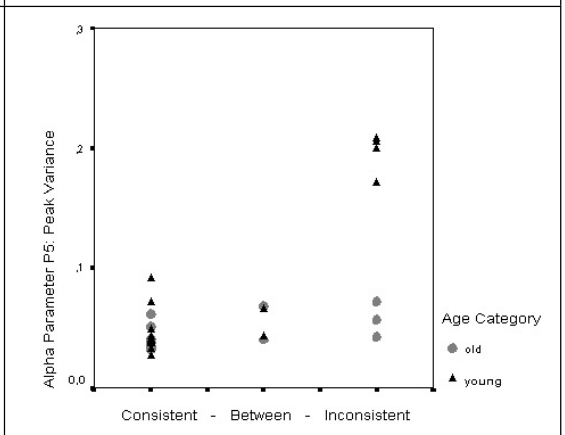
3.2. Experimental parameters

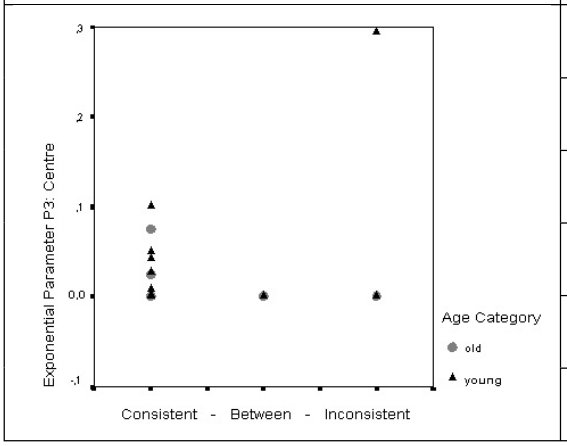
To test the construct validity of each experimental parameter for consistency the parameters are compared with an expert rating. An experienced neurologist sorted 29 butterflyplots from multichannel SEPs into three groups: consistent, in between and inconsistent. Figure 3.2 shows scatterplots for each parameter and group. A Kruskal-Wallis test was performed for each parameter, comparing it to the expert rate. Most parameters show a strong relation with the expert rating, except for the centre of the exponential function ($p = 0.197$). The means of the parameters for central height of the exponential function and for slope of the alpha function differ most significantly between groups ($p = 0.000$). The standard deviation of the exponential function ($p = 0.005$) and the location of the peak of the alpha function ($p = 0.002$) differ significantly between at least two groups as well.











Parameter	Kruskal-Wallis
P1	**,000**
P2	**,005**
P3	,197
P4	**,000**
P5	**,002**

Figure 3.2. Expert rate and experimental parameters. For all parameters, except P3 (Centre of the exponential function) the mean of the parameter differs per group of the expert rating.

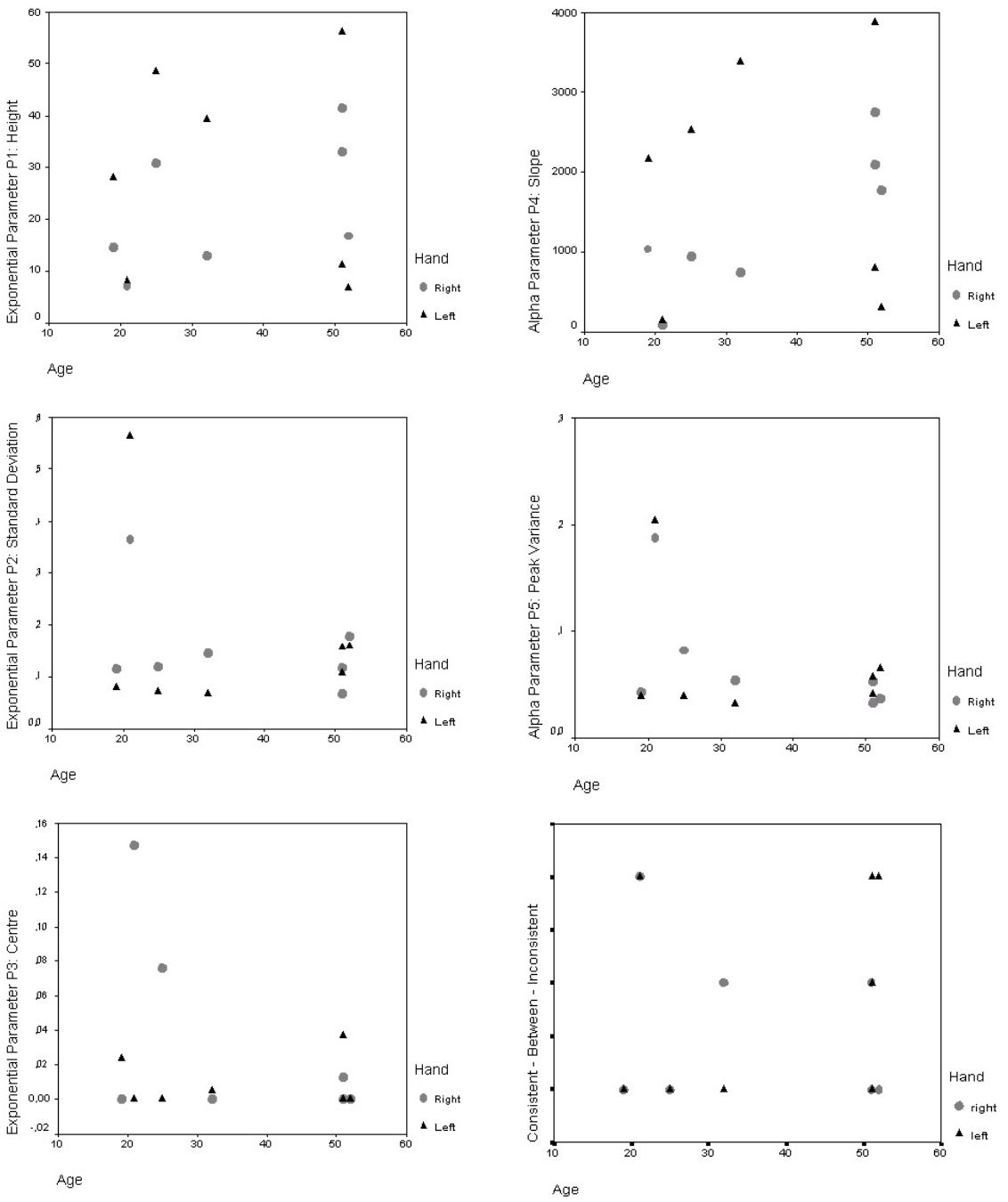


Figure 3.3. Relationship between Age and Consistency. Scatterplots P1 – P5 showing the distribution of scores on each respective parameter compared to age. Shown on the lower right is the relationship between Expert Rate and Age.

3.2.1. Experimental parameters and age

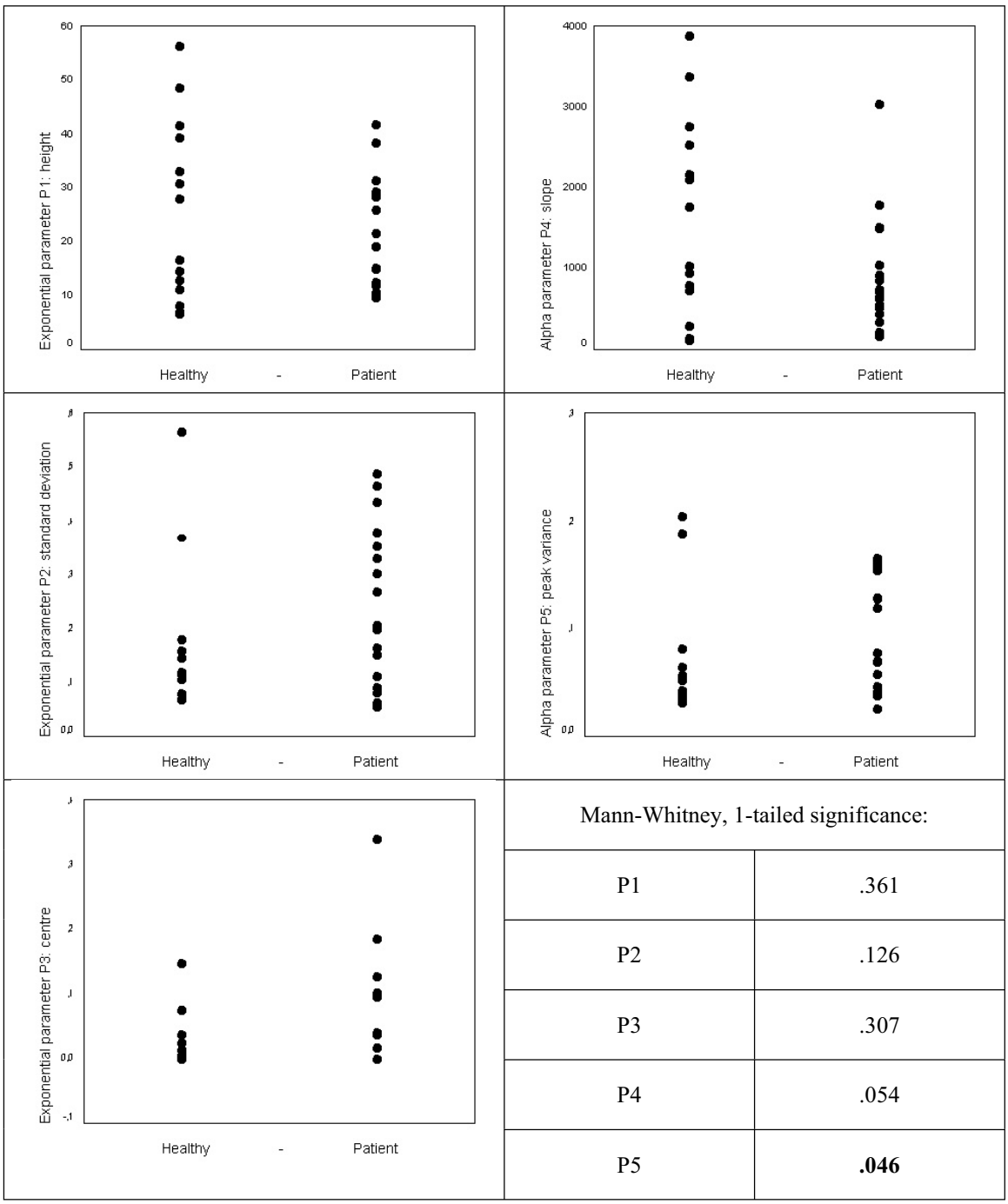
For the normal subjects, the scatterplots of age versus expert-rate and the experimental parameters are shown in figure 3.3. Most of the extreme values are measurements of subject 6 (age 21), for which the cause probably lies in higher than average muscle activity. The scatterplots show age has no effect on the experimental parameters. There is no difference in mean age between the three groups of the expert rating (Kruskal-Wallis, $p = .588$).

3.2.2. Experimental Parameters and Diagnosis

Figure 3.5 shows a comparison of patients probably suffering from CBGD and patients suffering from two other parkinsonian syndromes with healthy subjects. Levels of significance indicate only parameter 5 is able to make a distinction between the two groups. Parameter 4 is almost significantly different between controls and patients, but notice that unaffected hemispheres are also included in the patient measurements.

Figure 3.6 shows a comparison of patients diagnosed with CBGD with the group of patients with other parkinsonian patients as well as hemispheric differences. A Mann-Whitney test was performed and indicated that parameter 4, slope and parameter 5, peak variance are able to make a distinction between CBGD and other parkinsonian syndromes ($p = .001$ and $p = .028$, respectively).

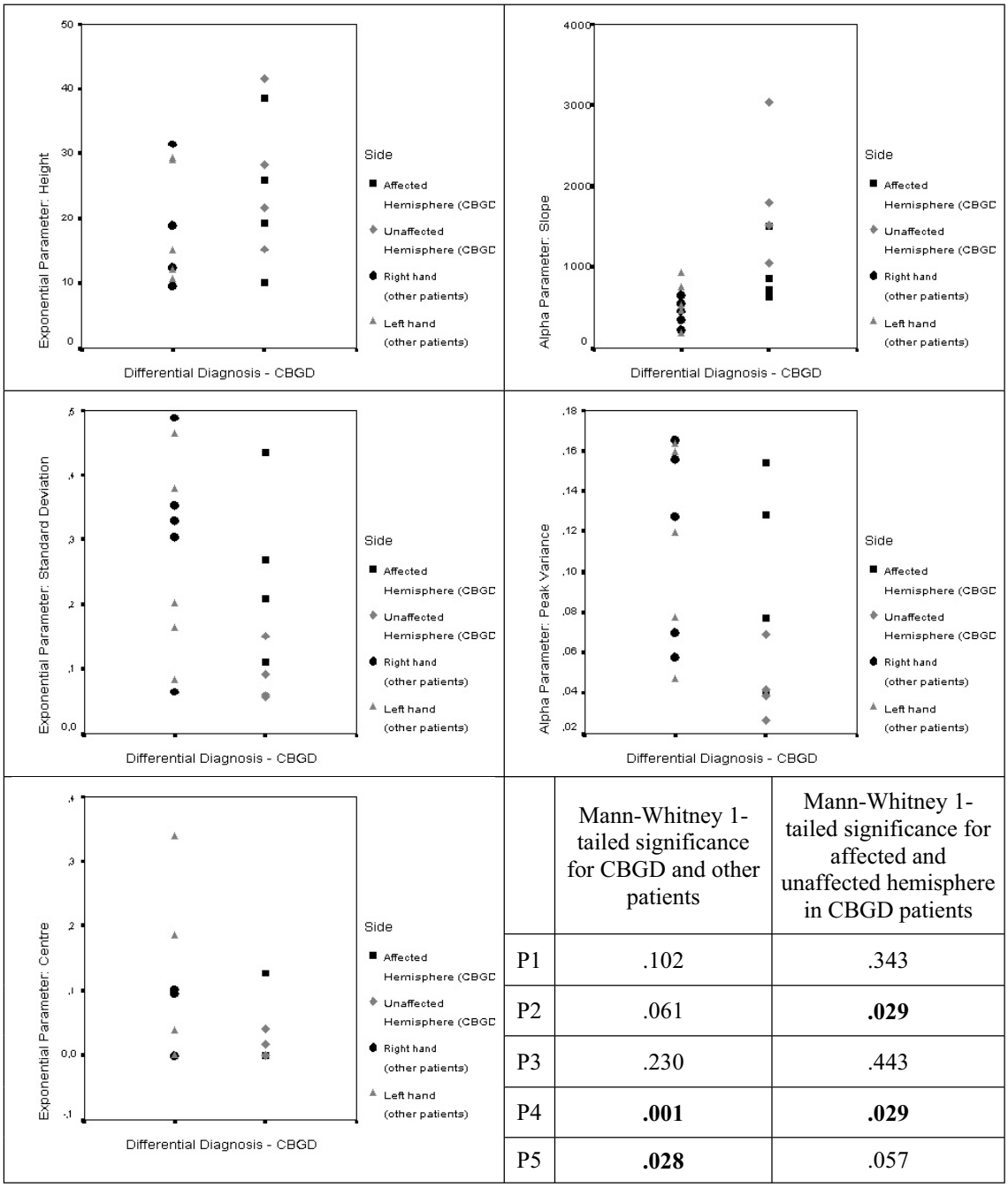
The comparison of affected and unaffected hemispheres on the mean values of the experimental parameters with a Mann-Whitney test shows that parameter 2, standard deviation and parameter 4, slope are able to differentiate between affected and unaffected hemispheres ($p = .029$ and $p = .029$, respectively). Note that the parameters for the affected hemispheres of CBGD patients are comparable to those for the other patients and all indicate a large degree of inconsistency.



Mann-Whitney, 1-tailed significance:

P1	.361
P2	.126
P3	.307
P4	.054
P5	**.046**

Figure 3.5. Healthy Subjects and Patients. The differences between the patient group and the healthy control subjects are shown for all five experimental parameters. The results of a Mann-Whitney test for 2 independent samples is shown in the lower right.



	Mann-Whitney 1-tailed significance for CBGD and other patients	Mann-Whitney 1-tailed significance for affected and unaffected hemisphere in CBGD patients
P1	.102	.343
P2	.061	**.029**
P3	.230	.443
P4	**.001**	**.029**
P5	**.028**	.057

Figure 3.6. Experimental Parameters and Differential Diagnosis. Comparison between patient groups and between affected and unaffected hemisphere in CBGD patients.

4. Discussion

4.1 Construct Validity

When comparing the experimental parameters to the expert rating, four of the five parameters seem to agree with the expert rating. These four parameters are likely to give a good summary of consistency of a SEP. This may still be improved by interpolating the raw data so as to enable the use of more bins in the histogram. Another possible flaw of the current technique is that it also uses the data before and during stimulus. The sample points before stimulus should provide no information and may only add noise to the complete set of data. The sample points during stimulus often show an increased amplitude and since we do not want to measure the stimulus but instead the reaction to the stimulus removing these sample points from the data may also further improve results.

4.2 Hypotheses

1. Consistency can distinguish between age categories.
2. Consistency can distinguish between normal subjects, CBGD patients and patients with other parkinsonian syndromes.
3. Consistency can distinguish between affected and unaffected hemispheres in CBGD patients.

The first hypothesis is proven false. Consistency can not distinguish between age categories as can be seen in figure 3.3.

The second hypothesis is partly true. One parameter appears to be able to distinguish between patients and healthy subjects: Parameter 5, the location of the peak of the fitted alpha function. Parameter 4, the slope of the alpha function, seems to be able to make this distinction too, but not as well as Parameter 5, probably because unaffected hemispheres of CBGD patients are included in the patient measurements. Parameter 4 and 5 are also able to distinguish between CBGD patients and other patients. Unfortunately the parameter values of the affected hemispheres of CBGD patients are comparable to those of other patients.

Probably, consistency is not primarily a measure of differentiated processing, but more of superfluous afferent somatosensory input caused by muscle tension in the afflicted hands.

Hypothesis 3 is also true: Parameter 2, standard deviation of the fitted exponential function and parameter 4, slope of the alpha function can distinguish between affected and unaffected hemisphere within CBGD patients. However, since the parameter values of affected hemispheres are comparable to the values of other patients this distinction has no clinical value. A usefull value might be the absolute difference between hemispheres. CBGD patients will probably have a larger difference between hemispheres than other patients.

4.3 Exponential Function versus Alpha Function

While the data presented here favours the slope of the alpha function there is no conclusive reason to dispose of the exponential function as yet. The parameters of the alpha function may be more informative but the parameters of the exponential function are easier understood. The main difference between the two functions is that the alpha function approaches zero as variance approaches zero, whereas the exponential function usually does not (see figure 2.3). To make a choice between the two it could be investigated what their behavior is when variance approaches zero. This can be done by greatly increasing the amount of bins. This in turn needs more sample points which may be achieved by interpolating the data.

4.4 Clinical Value

The clinical value of this tool is questionable, because it can not make a distinction between the affected hemispheres of CBGD patients and those of other patients. However, there is a large difference on parameter 4 between affected and unaffected hemispheres of CBGD patients. In other patients there is almost no difference on parameter 4 between hemispheres. Parameter 4 is able to distinguish affected from unaffected hemispheres quite well. Sensitivity – specificity charts are given in figure 4.1. If one has no preference for sensitivity or specificity a cut-off value of 1280 could be chosen to distinguish affected from unaffected hemispheres in CBGD patients (sensitivity = 0.75, specificity = 0.75). We tried to use the absolute difference between hemispheres on parameter 4 to separate CBGD patients from

patients with other parkinsonian syndromes. Without preference for either sensitivity or specifity, a usefull cut-off value is 250 (sensitivity = 0.75, specificity = 0.8).

The value of the fitted alpha-function's slope as a consistency measure may still be improved by only analysing the time-window around the components that are most affected in patients suffering from CBGD, for example by dropping all data before 18 ms and after 40 ms.

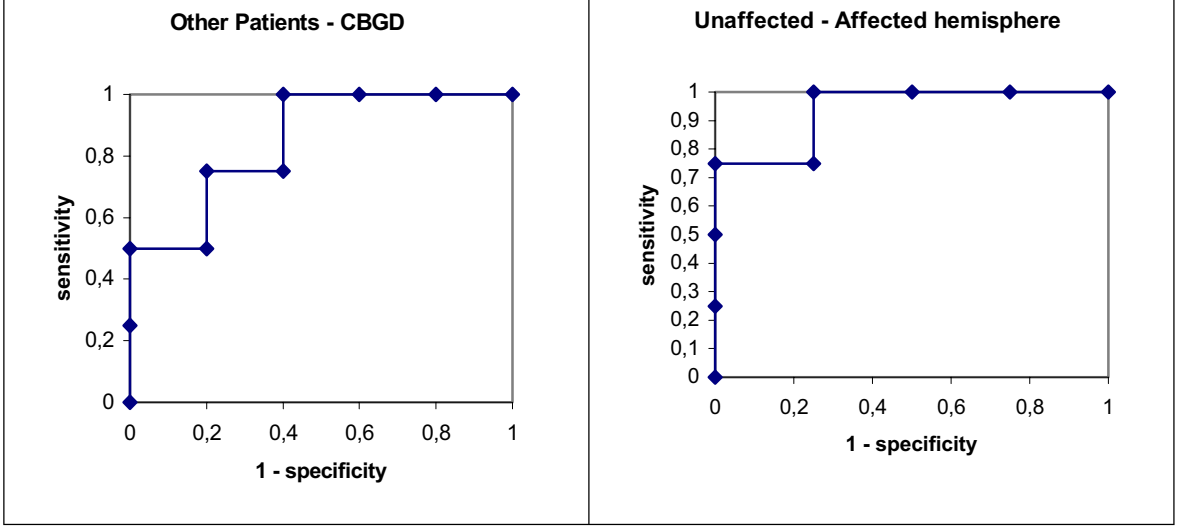


Figure 4.1. Sensitivity – specificity for parameter 4: slope as a diagnostic tool. These ROC-curves are based on the data for the alpha parameter slope as represented in figure 3.6 (upper-right). For the distinction between other patients and CBGD patients the absolute difference of the value of parameter 4 between hemispheres is used.

5. References

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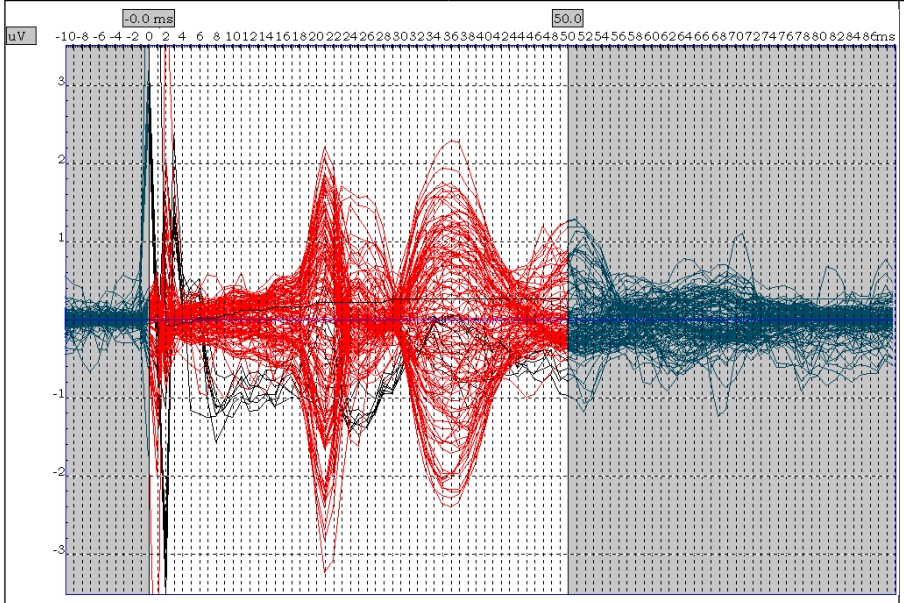
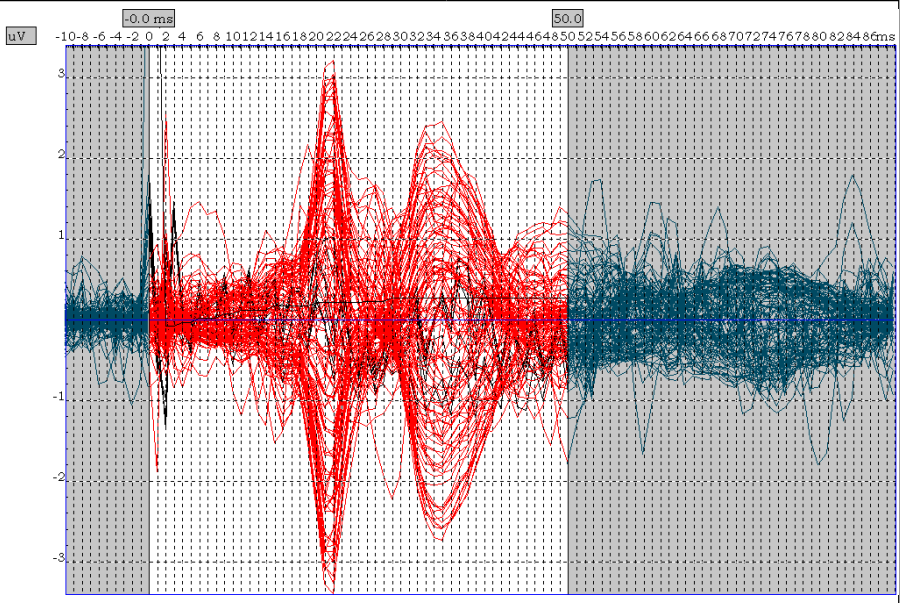
Appendix A: subject data

Only the first measurements of each hand of every subject is given here. Contact the authors for a complete set of data. The charts and numbers shown here are intended to give an idea of the relationship between the butterflyplots and the experimental parameters investigated.

Subject 1



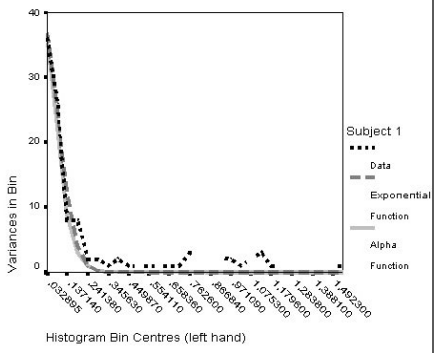


Left hand	Right hand

Subject: 1
Group: Normal Controls
Age: 25

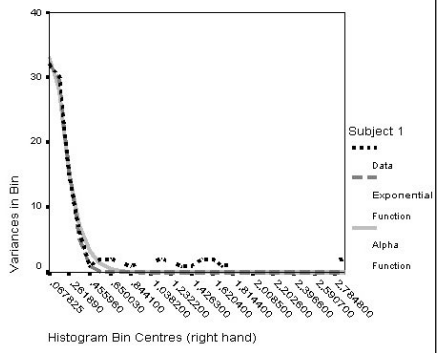
Exponential parameters
P1 (height): 53,9
P2 (SD): ,0676
P3 (centre): ,0000

Alpha parameters
P4 (slope): 2475
P5 (peak variance): ,0402

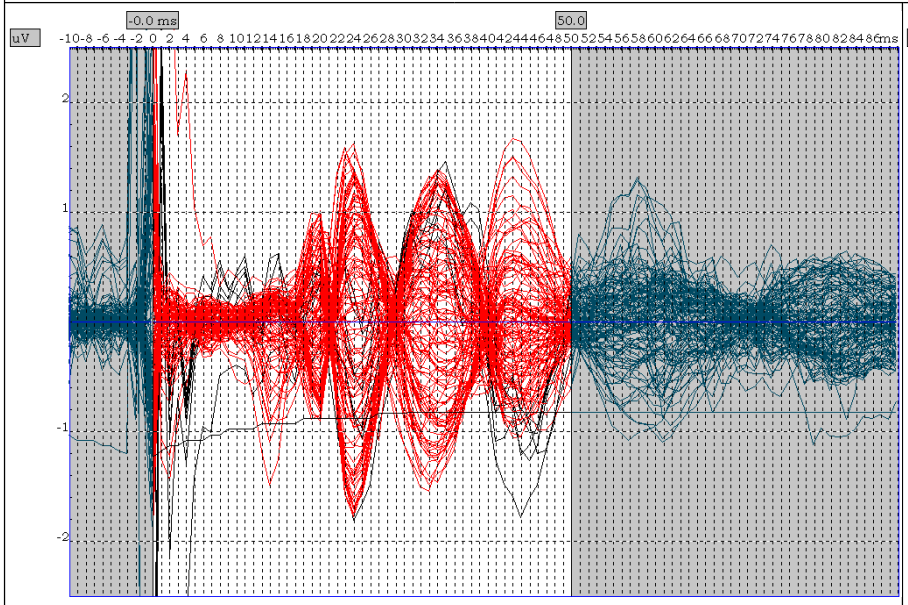


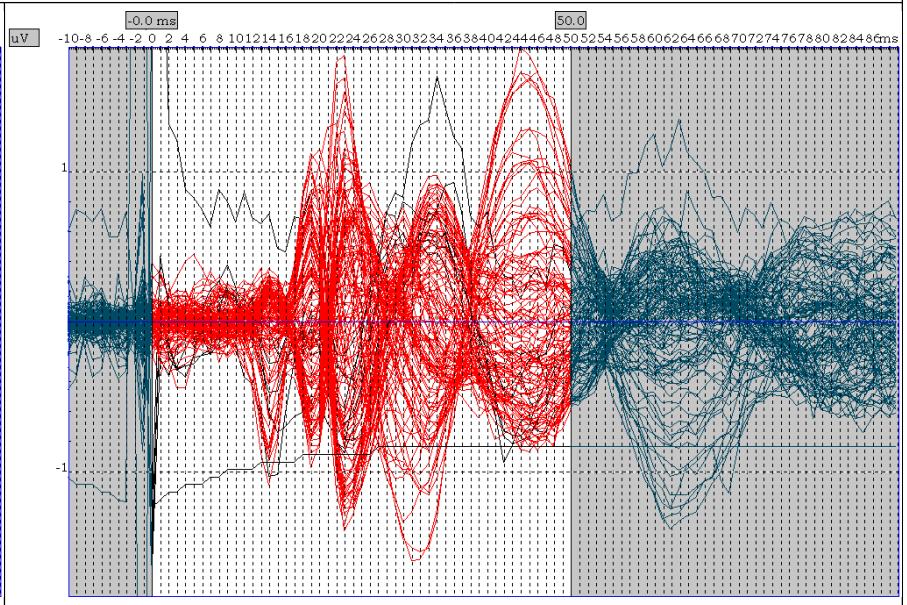
Exponential parameters
P1 (height): 38,7
P2 (SD): ,1116
P3 (centre): ,1014

Alpha parameters
P4 (slope): 1025
P5 (peak variance): ,0915



Subject 2



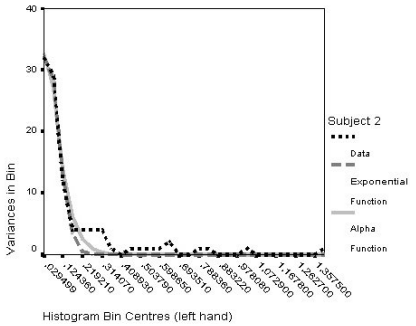


Left hand	Right hand

Subject: 2
Group: Normal Controls
Age: 19

Exponential parameters
P1 (height): 33,1
P2 (SD): ,0603
P3 (centre): ,0430

Alpha parameters
P4 (slope): 2259
P5 (peak variance): ,0413



Exponential parameters
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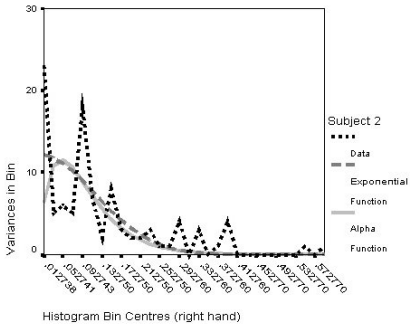
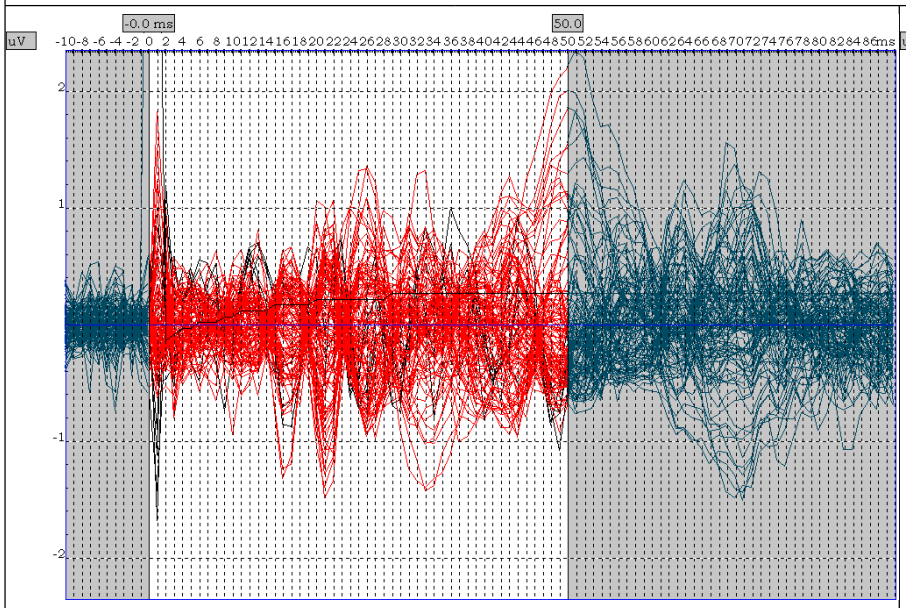
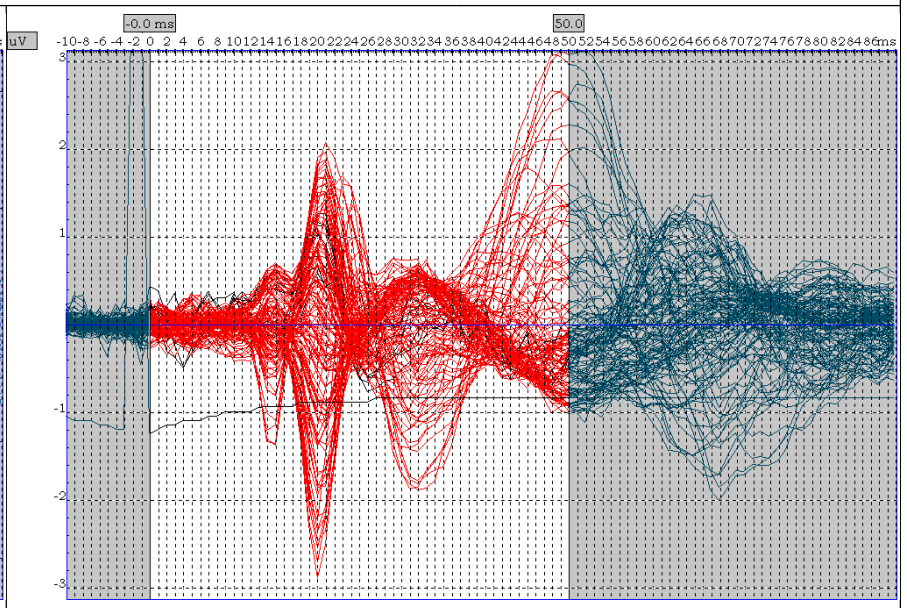
P2 (SD): ,1175
P3 (centre): ,0000

Alpha parameters
P4 (slope): 647
P5 (peak variance): ,0486



Subject 3





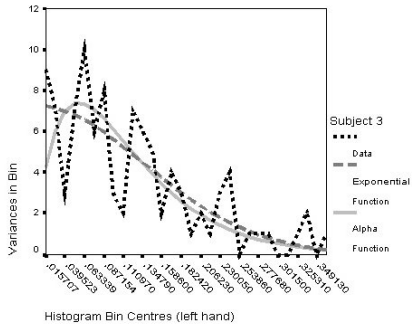
Left hand

Right hand

Subject: 3
Group: Normal Controls
Age: 52

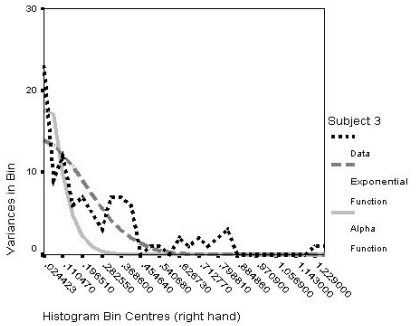
Exponential parameters
P1 (height): 7,3
P2 (SD): ,1373
P3 (centre): ,0000

Alpha parameters
P4 (slope): 356
P5 (peak variance): ,0565

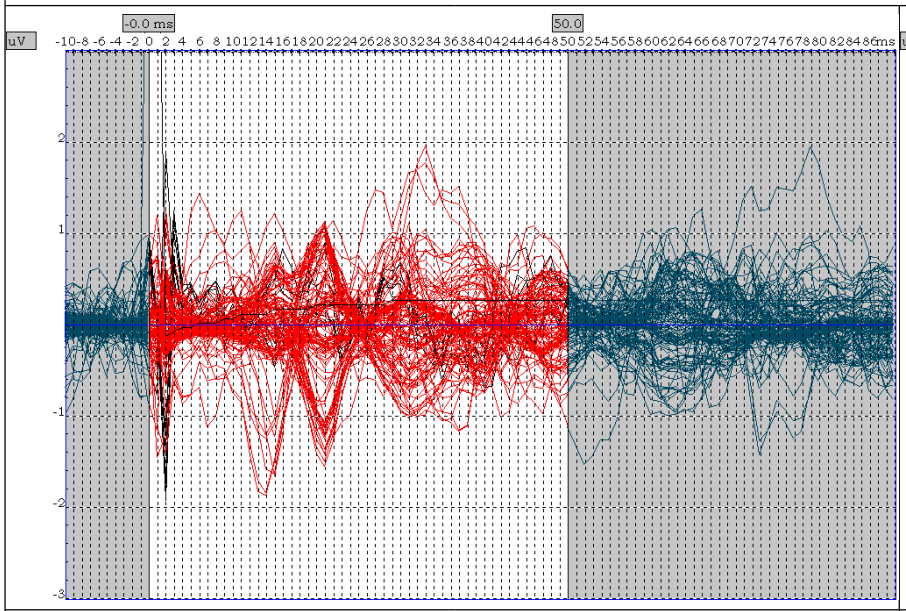


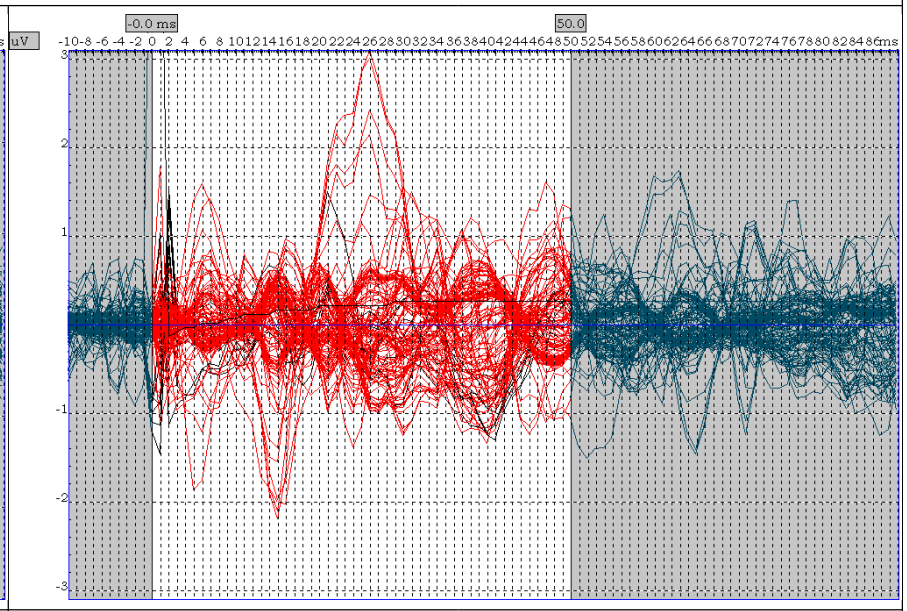
Exponential parameters
P1 (height): 14,0
P2 (SD): ,2091
P3 (centre): ,0000

Alpha parameters
P4 (slope): 1306
P5 (peak variance): ,0411



Subject 4





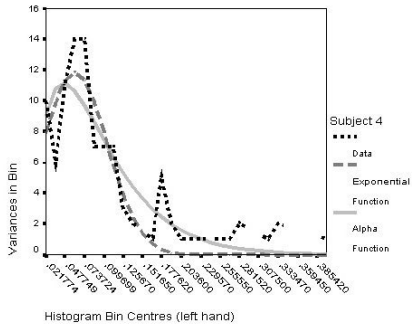
Left hand

Right hand

Subject: 4
Group: Normal Controls
Age: 40

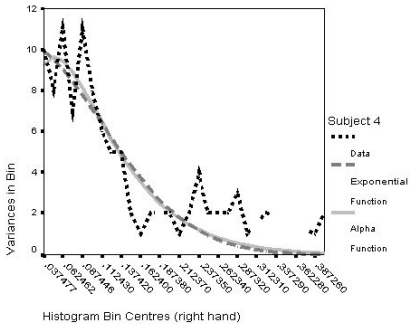
Exponential parameters
P1 (height): 11,3
P2 (SD): ,0614
P3 (centre): ,0705

Alpha parameters
P4 (slope): 663
P5 (peak variance): ,0456

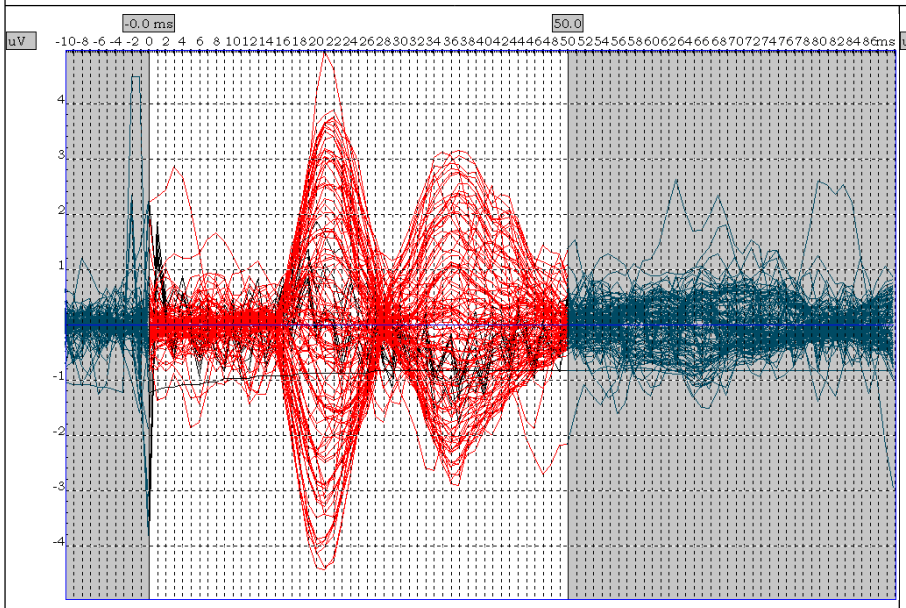


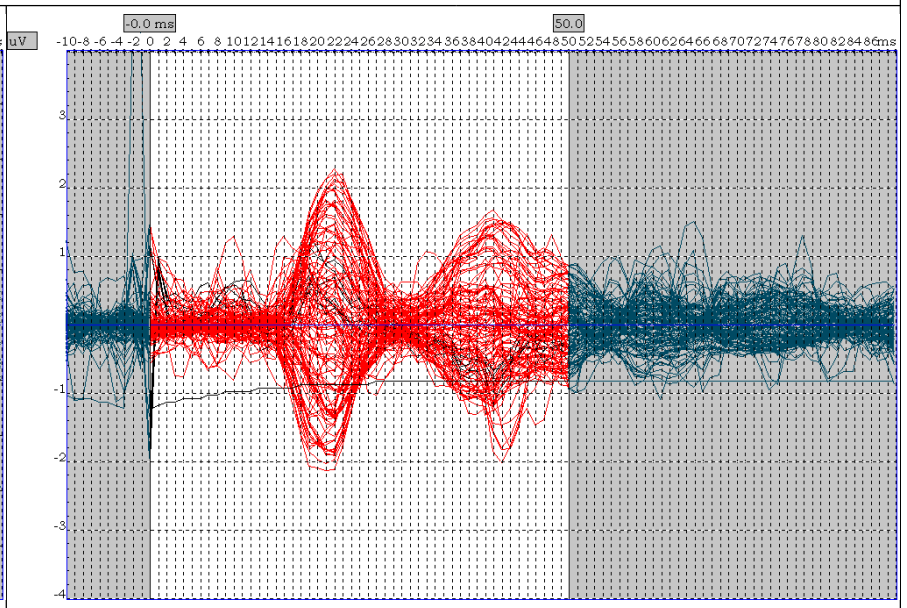
Exponential parameters
P1 (height): 9,2
P2 (SD): ,0767
P3 (centre): ,0771

Alpha parameters
P4 (slope): 511
P5 (peak variance): ,0512



Subject 5





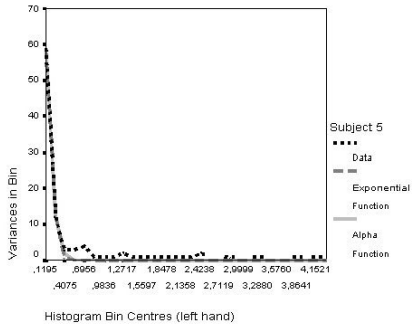
Left hand

Right hand

Subject: 5
Group: Normal Controls
Age: 52

Exponential parameters
P1 (height): 61,6
P2 (SD): ,1820
P3 (centre): ,0000

Alpha parameters
P4 (slope): 3433
P5 (peak variance): ,0615



Exponential parameters
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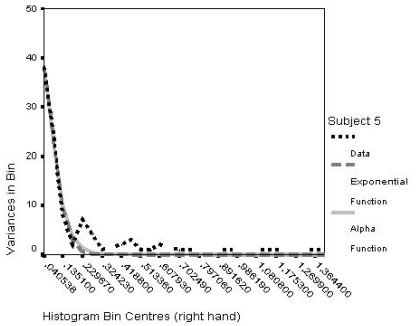
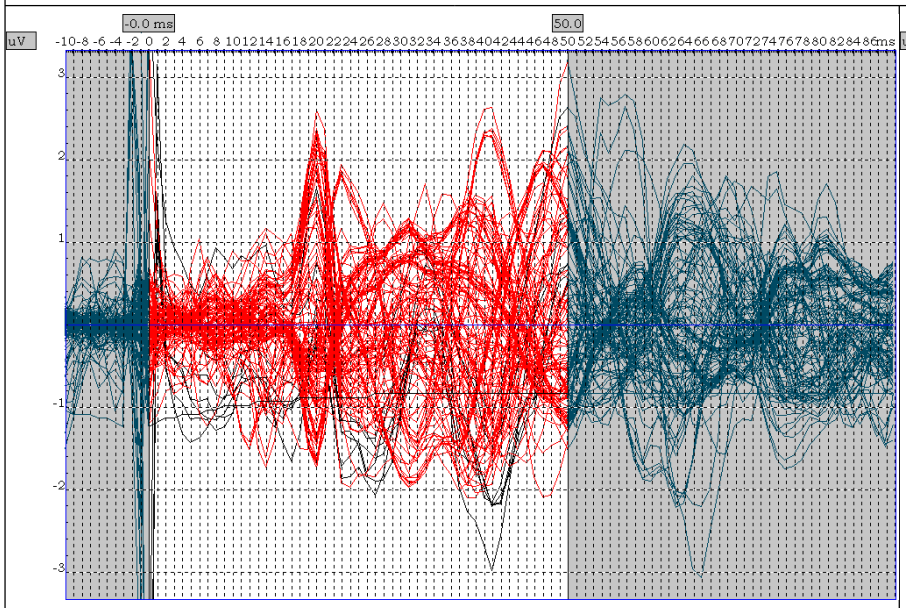
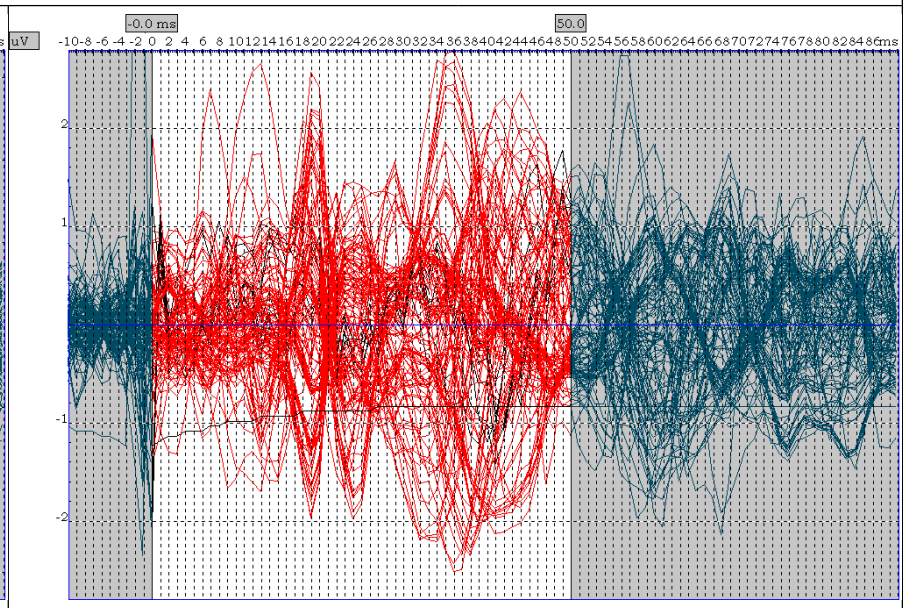
P2 (SD): ,0778
P3 (centre): ,0000

Alpha parameters
P4 (slope): 2795
P5 (peak variance): ,0371



Subject 6



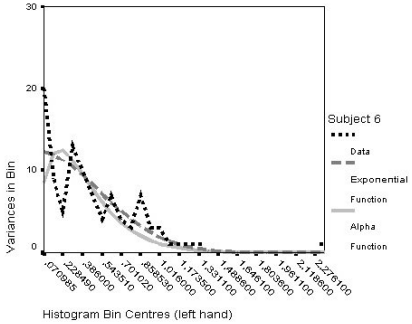


Left hand	Right hand

Subject: 6
Group: Normal Controls
Age: 21

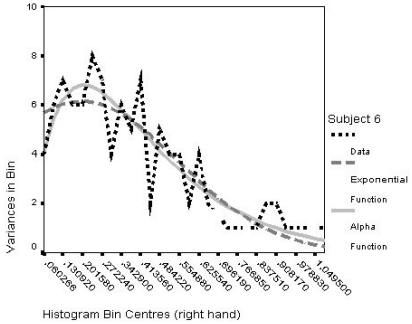
Exponential parameters
P1 (height): 6,9
P2 (SD): ,6135
P3 (centre): ,0000

Alpha parameters
P4 (slope): 171
P5 (peak variance): ,1997

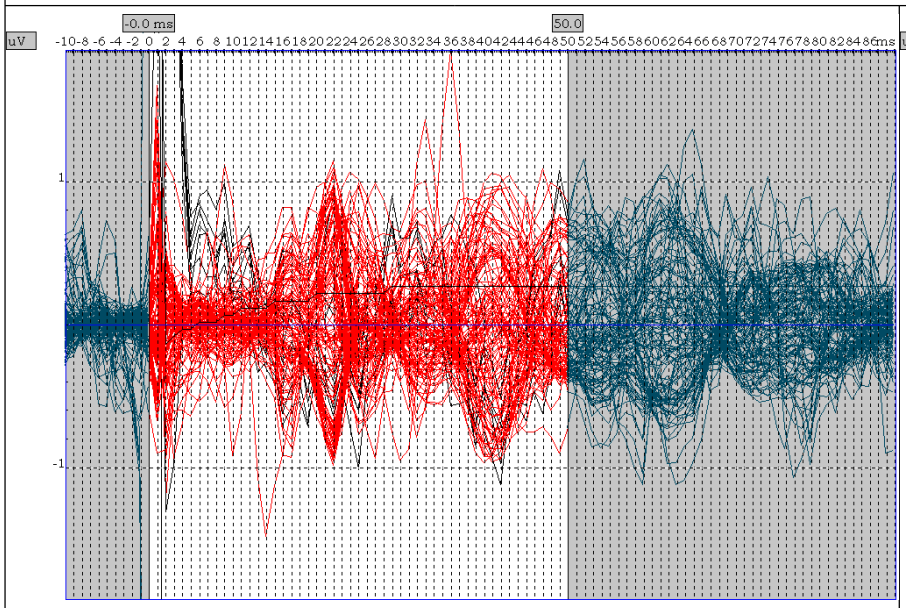


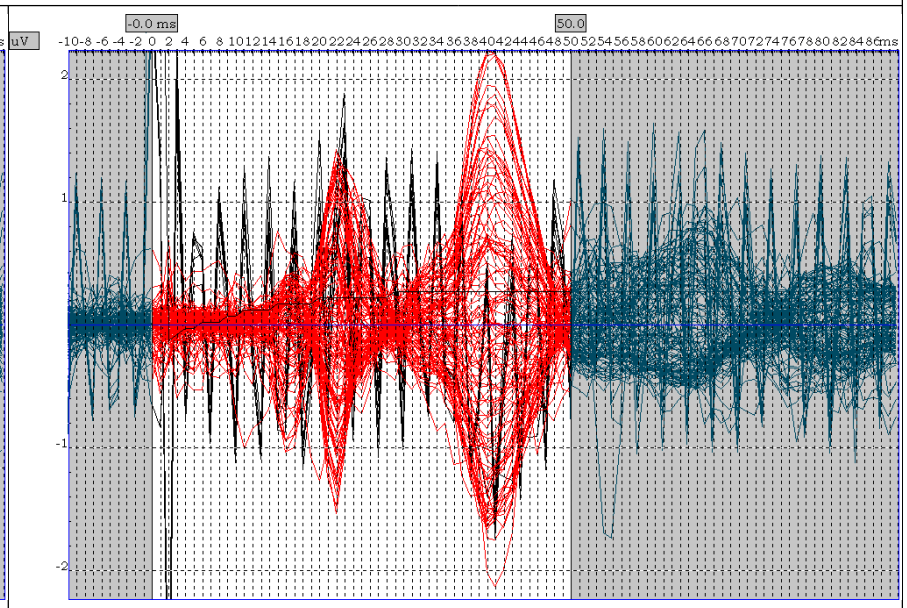
Exponential parameters
P1 (height): 7,2
P2 (SD): ,2061
P3 (centre): ,2948

Alpha parameters
P4 (slope): 90
P5 (peak variance): ,2054



Subject 7





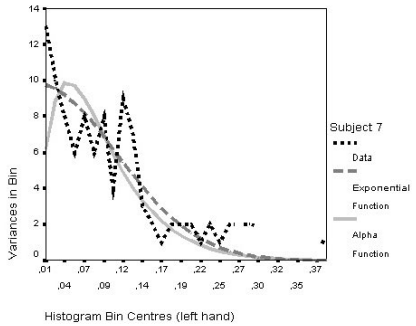
Left hand

Right hand

Subject: 7
Group: Normal Controls
Age: 51

Exponential parameters
P1 (height): 9,8
P2 (SD): ,1074
P3 (centre): ,0000

Alpha parameters
P4 (slope): 621
P5 (peak variance): ,0433



Exponential parameters
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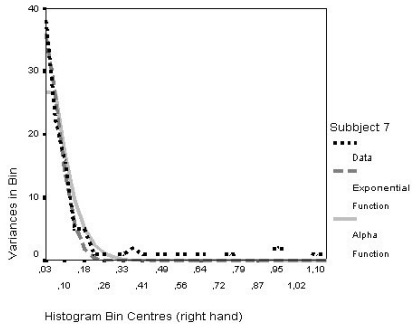
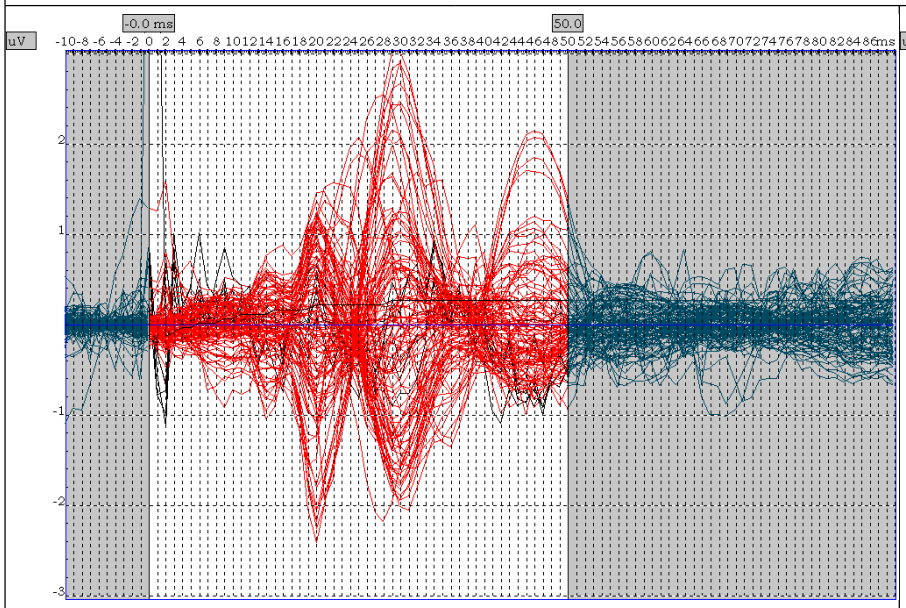
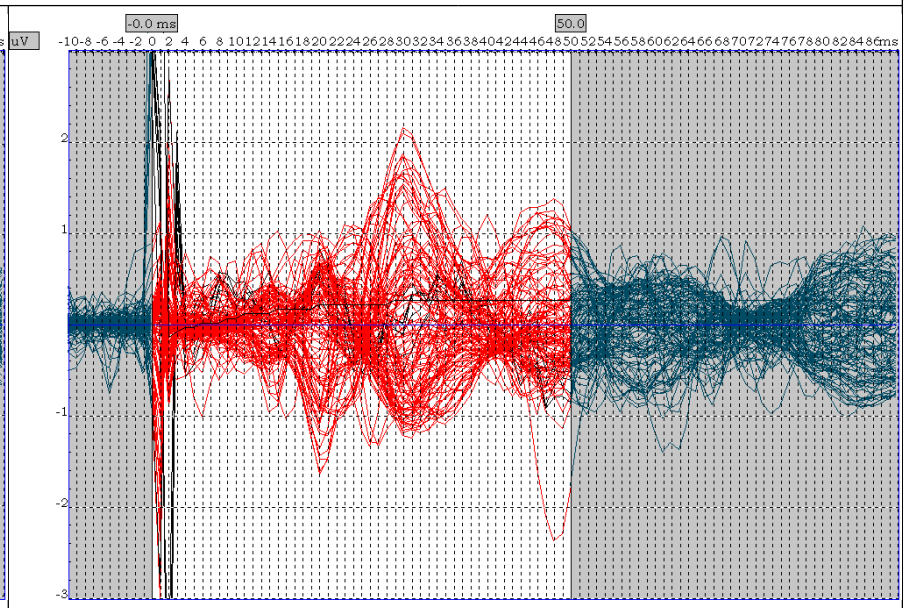
P2 (SD): ,0729
P3 (centre): ,0000

Alpha parameters
P4 (slope): 3198
P5 (peak variance): ,0313



Subject 8





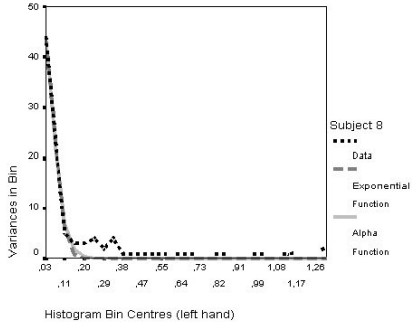
Left hand

Right hand

Subject: 8
Group: Normal Controls
Age: 32

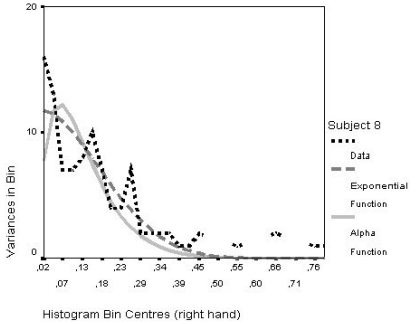
Exponential parameters
P1 (height): 48,1
P2 (SD): ,0546
P3 (centre): ,0024

Alpha parameters
P4 (slope): 4577
P5 (peak variance): ,0261

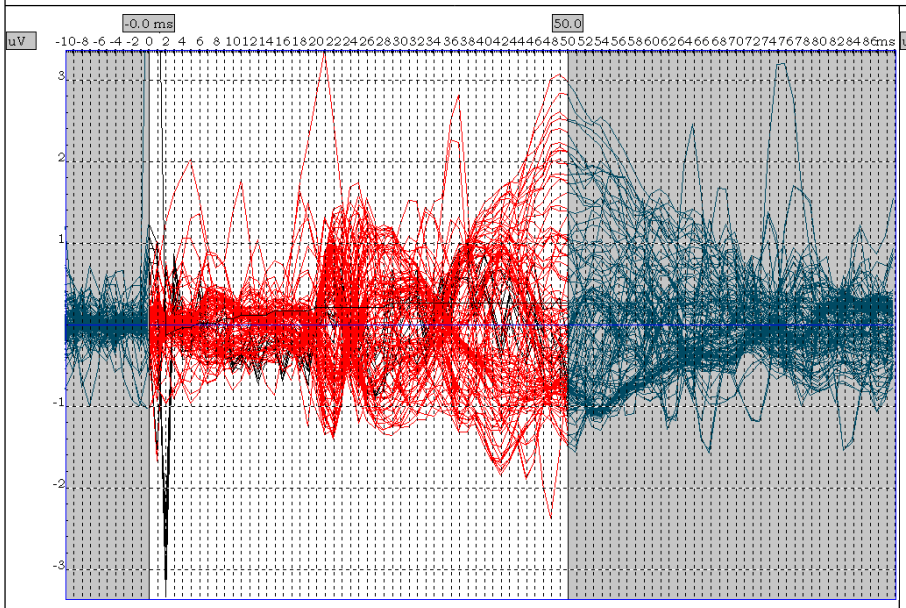


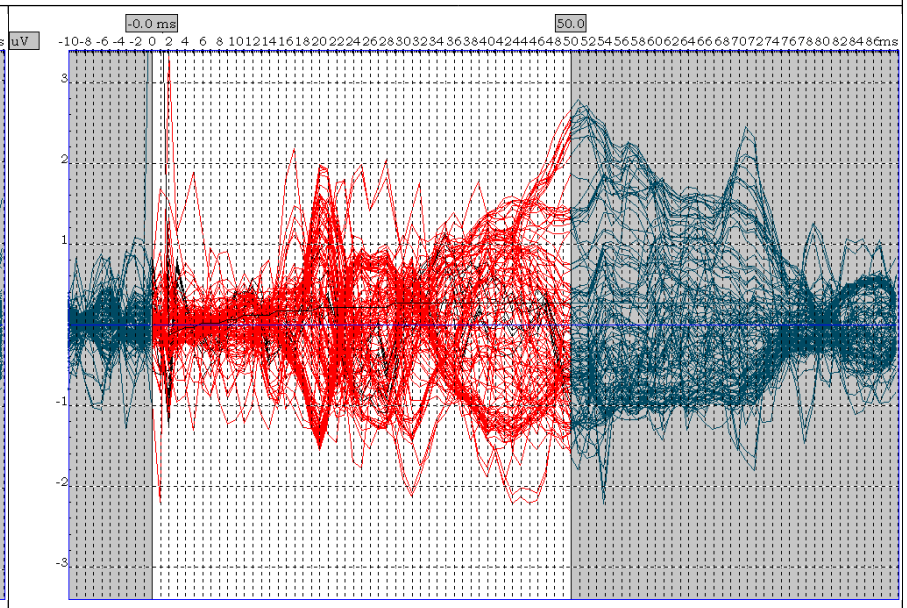
Exponential parameters
P1 (height): 11,8
P2 (SD): ,1734
P3 (centre): ,0000

Alpha parameters
P4 (slope): 514
P5 (peak variance): ,0651



Subject 9





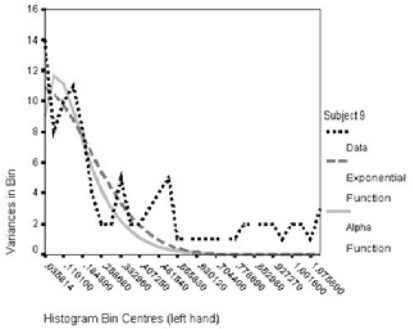
Left hand

Right hand

Subject: 9
Group: Other Patients
Age: 73

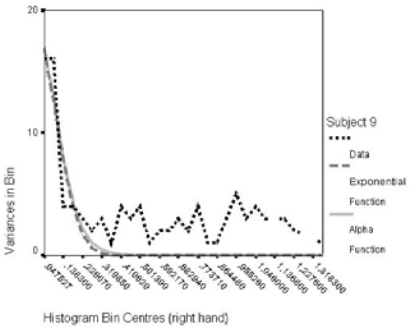
Exponential parameters
P1 (height): 11,1
P2 (SD): ,22
P3 (centre): ,0000

Alpha parameters
P4 (slope): 391
P5 (peak variance): ,0813

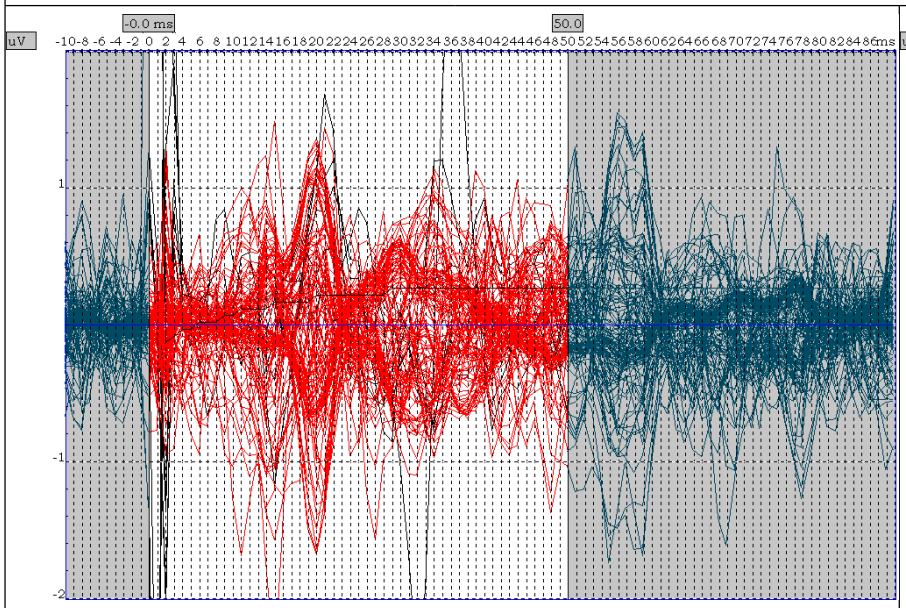


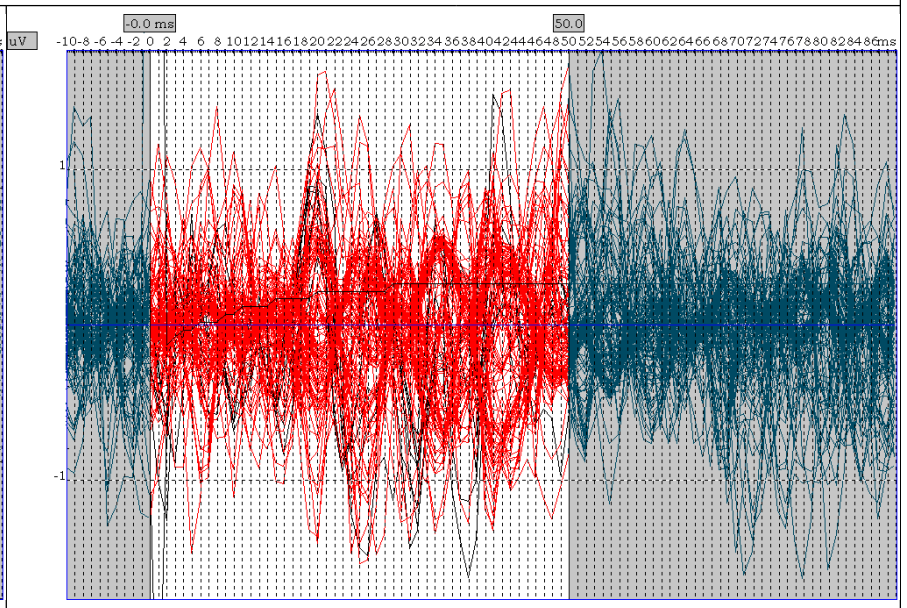
Exponential parameters
P1 (height): 18,8
P2 (SD): ,10
P3 (centre): ,0000

Alpha parameters
P4 (slope): 907
P5 (peak variance): ,0499



Subject 10





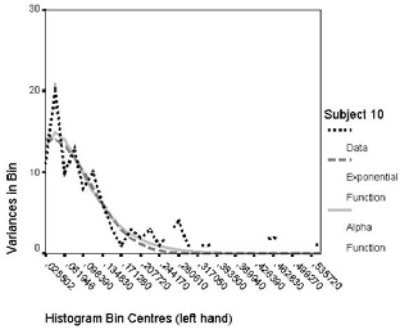
Left hand

Right hand

Subject: 10
Group: Other Patients
Age: 73

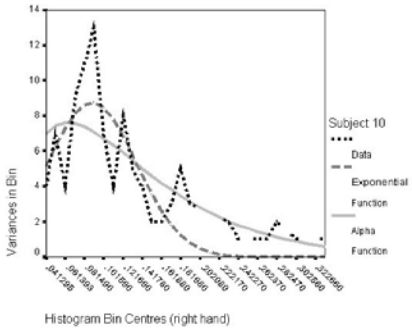
Exponential parameters
P1 (height): 14,1
P2 (SD): ,08
P3 (centre): ,0345

Alpha parameters
P4 (slope): 916
P5 (peak variance): ,0442

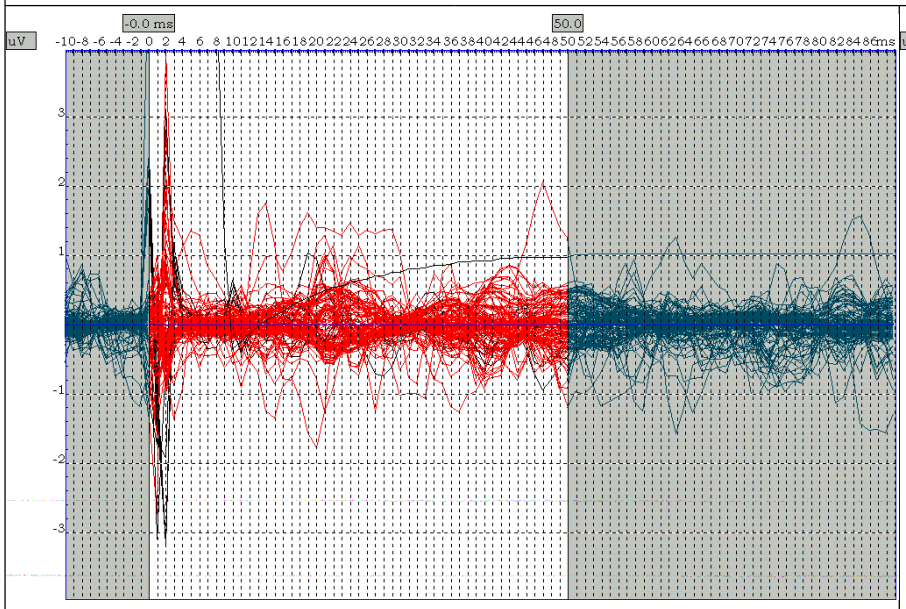


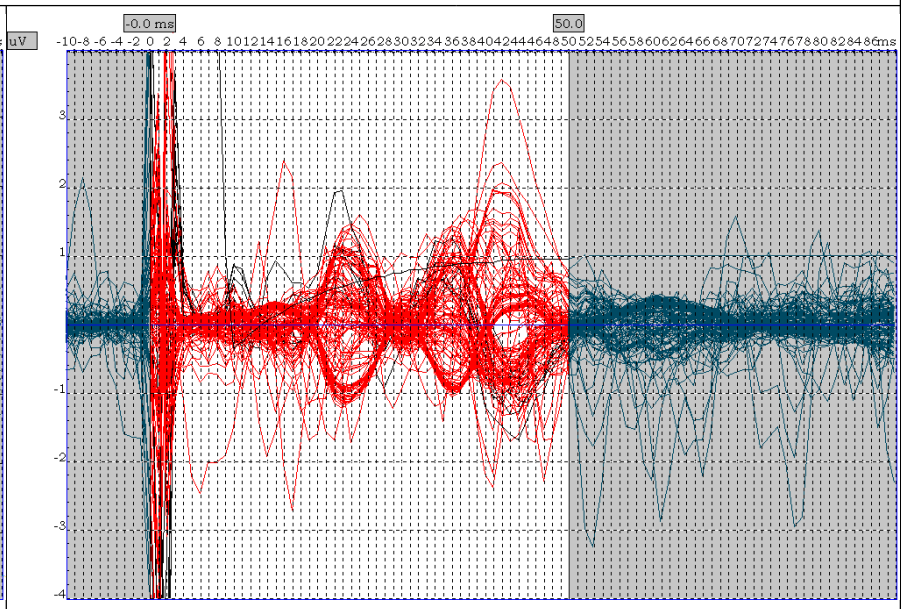
Exponential parameters
P1 (height): 8,7
P2 (SD): ,05
P3 (centre): ,0894

Alpha parameters
P4 (slope): 322
P5 (peak variance): ,0641



Subject 11





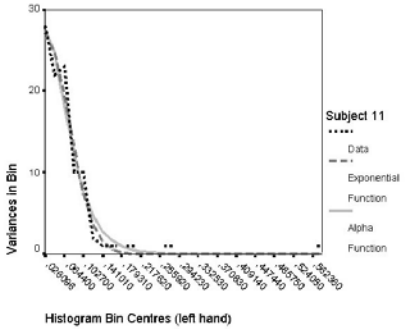
Left hand

Right hand

Subject: 11
Group: Probable CBGD
Age: 68

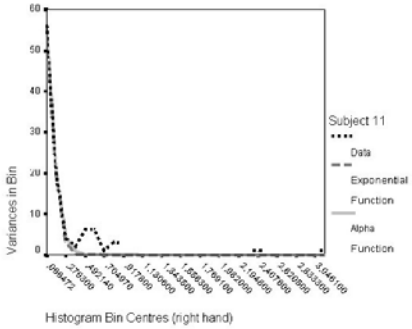
Exponential parameters
P1 (height): 27,2
P2 (SD): ,05
P3 (centre): ,0239

Alpha parameters
P4 (slope): 2619
P5 (peak variance): ,0289

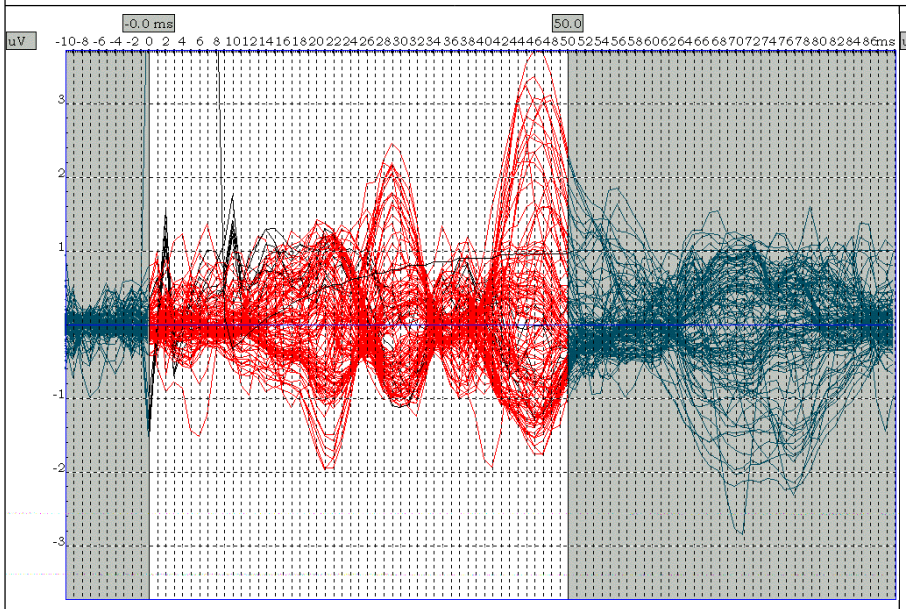


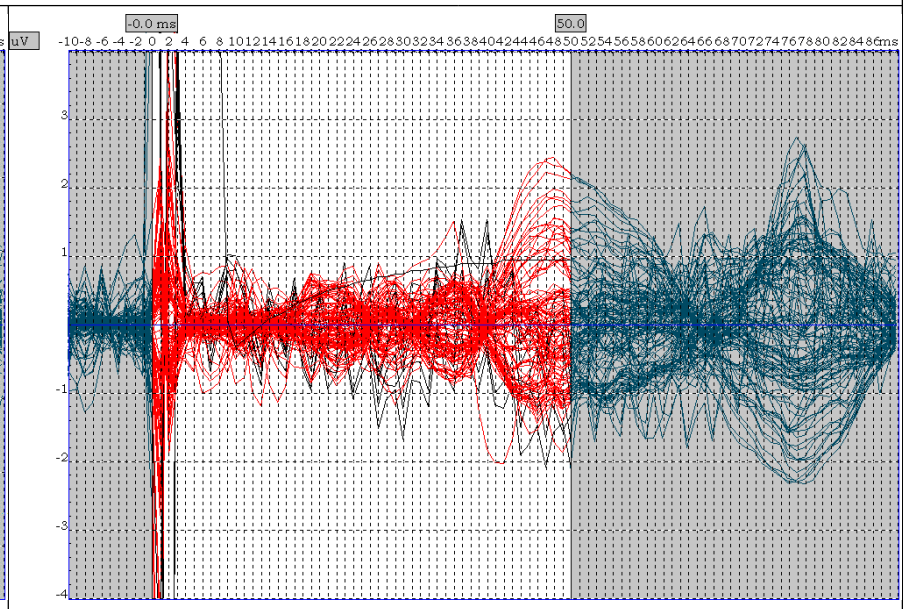
Exponential parameters
P1 (height): 66,5
P2 (SD): ,11
P3 (centre): ,0000

Alpha parameters
P4 (slope): 2895
P5 (peak variance): ,0538



Subject 12



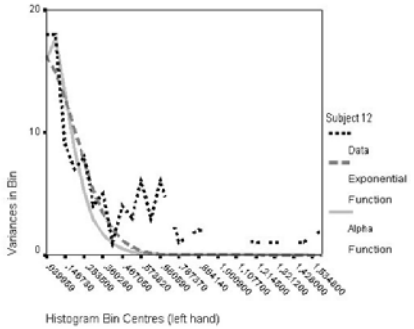


Left hand	Right hand

Subject: 12
Group: Probable CBGD
Age: 59

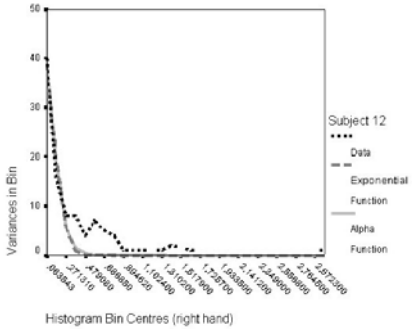
Exponential parameters
P1 (height): 16,6
P2 (SD): ,20
P3 (centre): ,0000

Alpha parameters
P4 (slope): 695
P5 (peak variance): ,0716

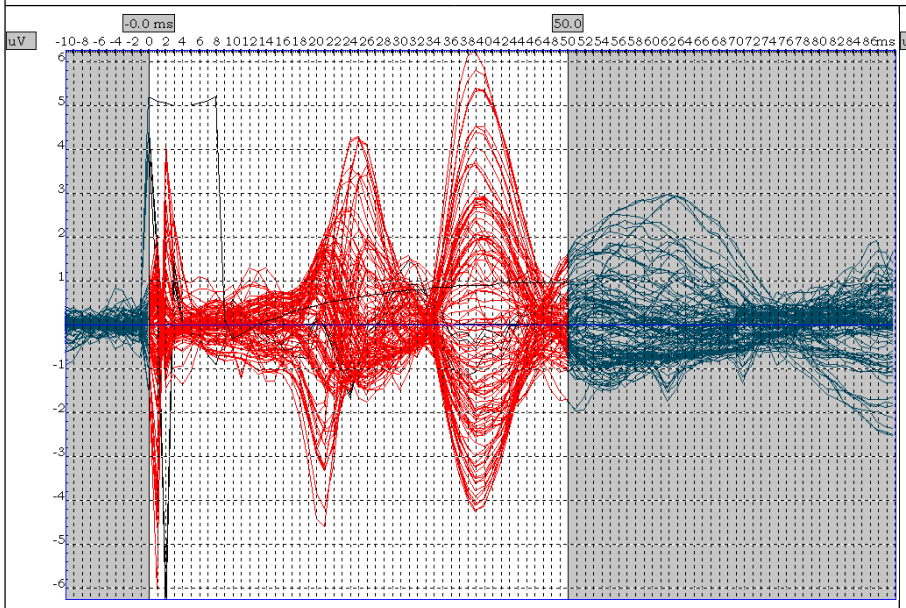


Exponential parameters
P1 (height): 43,0
P2 (SD): ,13
P3 (centre): ,0000

Alpha parameters
P4 (slope): 1707
P5 (peak variance): ,0621



Subject 13



Left hand

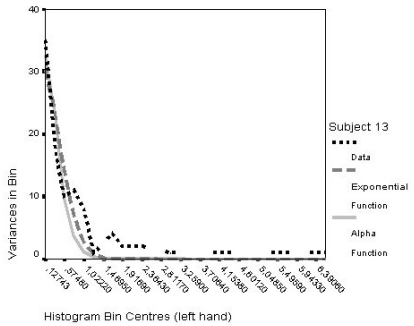
Subject:	13
Group:	Other Patients
Age:	64

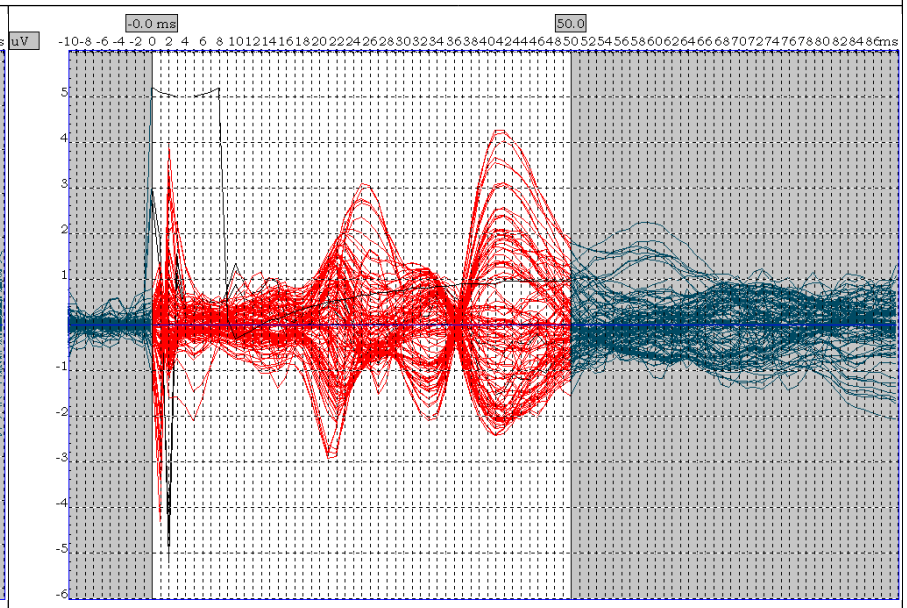
Exponential parameters

P1 (height):	31,4
P2 (SD):	,46
P3 (centre):	,0000

Alpha parameters

P4 (slope):	553
P5 (peak variance):	,1649





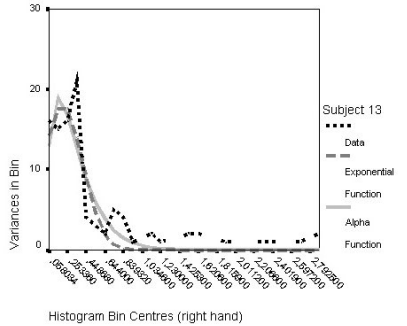
Right hand

Exponential parameters

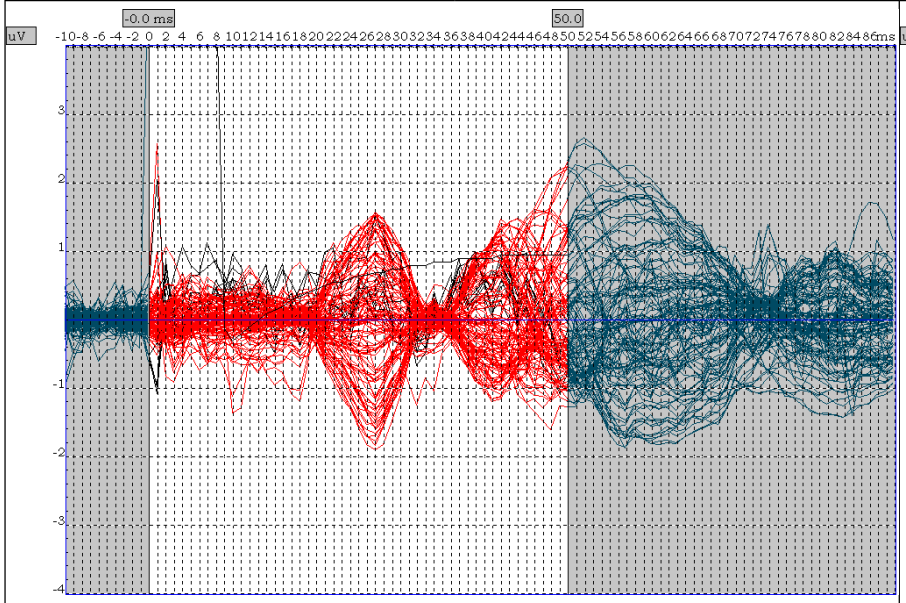
P1 (height):	18,1
P2 (SD):	,21
P3 (centre):	,2022

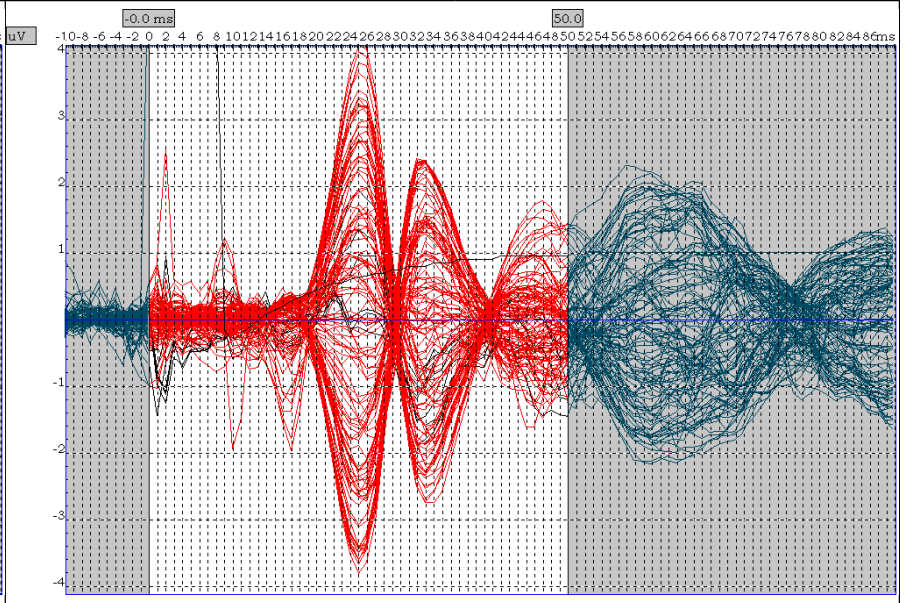
Alpha parameters

P4 (slope):	320
P5 (peak variance):	,1610



Subject 14





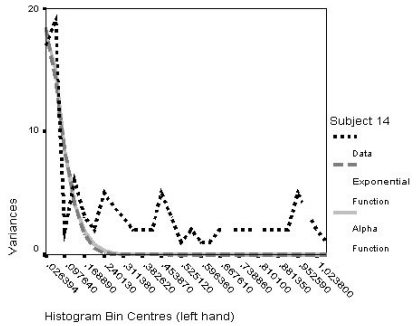
Left hand

Right hand

Subject: 14
Group: Probable CBGD
Age: 73

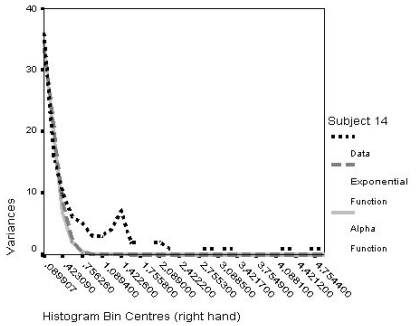
Exponential parameters
P1 (height): 19,6
P2 (SD): ,08
P3 (centre): ,0000

Alpha parameters
P4 (slope): 1454
P5 (peak variance): ,0346

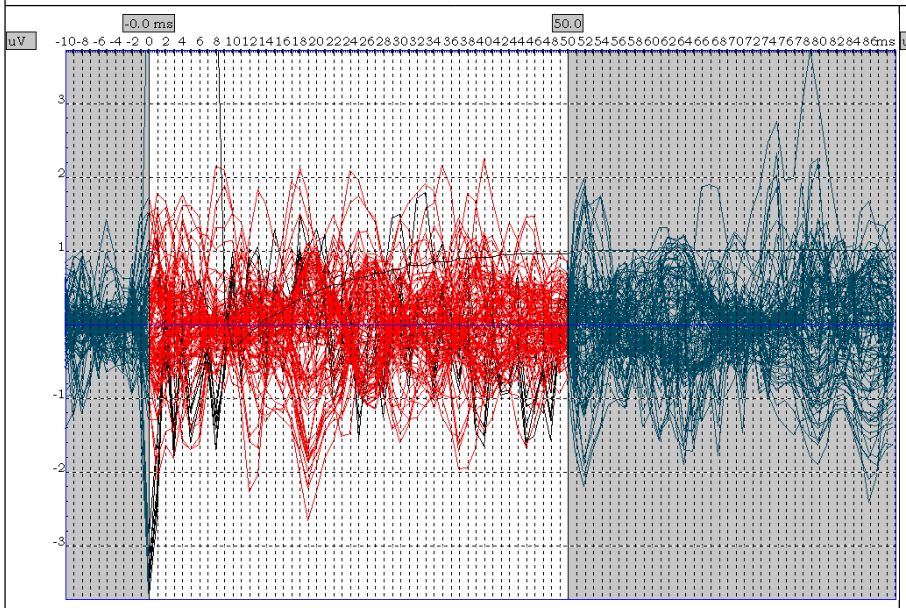


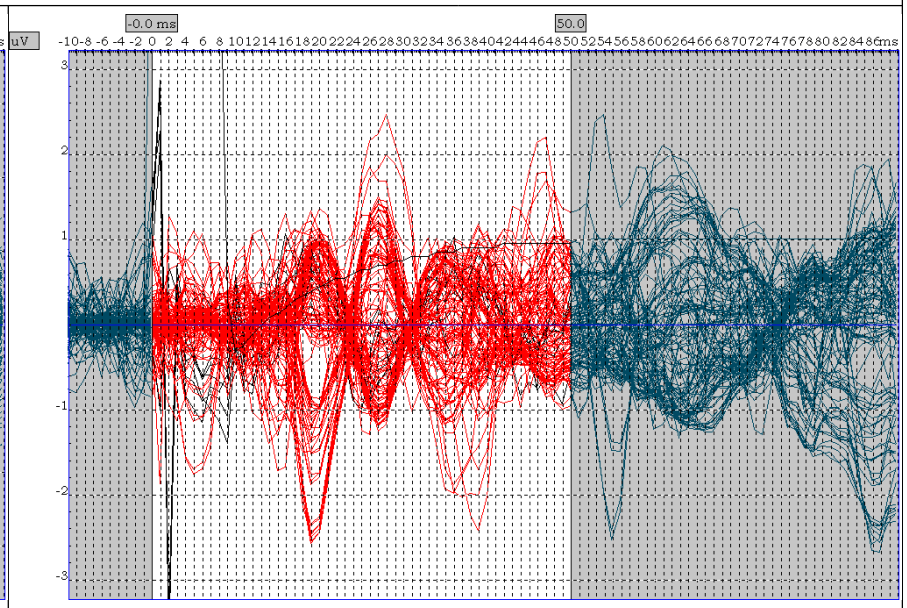
Exponential parameters
P1 (height): 35,8
P2 (SD): ,25
P3 (centre): ,0000

Alpha parameters
P4 (slope): 915
P5 (peak variance): ,1040



Subject 15



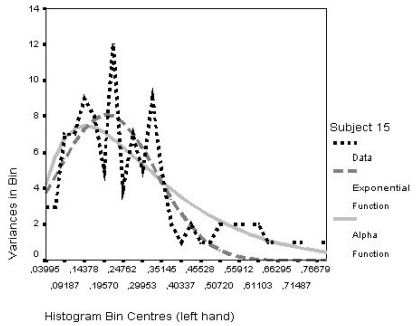


Left hand

Subject: 15
Group: Other Patients
Age: 57

Exponential parameters
P1 (height): 8,1
P2 (SD): ,13
P3 (centre): ,2038

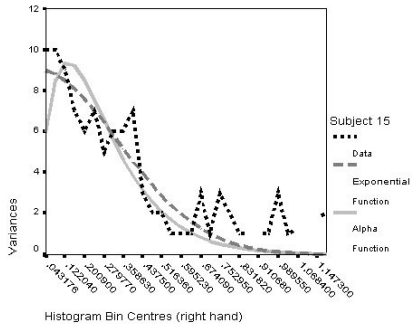
Alpha parameters
P4 (slope): 139
P5 (peak variance): ,1459



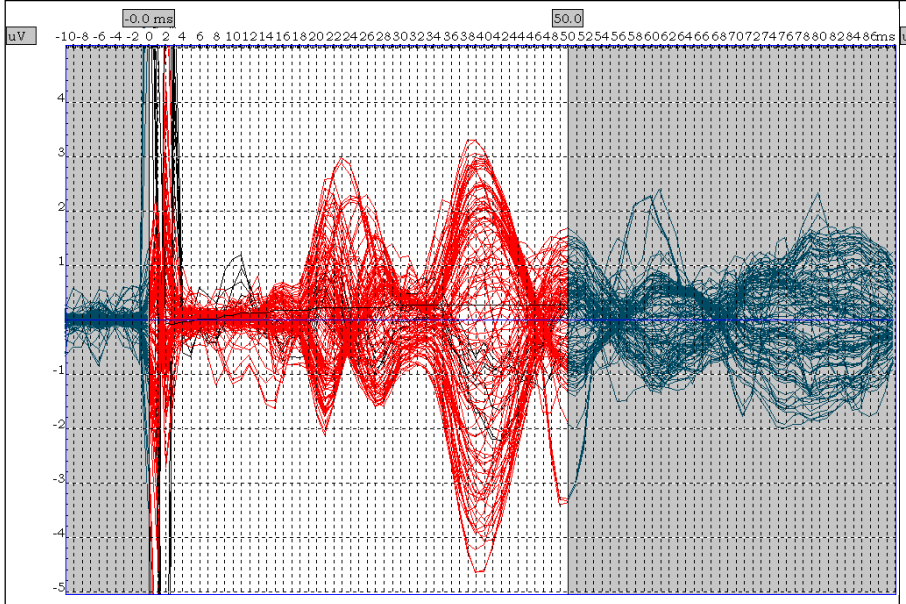
Right hand

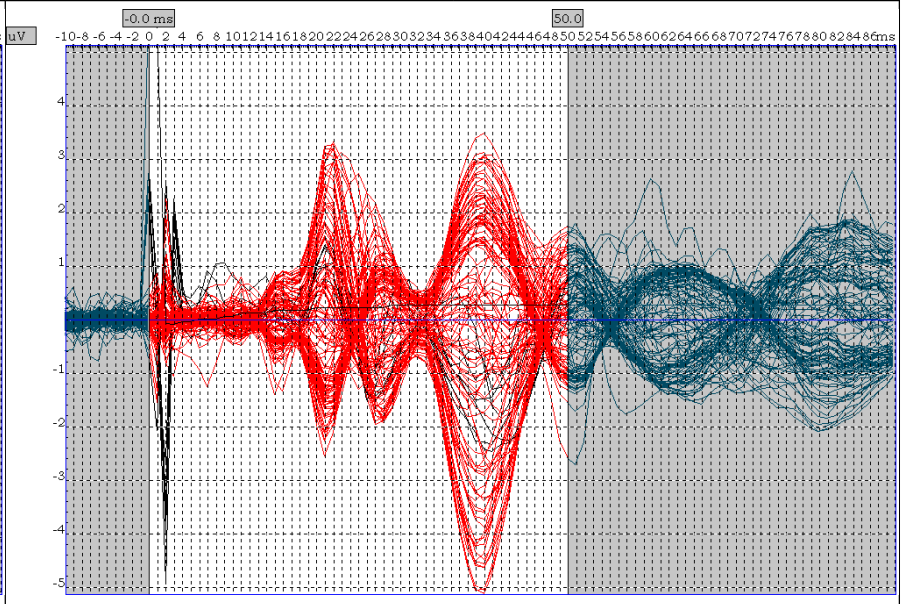
Exponential parameters
P1 (height): 9,0
P2 (SD): ,34
P3 (centre): ,0000

Alpha parameters
P4 (slope): 191
P5 (peak variance): ,1333



Subject 16



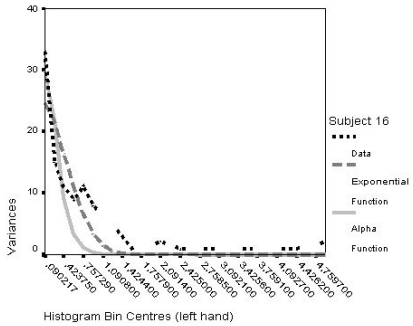


Left hand

Subject: 16
Group: Other Patient
Age: 68

Exponential parameters
P1 (height): 25,1
P2 (SD): ,46
P3 (centre): ,0000

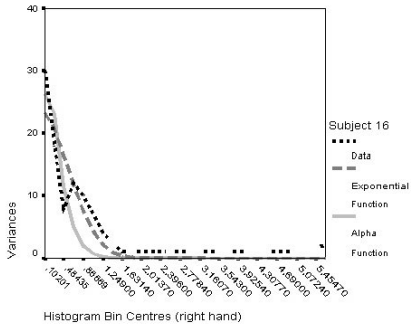
Alpha parameters
P4 (slope): 689
P5 (peak variance): ,1224



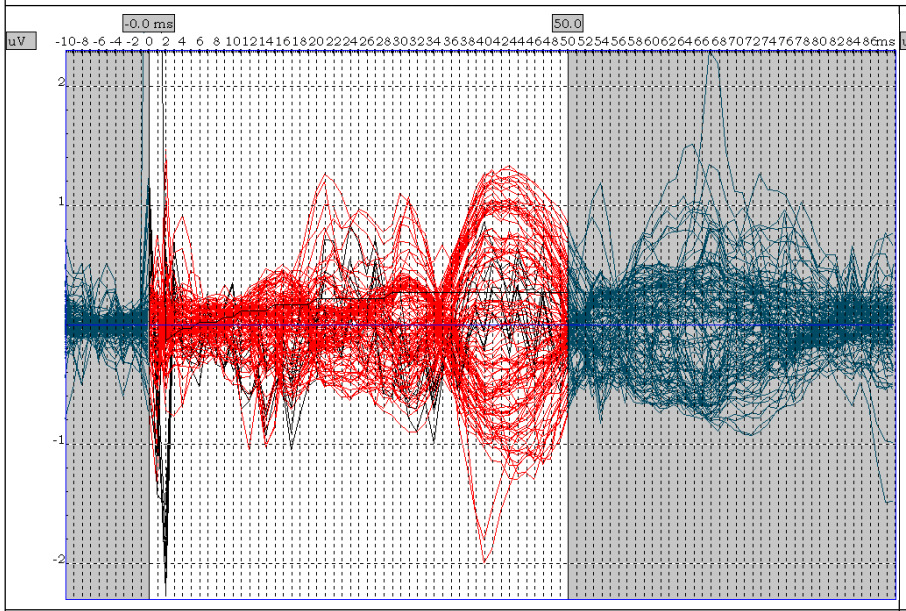
Right hand

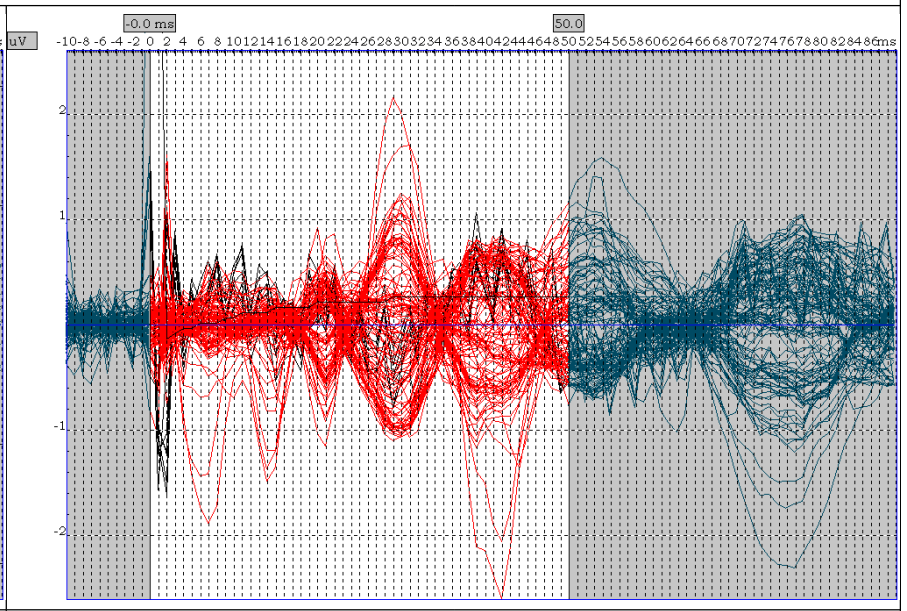
Exponential parameters
P1 (height): 23,6
P2 (SD): ,57
P3 (centre): ,0000

Alpha parameters
P4 (slope): 486
P5 (peak variance): ,1604



Subject 17





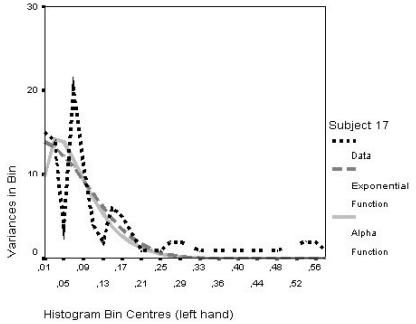
Left hand

Right hand

Subject: 17
Group: Probable CBGD
Age: 71

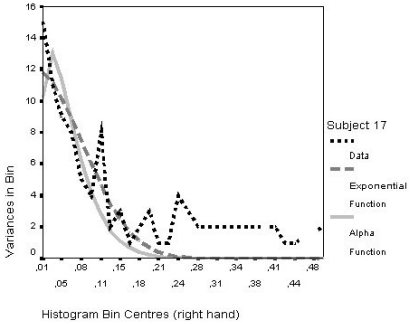
Exponential parameters
P1 (height): 14,0
P2 (SD): ,10
P3 (centre): ,0000

Alpha parameters
P4 (slope): 946
P5 (peak variance): ,0414



Exponential parameters
P1 (height): 11,9
P2 (SD): ,08
P3 (centre): ,0000

Alpha parameters
P4 (slope): 1240
P5 (peak variance): ,0285



Appendix B: Matlab functions

Function: Makeext.m

This function converts ASA .avr files to files that can be used in the other functions. It removes the first two lines with header-information and all lines indicated in electrodes.ext. Apart from the .avr-files the function needs three other files as input: rawfiles.ext, which tells the function where to find the .avr-files, filenames.ext, which tells the function where to save the results. It also needs a file 'electrodes.ext', which contains a sequence of zeroes and ones and tells the function which lines of the .avr-files from rawfiles.ext should be saved to the files mentioned in filenames.ext (a one) or not (a zero).

```
function madeext = makeext(rawfiles)

infiles = fopen('H:\mSEP\rawfiles.ext');
outfiles = fopen('H:\mSEP\filenames.ext');
electrodefile = fopen('H:\mSEP\electrodes.ext')
ge = fgetl(electrodefile);
goelectrodes = sscanf(ge,'%f');

while (feof(infiles))<1
   inputfile = fopen(fgetl(infiles));
   outputfile = fgetl(outfiles);
   line = fgetl(inputfile);
   line = fgetl(inputfile);
   n = 0;
   temparr = [];
   while (feof(inputfile))<1
      n = n + 1;
      line = fgetl(inputfile);
      linevector = sscanf(line,'%f');
      linevector = linevector';
      if (goelectrodes(n))
         temparr = [temparr;linevector];
      end
   end
   dlmwrite(outputfile,temparr,'\t');
end

fclose all;

madeext = 1;
```

Function: Mseph.m

This function calculates a table with two columns for each input-file mentioned in ‘filenames.ext’ (which should be the same list used for the makeext-function). The first column contains the amount of variances in each consecutive bin in a histogram. The second column contains the location of the centres of the bins. The amount of bins must be specified when running the function. This function needs the file filenames.ext and the input-files mentioned in filenames.ext as well the next function described. If no variable name is specified when the mesph-function is called, the result is stored in the standard variable ‘ans’. The result of the function should be saved to a file with a command such as mentioned in the comment at the end of the function. This file can be read in SPSS and Excel for further processing.

```
function hvars = mseph(histbins)

filenames = fopen('H:\mSEP\filenames.ext')

while (feof(filenames))<1
   temparray = [];
   temparray = dlmread(fgetl(filenames),'\t');
   hvars = [hvars;temphistvar(temparray,histbins)];
end

hvars = hvars';

% dlmwrite('H:\mSEP\varhists.dat',hvars,'\t')
```

Function Temphistvar.m

This function performs a task for the function mseph.m which gives it all the necessary input.

```
function h = temphistvar(dataarray,histbins);

tempvar = var(dataarray);
[temph,bincentres] = hist(tempvar,histbins);
h = [temph;bincentres];
```