Biomarkers Notes

Abstract

* statistically significant correlation is evident in 37 of 66 (56%) comparisons performed between 12 markers of different natures
* Different EEG markers reflect partly the same features in brain functioning

Introduction

* Mental disorders cause only mild alterations in EEG which are difficult to detect
  + Different advanced methods have had to be developed
  + Many different methods because EEG is complex, stochastic, nonstationary, and nonlinear
* Changed caused by mental disorders are seen in traditional EEG markers based on powers of EEG frequency bands
  + EEG alpha power is associated with depression severity
  + Various mental disorders are seen in differences in EEG frequency bands powers
* Fractality, complexity, and frequency balance are more complex EEG markers
  + Can detect Alzheimer’s, schizophrenia, and others
  + “The combination of nonlinear markers Higuchi’s fractal dimension (HFD), Detrended fluctuation analysis (DFA), correlation dimension, and Lyapunov exponent markers provides a classification accuracy of depression of 90% which is higher than the classification accuracy for the linear EEG band powers markers 76.6%”
* Two possible explanations
  + Disorder causes psychological changes which are reflected by different features of EEG signal, where each marker detects a specific EEG feature
  + Different EEG markers reveal the same EEG features and similar declinations in brain functioning
* Need to select important markers in EEG signal
  + Mild alterations are expected in EEG, don’t want these to be undetected
  + Selection of EEG markers is probably more important than actual method used to interpret markers
  + Want to investigate if different EEG markers reveal same EEG features and overlap in regards to state of the brain
  + Correlation between different EEG markers indicating various features of the signal is investigated
* Markers
  + Four from band power – these markers describe the power of the signal inside the fixed EEG frequency bands. Not sensitive to pattern of the signal
    - Theta band power (TBP)
    - Alpha band power (ABP)
    - Beta band power (BBP)
    - Gamma band power (GBP)
  + Four dynamics markers – describe pattern and complexity of signal
    - HFD describes self-similarity of signal
    - DFA describes self-correlation of signal and determines self-affinity of signal
    - LZC describes randomness of signal
    - SASI describes balance of low-frequency and high-frequency oscillations in the signal
  + Four functional connectivity markers – describe connectivity between different brain areas using multichannel data
    - Magnitude-squared coherence (MSC) describes intensity of coherence between two signals
    - Imaginary part of coherency (ImC) characterizes phase relationships in the coherence between two complex signals
    - Synchronization likelihood (SL) describes dynamical interdependencies between two signals
    - Mutual information (MI) describes coherence of the information between two signals and can be considered a spatial analog of entropy
  + Classifications
    - Linear - TBP, ABP, BBP, GBP, SASI, MSC, ImC
    - Nonlinear - HFD, DFA, LZC, SL, MI
    - Time domain - HFD, DFA, LZC, SL, MI
    - Frequency domain - TBP, ABP, BBP, GBP, SASI, MSC, ImC
    - Phase-sensitive - ImC, SL
    - Phase-insensitive - MSC and MI

Methods

* Participants
  + 80 in total, 38 F and 42 M
  + 19-75 in age, mean of 37 +/- 15
* EEG Recordings
  + Neuroscan Synamps2
  + Extended international 10-20 system, 30 electrodes
    - Linked mastoids are used as reference
* EEG Processing
* EEG Analyses
  + Calculation of band power markers
    - PSD of recorded signal calculated using Welsh’s averaged periodogram method
    - Markers were calculated as mean of PSD over the frequencies within fixed frequency bands
      * TBP 4-7 Hz
      * ABP 8-12 Hz
      * BBP 13-30 Hz
      * GBP 31-45 Hz
  + Calculation of Dynamics Markers
    - Nonlinear were calculated in time domain
    - Nonlinear marker was determined as mean value of calculations’ results over ten segments
    - HFD calculated using Higuchi’s original algorithm with kmax = 8
    - DFA was calculated according to the published by Peng et al. algorithmsapplying the adaptation to EEG described by Bachmann et al
    - LZC performed based on principles and algorithms published by Lempel and Ziv and Zhang et al.
    - SASI calculated in frequency domain summarizing PSD over the lower and higher EEG frequency bands and excluding the central alpha band from calculations
  + Calculation of functional connectivity markers
    - SL calculated in time domain
    - MSC and ImC calculated in frequency domain
* Statistics
  + 435 combinations were performed per marker for a subject

Results

* Band power markers
  + Correlation is statistically significant between markers of closer frequency bands
  + Four of six combinations indicate statistically significant correlations
* Dynamics markers
  + HFD has significant correlation with all three (DFA, SASI, and LZC) (ordered by correlation, descending)
  + Correlations between the other three are insignificant
* Functional Connectivity Markers
  + SL has significant correlation with all three (MI, ImC, MSC) (ordered by correlation, descending)
  + MSC and ImC, ImC and MI are also correlated
  + Five out of six significant (all but MSC and MI)
* Markers of Different Categories
  + Significant correlation in 37 of 66 comparisons between the 12 markers
  + Level of correlation varies from 0.97 to 0.38

Discussion

* Effectiveness of a marker, Ei, is estimated as product of number of markers, Ni, correlated with marker I and the average value of the corresponding correlation coefficients, Ri
  + E = NR
* A graph of different numbers

  Description automatically generated with medium confidence
  + First group (HFD, SL, MI, ABP) contains markers expected to incorporate a wide scale of EEG features
  + Second group (DFA, TBP, BBP, and ImC) covers more specific part of EEG features
  + Third group (GBP, MSC, LZC, SASI) are useful for detection of only specific EEG feature
* First group
  + HFD has highest effectiveness, incorporates maximal part of information from EEG signal
  + ABP is most effective band power marker, and is the most commonly used band power marker
  + Having SL and MI (two functional connectivity markers) shows that phase relations and power and important in brain functional connectivity
* Second group
  + DFA has high classification accuracy for depression
  + DFA combined with ABP can identify Alzheimer’s
  + ImC + cluster-span threshold is optimal in graph theory analyses of depression