# Fat tails and the need to disclose distribution parameters of qEEG databases

1

2

3 Guilherme Wood<sup>a</sup>, Klaus Willmes<sup>b</sup>, Jan Willem Koten<sup>a</sup> and Silvia Erika Kober<sup>a</sup> 5 6 <sup>a</sup> Institute of Psychology, University of Graz, Graz, Austria <sup>b</sup> Neurological Clinic—Neuropsychology, RWTH Aachen, Germany 7 9 10 11 Corresponding Author: 12 Full name: Guilherme Maia de Oliveira Wood 13 Department: Neuropsychology/Neuroimaging 14 Institute/University/Hospital: Institute of Psychology 15 Street Name & Number: Universitaetsplatz 2 City, State, Postal code, Country: Graz, Austria, 8010 16 17 Tel: +43 316 380 8503 E-mail: guilherme.wood@uni-graz.at 18 19 20 21 Number of Tables: 2 22 Number of Figures: 3 23 Word count: 5260 24 Keywords: fat-tailed distribution, qEEG, neurometry, neurofeedback, false-positives, QRP

# **Abstract**

1

2

3

4 5

6

7

8

9

10 11

12

13

14

15 16

17

18

19

20

21

Neurometry (a.k.a. quantitative EEG or qEEG) is a popular method to assess clinically relevant abnormalities in the electroencephalogram. Neurometry is based on norm values for the distribution of specific EEG parameters and believed to show good psychometric properties such as test-retest reliability. Many psychometric properties only hold under the Gaussian distribution and become problematic when distributions are fat-tailed. EEG signals are typically fat-tailed and do not show fast convergence to a Gaussian distribution. To circumvent this property of EEG, log-transformations have frequently, but not always been employed. In Monte Carlo simulations, we investigated the impact of fat-tails (i.e. deviations from Gaussian) on the cut-off criteria and changeability of what in neurometry is termed "abnormal EEG". Even slight deviations from the Gaussian distribution as measured by skewness and kurtosis lead to large inflation in the number of false positive qEEG findings. The more stringent the cutoff value adopted, the larger the inflation. Moreover, "abnormal EEG" seems to recover spontaneously at rates not compatible with the alleged test-retest reliability of qEEG. Alternative methods should be employed to determine cut-off values for diagnostics purposes, since a large number of false positive results emerge even when slight deviations from the Gaussian distribution are present. We argue that distribution properties of qEEG databases should be disclosed in much more detail by commercial providers to avoid questionable research practices and promote diagnostic transparency. We provide recommendations for the improvement of psychometric properties of existing qEEG databases.

# Introduction

22

23

24

25

26

27 28

29

30

31

32

33

34

35

36 37

38

39

40

41

42

43

44

45 46

47

48

Neurometry (a.k.a. quantitative EEG or qEEG) is the popular name given to the adaptation of classic psychometric measurement models to the evaluation of EEG data [1]. Typically, EEG parameters are measured in a "large" sample and norm values are calculated and employed as a reference to classify EEG signals as normal or abnormal and suggest specific forms of "cure" to "normalize" EEG classified as deviant. More or less extreme cut-off values are used to classify the EEG of individuals as "normal" and "abnormal" [2] and in case of abnormality, an intervention such as neurofeedback [3] can be applied to "normalize" the EEG. Several parameters of EEG have been treated in this way: absolute and relative frequency power, coherence, phase, and event-related potentials [4]. A PubMed search for the term "qEEG" alone yields to the present time point over 1000 entries. The rationale behind the construction of normative databases is strongly dependent on assumptions regarding the distribution of EEG population parameters. Ideally, these parameters converge quickly to a Gaussian distribution and the true population values for mean and variance of the EEG can be estimated with reasonable effort. Results acceptable for diagnostic purposes can be achieved for the mean with sample sizes of n = 30 and the variance with  $n = 750^{1}$  [5]. An estimate of the variance is paramount for the development of norms, since the standard deviation serves as the unity to describe how far an observation is from the mean. The proportion of observations more extreme than a z-score of  $\pm$  2 or 3 is given by the density function of the Gaussian distribution (i.e.  $\cong$  5% and 0.1%, respectively) and serves well as a cut-off value for diagnostics. An inaccurate estimate of the variance leads to imprecise z-scores and cut-off values that are useless for individual diagnostics because the proportions of values exceeding the cut-off values may be much higher or lower than expected. Test-retest reliability measures provide the basis for measurement of intervention effects, since they estimate the expected changes in test scores which are due to measurement error alone. One important caveat for the usefulness of test-retest reliability is the homoscedasticity of measurement error. When skewness and kurtosis deviate from a Gaussian distribution, measurement error becomes more heteroscedastic because of one or both of the distribution's tails, and test-retest reliability estimates become invalid for observations far from the mean. In the

<sup>1</sup> This is the n when considering a reasonably useful estimate that will not deviate more than d = 5% from the correct value with a confidence of 95%. Taking a less stringent accuracy criterion may not be problematic when evaluating estimates close to the mean, but problematic for more extreme observations. While an error of 10% is still fine when observations are  $1\sigma$  away from the mean, an error of 10% when estimating an observation  $2\sigma$  away from the mean is much more pronounced.

50

51

52

53

54

55

56

57

58

59

60

61

62

63

64

65

66

67

68

69

70

71

72

73

74

75

76

77 78

79

80

81

present study, we will investigate the impact of deviations from a Gaussian distribution to the practice of comparing EEG with EEG norms using cut-off values. Authors active in the development of neurometric tools tend to underscore that EEG parameters such as absolute power, relative power, phase, and coherence follow a Gaussian distribution. As reported for instance by [6] and [7] (Table 1, p. 101), skewness and kurtosis deviate from normality to a certain degree in qEEG databases, but for decades this has been treated as negligible, but a psychometric proof of this claim was never presented. To the contrary, publications on qEEG databases rarely present information on the higher moments of the distribution of EEG parameters. This is highly problematic, since EEG data can show fat-tailed distributions such as a lognormal distribution [8] and require the use of mathematical transformations to achieve a Gaussian distribution. The lognormal distribution can behave differently according to its standard deviation [9]. The lognormal distribution with a small standard deviation is almost symmetric around the mean and behaves indeed very similarly to the Gaussian, but starts very quickly to behave as a fat-tailed distribution, when its variance increases. When the distributions are truly lognormal, the logarithm of raw values behaves as a Gaussian and the assumptions for diagnostics are met. Obviously, transformations have to be chosen taking into consideration the properties of data at hand and only wrong transformations can damage data properties. Crucially, there is evidence from Box-Cox investigations, that EEG parameters can be distributed in a more extreme way than lognormal [10] (Table 2, p. 210). In such cases, a log-transformation is unable to bend the data distribution to a Gaussian and many of the properties of fat-tailed distributions will remain in the data even after a log-transformation and several of the measurement assumptions cannot be met for any practical purpose. One characteristic of fat-tailed distributions is the higher probability density of observations far from the mean in comparison to the Gaussian distribution. The more fat-tailed a distribution is, the more observations are farther than 2, 3, 4 standard deviations from the mean, rendering these values useless as cut-offs (Fig. 1). For instance, under a fat-tailed log-normal distribution with mean 0 and standard deviation 1, many more observations will be more extreme than 2 or 3 standard deviations than in a Gaussian distribution (i.e. 25% and 14%, respectively, and not only 5% and 0.1%, as under a Gaussian). These values illustrate how large the inflation in the number of false positives is when taking  $2\sigma$  (0.25/0.05 = 500%) or  $3\sigma$  (0.14/0.001 = 14000%) as cut-off values for neurometrics. When considering cut-off values based on the standard deviation, fat-tailed distributions lead to the inflation of occurrence of observations more extreme than the cutoff.

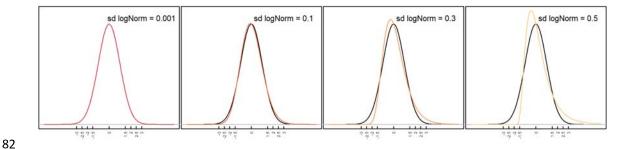


Figure 1. Comparison of the densities of the Gaussian distribution (black line) and lognormal distributions, the latter with increasing variances. Note that at very small variance values the lognormal is indistinguishable from the Gaussian, but small increases in variance lead to large deviations at the tails.

84

85

86

87

88

89

90

91

92

93

94

95

96

97

98

99

100

101

102

103

104

105

Moreover, estimating the moments of fat-tailed distributions (mean, standard deviation, skewness and kurtosis) is not an easy task because of slow convergence. Even after collecting many thousands of observations, sample estimates can be far away from the true population value. While one can rely on n = 30 to provide a not too bad estimation of the population mean of a Gaussian distribution, some common fat-tailed distributions would need no less than 10<sup>9</sup> observations for estimation of the mean [9]. Even if many fat-tailed distributions converge to a Gaussian distribution when n approaches infinity, slow convergence implies sample sizes prohibitively large by many orders of magnitude in comparison to the Gaussian. For fat-tailed distributions, the empirical distribution does not reflect the true statistical properties of the population, since typical sample sizes of hundreds or even some thousands of participants are too small to allow useful estimation. This is problematic especially at the extremes of the distribution, which are central for diagnostics of "abnormal" EEG. Fat-tailedness also interferes with the computation of score differences, which are essential when comparing qEEG scores obtained before and after an intervention. Due to an intervention, neurometrics specialists aim at a "normalization" of the EEG, which is expressed by a correction of extreme scores obtained prior to a treatment to levels typically observed in the population. Database providers use to report good or even excellent test-reliability scores for qEEG parameters [11, 12, 13]. Thanks to the test-retest reliability of gEEG databases, one can compute the critical difference of qEEG scores, which is the smallest non-trivial score difference, i.e. a score too large to be attributed to chance alone. In this sense, the critical difference helps accounting for the effects of regression to the mean and can therefore be taken as genuine evidence of the effectivity of a therapeutic intervention and is a great tool to evaluate the effects of heteroscedasticity on diagnostics and evaluation practices typical in neurometry. Under the Gaussian distribution, individual measurement

error (i.e. SE =  $z_{\alpha}\sqrt{1-\rho}$  for z-transformed variables with  $\sigma$  = 1) is homoscedastic, so that the probability of test scores to surpass the critical difference by chance is the same for any test score regardless of how far it is from the mean. This is not true, however, when distributions are fat-tailed. In case of variables with excess skewness and kurtosis, heteroscedasticity generates larger critical differences far away from the mean than closer to it and give rise to the artificial impression of large improvements where there is none. In the following, we will employ descriptions of qEEG distributions from the literature and test their susceptibility for inflation of positives and tail heteroscedasticity using Monte Carlo simulations.

# **Materials and Methods**

115

116

117

118119

120

121

122

123

124

125

126

127

128

129

130

131

132

133

134

135

136

137

138

139

140

141

142

143

The degree of deviation from a Gaussian distribution observed in popular qEEG databases can be estimated using the empirical values of variances, skewness, and kurtosis reported in the literature (e.g. [6], Table 2.2, p. 16 and [7], Table 1, p.  $101^2$ ). These authors published skewness and kurtosis of their database as percentage value in relation to the moments of a Gaussian. Inspection of some of these values reveal deviations from Gaussian in the order of 0% to 50%. Although it is not explicitly reported in these publications, we assume that the sample moments are higher than the Gaussian because of the well-known fat-tail properties of EEG signals [8, 10]. This means that simulations with kurtosis values covering the interval between 3 and 4.5 are required to understand the diagnostic properties of qEEG data, considering that the Gaussian distribution has a kurtosis of 3.

#### Monte Carlo simulation of cut-off values

We investigated the proportion of observations more extreme than typical cut-off values used to classify gEEG as normal or abnormal. Typical cut-off values of  $2\sigma$  and  $3\sigma$  as well as cut-off values of 1.5σ and 2.5σ were included in the simulations to improve the visualization of results. Nine different values ranging from 0.001 to 0.5 were used as the standard deviation to generate data with a lognormal distribution. Data drawn from a lognormal distribution with a very small value of sigma yields moments very close to the normal distribution (skewness<sub>lognormal</sub>  $\sigma = 0.001$ , kurtosis<sub>lognormal</sub>  $\sigma \cong$ 3) while those of a lognormal distribution with a larger standard deviation = 1 are much higher (skewness = 5.75, kurtosis = 80.5) than those of a Gaussian. Simulated data were z-standardized to have a mean value of 0 and a standard deviation of 1 to allow the calculation of the cut-off values of 1.5, 2, 2.5 and 3 $\sigma$  and the comparison with the Gaussian distribution. Comparisons consisted of counting the number of values more extreme than the cut-off value in the lognormal and in the Gaussian distribution and dividing the first by the second number. When both values are comparable, this index is approximately one. When the lognormal distribution generates more positives, the value gets bigger than one and indicates an inflation of positives in comparison to the Gaussian. Finally, when the lognormal distribution generates less positives, the value gets smaller than one and indicates a deflation of positives in comparison to the Gaussian. In total, 36 conditions (4 cut-off values \* 9 variance levels) were simulated with k = 10000 repetitions in each cell. In each repetition, one comparison of lognormal and Gaussian data was performed. Sample size was set at n

<sup>2</sup> Thatcher (2010, Table IV, p 141) presents even higher skewness and kurtosis values for a LORETA normative database.

= 1000 observations to reproduce the size of a large qEEG database. In the Supporting Information file, simulations of the inflation of false-positive values observed under other fat-tailed distributions (Chi²-square, T distributions) are presented.

Monte Carlo simulation of score changes and test-retest estimates: Aim of this simulation is to understand the effect of non-normality on the interpretability of test score differences. Usually, clinically relevant improvements in test-scores are attributed to the effectiveness of the intervention, but this must not be the case. For each test score difference there is a probability p of a false positive, i.e. test-scores show an improvement, which is due merely to random numeric fluctuation. One way to evaluate improvements in performance due to an intervention is the computation of the so-called critical difference in test scores [14]. The critical difference describes the minimal size of test score difference that is associated with a (low) probability  $p = \alpha$  of being produced by measurement error alone. Formula (1) illustrates the calculation of the critical differences ([15], adapted from formula 7.2.10, for z-transformed variables with  $\alpha = 1$ ), where Y represents the qEEG scores typically obtained before and after an intervention. As can be seen in (1), the critical difference is inversely related to the test-retest reliability  $\rho_{jj}$  of test-scores. The larger the test-retest reliability of test scores, the smaller the smallest meaningful difference score.

161 
$$crit\left(Y_{pre}-Y_{post}\right)=z_{1-\alpha/2}\sqrt{2(1-\rho_{jj})} \tag{1}$$

QEEG parameters typically are reported to show moderate to high test-retest reliabilities [11, 12, 13]. Under homoscedasticity, the size of observed differences between test scores is independent of the absolute value of the scores. For a Gaussian distribution, the size of test score differences observed for each test score is comparable and the test-retest reliability can be used to determine an upper bound for the size of test score differences that is caused by random fluctuation alone. This value is valid in the whole range of possible test score values. Under heteroscedasticity, this is not the case. We generated pairs of variables with mean = 0, variance = 1, and with test-retest correlation  $\rho_{jj}$ . We then established the critical difference given the size of the  $\alpha$ -level and the test-retest correlation  $\rho_{jj}$ . Correlations of the same size as the test-retest reliability estimates published in the literature were employed to calculate the critical difference. These variables were drawn either from a Gaussian distribution or from nine different log-normal distributions with the same degree of logarithmic compression as those employed in the simulation of cut-off values (see above). Four different test-retest correlation values were employed ( $\rho_{ij}$  was set to 0.5 (poor reliability), 0.7 (acceptable

reliability), 0.8 (good reliability), and 0.95 (excellent reliability)) and 9 degrees of logarithmic compression (see Table 1). The number of repetitions for each experimental cell in the design was k = 10000. The first variable in each pair represented the pre-test score and the second the post-test score. The difference  $D_{Ypre-Ypost}$  was calculated. The presence of heteroscedasticity was evaluated applying the Breusch-Pagan test [16, 17] to a linear model relating  $D_{pre-post}$  to the pre-test score. The rationale is that under the Gaussian distribution, the model should have no predictive power and yield a beta coefficient of 0; the residuals of this model will be strictly homoscedastic. Under logarithmic compression, the regression coefficient will be different from 0 and the residuals will assume increasing levels of heteroscedasticity. Moreover, under an excess of skewness and kurtosis, the number of difference scores fulfilling the condition  $D_{pre-post} > crit (Y_{pre} - Y_{post})$  should increase, particularly far from the distribution mean.

#### Statistical analysis

Simulations were programmed in R [18] using the packages base, stats v4.1.0, moments v.014 and Imtest v. 0.9-39. The scripts employed to generate data are available in the Appendix. In simulation 1, probabilities of reaching a value higher than the cut-off were calculated using the cumulative density function of the normal distribution and were compared with the empirical probability values obtained for the different instances of the lognormal distribution.

# Results

196

197

198

199

200

201

202

203

204

205

206

207

208

209

210

211

212

213

214

215

216

217

Monte Carlo simulation of cut-off values: The proportion of values exceeding the cut-off were obtained by thresholding log-normally distributed data with different variances using cutoff values between 1.5 and 3 standard deviations (Table 1 and Fig. 2). As can be seen in Figure 2, none of the cut-off values leads to a number of positives comparable to that of the Gaussian. Results of Simulation 1 show clearly how badly one can misinterpret the diagnostic value of EEG parameters, when these data deviate from a Gaussian distribution. A mismatch between the Gaussian and the lognormal distribution manifests itself in different directions and intensities depending on the cut-off value employed. On the one hand, liberal cut-off values (cut-off = 1.5) lead to an underestimation of the number of positive cases, which is worse when the kurtosis of the lognormal distribution is virtually the same as the Gaussian. Under these circumstances, the number of positives detected is only 36% of the expected. On the other hand, more conservative cut-offs produce a gross overestimation of positives, ranging between 400% and 3000%. Even in the case of a cut-off =  $2\sigma$ , which generates the mildest misestimations, an inflation of 7 % in the number of cases can be observed, even when the kurtosis is as expected from a Gaussian distribution. The size of the inflation increases rapidly and reaches 50% even when the kurtosis of the lognormal distribution is only 20% higher than that of a Gaussian.

Table 1. Skewness and kurtosis of artificial data reproducing the typical properties of qEEG data

SD of EEG distribution	0.001	0.100	0.157	0.214	0.271	0.329	0.386	0.443	0.500
Skewness	0	0.30	0.48	0.65	0.84	1.00	1.24	1.47	1.71
Kurtosis*	1	1.04	1.11	1.22	1.37	1.57	1.82	2.15	2.55

<sup>\*</sup>Kurtosis is expressed as kurtosis(simulation)/kurtosis(Gaussian)

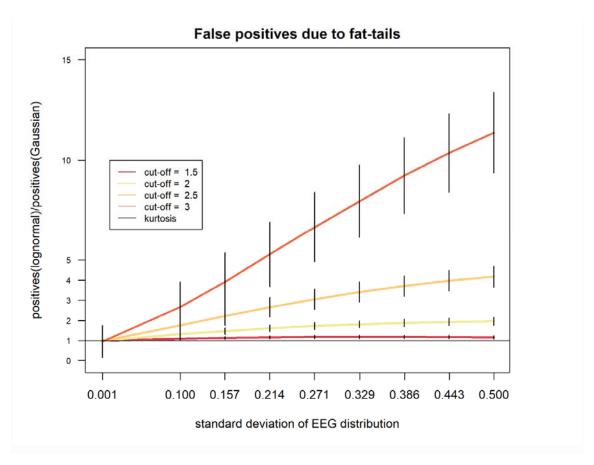


Figure 2. Inflation of the number of positive observations more extreme than cut-off values. The y-axis represents the proportion of values in EEG data exceeding the cut-off value divided by the expected frequency of a Gaussian distribution. In this simulation the cut-off values were set at 1.5, 2, 2.5 and  $3\sigma$ .

Figure 3 depicts the deviations from a Gaussian distribution observed when increasing the logarithmic compression of the data. It is evident that the extremes of the distribution deviate the most and are therefore more affected by the properties of the distribution.

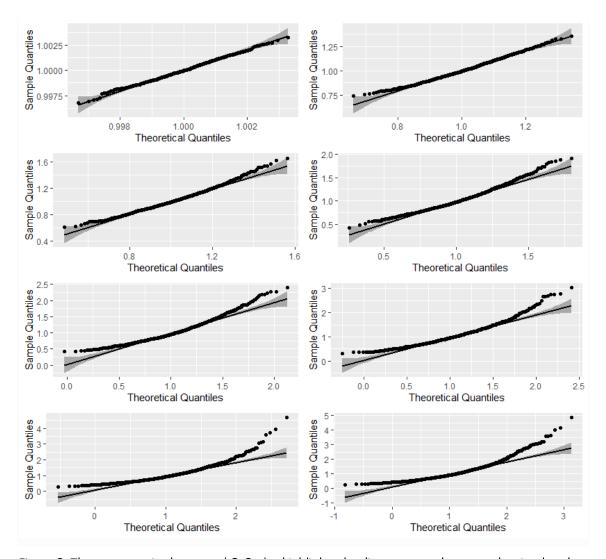


Figure 3. The curvature in the normal Q-Q plot highlights the disagreement between the simulated data and the Gaussian model.

Monte Carlo simulation of score changes and test-retest estimates: Table 2 depicts the average p-values obtained when testing for heteroscedasticity with the Breusch-Pagan test. An excess of kurtosis of 15% to 20% leads to systematic heteroscedasticity regardless of the level of test-retest reliability. Interestingly, the lowest levels of heteroscedasticity were observed when test-retest reliability is very high ( $\rho_{jj}=0.95$ ). Still, even under these optimal test-retest reliability conditions significant heteroscedasticity is observed as an excess of kurtosis reaches 27%. Given these results, it is informative to compare the slope of the linear regression of D<sub>pre-post</sub> on the pre-test score Y<sub>pre</sub>. As expected, this slope is 0 under the Gaussian distribution. Table 2 presents the slope values as  $\log_{10}(1 + \log_{10})$ . When using this scaling, values larger than 0 in Table 2 reveal a positive correlation between

the pre-test scores and the critical differences. The larger the pre-test score, the larger are the  $(Y_{pre}-Y_{post})$  differences. Values in Table 2 increase for all test-retest reliability levels depending on the kurtosis excess. Finally, we computed the number of cases in which  $D_{pre-post} > crit$   $(Y_{pre}-Y_{post})$  and the pre-test scores were larger than  $2\sigma$ . Table 2 shows that the stronger the kurtosis excess, the larger the proportion of values  $D_{pre-post} > crit$   $(Y_{pre}-Y_{post})$ . Numerical values depict the multiplicative factor related to each cell in the design. The value of 1 indicates that the number of cases is comparable to that obtained under Gaussian distribution. As can be observed, the proportion of values exceeding the critical difference is larger than under the Gaussian for each level of logarithmic compression. More importantly, the higher the test-retest reliability, the larger the number of observations with high levels at pre-test and a large pre-post difference (i.e. a case showing what neurometricians call "normalization of EEG"). The values presented in Table 2 show that an inflation of more than 30% is observed with very small kurtosis excess and this inflation increases up to 370% in case of larger kurtosis excess and excellent test-retest reliability.

Table 2: Heteroscedasticity, dependency on initial scores, and inflation of false positives as a function of the standard deviation of log-normal distribution used in the simulations

SD of EEG	Breusch-Pagan test									
	0.001	0.100	0.157	0.214	0.271	0.329	0.386	0.443	0.500	
$ \rho_{jj} = 0.5 $	-0.43	-1.13	-1.97	-3.02	-4.26	-5.49	-6.82	-8.06	-9.23	
$ \rho_{jj} = 0.7 $	-0.43	-1.26	-2.27	-3.63	-5.08	-6.72	-8.33	-9.96	-11.63	
$ \rho_{jj} = 0.8 $	-0.43	-1.15	-1.99	-3.11	-4.34	-5.67	-7.02	-8.48	-9.60	
$ \rho_{jj} = 0.95 $	-0.44	-0.63	-0.89	-1.23	-1.58	-1.94	-2.34	-2.69	-3.03	
		SI	ope of the	e differenc	e D <sub>pre-post</sub> o	on the pre-	test score	s Y <sub>pre</sub>		
	0.001	0.100	0.157	0.214	0.271	0.329	0.386	0.443	0.500	
$ \rho_{jj} = 0.5 $	0	0.02	0.03	0.04	0.05	0.06	0.06	0.07	0.08	
$ \rho_{jj} = 0.7 $	0	0.01	0.02	0.03	0.04	0.04	0.05	0.06	0.06	
$ \rho_{jj} = 0.8 $	0	0.01	0.02	0.02	0.03	0.04	0.04	0.05	0.05	
ρ <sub>jj</sub> = 0.95	0	0.01	0.01	0.01	0.01	0.02	0.02	0.02	0.03	
	(Values exceeding the critical difference / Gaussian) -1									
	0.001	0.100	0.157	0.214	0.271	0.329	0.386	0.443	0.500	
$ \rho_{jj} = 0.5 $	0	0.01	0.32	0.15	0.27	0.34	0.32	0.41	0.30	
$ ho_{jj}$ = 0.7	0	0.23	0.55	0.66	0.69	0.69	0.61	0.96	0.93	
$ \rho_{jj}$ = 0.8	0	0.36	0.35	0.49	0.68	0.89	0.86	0.87	1.03	
$\rho_{ii} = 0.95$	0	0.24	0.53	0.49	0.54	0.75	0.69	0.92	1.07	

# **Discussion/Conclusion**

252

253

254

255

256

257

258

259

260

261

262

263

264

265

266

267

268

269

270

271

272

273

274

275

276

277

278

279280

281

282

In the present study, we investigated how fat-tails of EEG data impact diagnostic criteria based on the assumption of a Gaussian distribution. Two main results emerged from our simulations. First, usual cut-off values based on standard deviations lead to a dramatic inflation in the number of falsepositives even when deviations from the Gaussian distribution are quite modest. Second, the same modest deviations from the Gaussian distribution can lead to strong estimation bias in the extremes of the distribution, which leads to heavy misestimation of individual scores. In the following we will discuss these results in more detail. The outcomes of Simulation 1 provide clear evidence that the diagnostic value of qEEG parameters can be badly overestimated, when these data deviate from a Gaussian distribution. When the cut-off is 1.5σ, the lognormal produces considerably less positives than the Gaussian, while cut-off values of  $2.5 \sigma$  and  $3\sigma$  produce dramatic inflation in the number of positives. In case of  $2\sigma$ , the number of positives is close to the expected when the lognormal distribution resembles the Gaussian the most (i.e. only 7 % excess of positives), but it starts to deviate from these estimates rapidly, when the standard deviation increases even only by a small amount. Interestingly, even when the kurtosis is very close to the Gaussian, there is a mismatch in the proportion of positives at each cut-off value. The more conservative the cut-off value (i.e.  $2.5\sigma$  or higher), the larger the inflation in the number of positives observed when data are lognormal. Even when the shape of the lognormal distribution looks almost indistinguishable from the Gaussian, there is an increase of 1806% in the number of positives. These results show clearly that even apparently harmless small deviations from the skewness and kurtosis of a Gaussian can lead to systematic misinterpretation of test results and a dramatic increase in the number of false positives. Apparently, no deviation from the Gaussian distribution is too small to have no severe consequences for diagnostics. Since the distribution parameters we employed in the present study come from published qEEG databases, one can be certain that the inflation of false positives occurs on a daily basis, as it is practiced world-wide and fulfills the prerequisites to be considered at least as Questionable Research Practice [19]. The only way to circumvent this problem is to ascertain that the qEEG data basis has exactly the desired properties and can be trusted to produce an acceptable number of false-positives. For too long, the necessity to enforce higher standards for the commercially availability of qEEG databases has been neglected and the relevance of deviant results downplayed. One possible reason for that is the uncritical willingness to believe in

284

285

286

287

288

289

290

291

292

293

294

295

296

297

298

299

300

301

302

303

304

305

306

307

308

309

310

311

312

313

314

315

the power of "neurotechnology", the so called "neuroenchantment" [20], that affects both laymen and specialists. Skewness and kurtosis alone are not sufficient to characterize data distributions in general. The reason for that is straightforward: Skewness and kurtosis offer only a global description of distribution parameters and do not reveal all the measurement properties necessary to define cut-off values for diagnostic purposes. Moreover, as shown by our Simulations 1 and 2, popular cut-off values for the interpretation of skewness and kurtosis values [21, 22] are not appropriate for the construction of test norms. As shown in the present study, skewness and kurtosis only deviated modestly from the expected values of a Gaussian distribution. Nonetheless, these deviations were sufficient to engender severe discrepancies between the density functions and inflation in the number of positives. Accordingly, even slight deviations from the Gaussian distribution led to a dramatic increase in the number of observations with values more extreme than the usual cut-off values. Inflation of the number of individuals with the diagnosis label of "abnormal" EEG increases dramatically with the distance between the cut-off value and the mean. While a cut-off value of 2 standard deviations leads to an inflation of 7% to 81%, a cut-off value of 3 standard deviations leads to an inflation of over 1800% in the number of individuals with an EEG classified as "abnormal". The results of the numerical simulation are in line with empirical findings of a large number of false positive qEEG results (see [23] for a review). If our simulations are accurate, in the clinical setting, such cut-off values misguide the majority of all diagnostic recommendations. Depending on the EEG parameter, the number of false positives is much larger than the number of correct positives, meaning that interventions such as neurofeedback may have been futile in the majority of the studies using qEEG hitherto. Therefore, it is crucial for companies offering qEEG services to provide sufficient evidence that the data they employ to calculate norms do follow a Gaussian distribution, if cut-off values of 2 or even 3 standard deviations are going to be employed in the future. Since evidence of normality of these data has barely been presented in the past, the general validity of research and clinical diagnostics based on qEEG is more than questionable. Not only the initial diagnostics by means of neurometry seems to be problematic, but also the evaluation of intervention outcomes. As revealed by Simulation 2, heteroscedasticity leads to a considerable inflation of the number of cases showing "spontaneous" improvement in qEEG parameters. Not only the probability of having the EEG classified as "abnormal" is highly inflated, but also the probability that by a second evaluation the EEG will be classified as "normalized", in both cases by force of randomness alone. Here, test-retest reliability estimates lead to false confidence in the usefulness of non-Gaussian qEEG for individual diagnostics. As revealed by Simulation 2, the

317

318

319

320

321

322

323

324

325

326

327

328

329

330

331

332

333

334

335

336

337

338

339

340

341

342

343

344

345

346

347

348

probability of observing large fluctuations in qEEG scores, when the first measurement was far from the average, is highly inflated, particularly when test-retest reliability is excellent. These results seem to contradict common wisdom on the impact of test-retest reliability on the stability of test scores. The intuition of contradiction is correct in case of a homoscedastic Gaussian distribution, but not valid under heteroscedasticity, particularly when the measurement error is much larger at the tail. Exactly this was shown by Simulation 2. When considering the outcomes of both Simulation 1 and 2 together, a pattern of generation of false positives emerges, which implies for the client, first, an expectation of need for an intervention and then the conviction of benefit from that intervention. Our results are not completely new, since [24] already observed a high number of false positive results when analyzing EEG data from typical participants. Those early results fit the results of the present stimulation, but did not get any attention in the meantime. Up to now, the study by [24] was cited only 16 times according to google Scholar. The consequences of this for the clinical practice of neurometry are manifold: most of the diagnostic decisions based on the popular cut-off criteria as performed hitherto are probably wrong, with ethical and legal implications for the therapeutic use of qEEG. Comparisons of skewness and kurtosis as performed in the past are insufficient to guarantee that qEEG norms are useful for clinical and scientific applications. A much more detailed approach is necessary to ascertain the psychometric properties of data, particularly regarding the properties of the tails of data distributions, since these are particularly relevant for diagnostic purposes. Since lognormal distributions may converge slowly, authors are ethically obligated to present much more robust arguments that the sample estimates of their databases are stable and close enough to population values. In other words, qEEG based diagnostic decisions of "abnormal EEG" as performed hitherto based on cut-off values of 2 or 3 standard deviations has a good chance of being dramatically inflated -and therefore wrong- in a large proportion of the cases. To dismiss such concerns regarding the legitimacy of qEEG, a much better description of the properties of the distribution of normative data is necessary and a more adequate way to account for the instabilities observed at the tails of the distribution should be taken seriously. An inflation of the number of false positive diagnoses of abnormal QEEG has both material and immaterial costs for its users. Material costs can be substantial, for neurofeedback treatment typically takes several sessions to be completed (see tables in Marzbani et al. 2016 for a summary of treat duration), requires the utilization of specialized equipment and time of an expert neurofeedback trainer. In a recent study, Kalokairinou and colleagues (2022) found out that about 73% of users paid for neurofeedback out-of-pocket. As observed by Kalokairinou and colleagues (2022), about 80% of neurofeedback users use it for indications not adequately supported by

350

351

352

353

354

355

356

357

358

359

360

361

362

363

364

365

366

367

368

369

370

371

372

373

374

375

376

377

378

379

380

scientific evidence although more than half (57.6%) considered neurofeedback to be a scientifically well-established therapy. This disconnection between scientific evidence and experiences of users can be considered part of the immaterial costs of neurofeedback. These immaterial costs may be even more substantial for the individuals with a false diagnose of "abnormal" EEG. These persons are confronted with concerns regarding their health and cognitive capabilities. False positive diagnosis is known to induce psychosocial harm in affected individuals (Wakefield, 2010, 2015). Although not as grave as a diagnostic of psychiatric disorder, some form of psychosocial harm can be expected from false-positive EEG diagnosis as well. Recommendations Describe extensively the distribution of qEEG parameters. Thoroughly describing the properties of higher moments of the distribution of normative EEG data is essential to guarantee that the diagnostic process is transparent and the number of false-positives is reduced to more reasonable levels. Conventional tests such as the Shapiro-Wilks test may not be sufficient to describe fattailedness [25]. In line with the recommendations by [26] to discourage Questionable Research Practice, providers of gEEG databases should disclose in detail all the properties of the data they contain. This means reporting skewness, kurtosis as well as confidence intervals for every parameter listed in gEEG databases. QQ-Plots should always be presented when databases are published or services sold. Cut-off values based on the percentiles of the EEG distribution could be an alternative. Depending on the properties of qEEG data distributions, percentile values could be used instead of the standard deviations. On the one side, percentiles force the developers of databases to put more effort in data collection when creating databases stratified for age, schooling, and sex of participants, since only in large samples it is possible to uniquely determine the 95th and 99th percentiles that are so important for practical purposes. On the other hand, the percentile values are as intuitive as standard deviations and have a straightforward meaning even for members of the family of fat-tailed distributions. However, the usability of percentile values can be limited by heteroscedasticity. If the values in the tails show larger variability than those close to the center, the meaning of extreme percentile values may also be limited, since the true value of that observation is accompanied by a large interval of uncertainty. Log-transformations are not necessarily sufficient. Some distributions cannot be bent to the shape of a Gaussian by the logarithm [9]. As shown by [10], the distribution of EEG parameters may deviate from Gaussian in ways more extreme than logarithmic compression. In these cases, the logarithm

382

383

384

385

386

387

388

389

390

391

392

393

394

395

396

397

398

399

400

401

402

403

404

405

406

407

408

409

410

411

412

may reduce the degree of fat-tailedness, but as our results clearly show, the remaining fat-tailedness can still be sufficient to inflate considerably the number of (false) positives. Therefore, one should ideally always determine the transformation capable of adequately bending the shape of the distribution of qEEG data into the Gaussian. One practical way to do that is to use other families of transformations [27, 28, 10]. However, this step of data processing is not trivial, since estimating distribution moments and properties when distributions are more pronouncedly fat-tailed requires much more data than the usual few hundreds or thousands available in gEEG data bases. Since the transformations assume that available data are representative of the population distribution parameters, large misestimation problems are still likely. Include gEEG norm construction in the CRED check-list for the quality of neurofeedback studies [29]. One should take the matter of designing norms for EEG data much more seriously than hitherto. When disclosing the real sample properties of qEEG databases, it is possible that most studies of the past have employed too liberal criteria to define clinical samples. This can produce gross distortions in correlations between treatment outcomes and other outcome measures, distortions in the response to treatments, etc. All these factors decrease the quality of neurofeedback services, lead to useless and expensive treatments and jeopardize reproducibility of study results. For all these reasons, we believe that good quality qEEG norm parameters have to be checked during neurofeedback studies. The "Consensus on the reporting and experimental design of clinical and cognitive-behavioral neurofeedback studies" (CRED-nf checklist) contains a checklist for registering and publication of NF studies (Ros et al., 2020). Here we argue that in future versions of the CRED the use of safe neurometry instruments should be included as a positive point and the use of problematic databases a negative point to be included in the characterization of the quality of neurofeedback studies. A new business model and more training are necessary to improve qEEG guided practices. Since accuracy of qEEG based diagnostics depends on the higher moments of the distribution of qEEG parameters, these have to be thoroughly disclosed in much more detail than is usually the case to allow clients an informed choice. Users of qEEG databases have to receive better training on when and under which circumstances gEEG is relevant for diagnostic decisions and the evaluation of interventions.

# Limitations

One important limitation of the present study is the limited availability of information on the distribution of qEEG data available in the literature. With more precise and transparent numerical values, the estimates we can provide will become more accurate. Still, our main results as well as their alarming consequences for the practice of qEEG would not be challenged, just become some decimal places more precise. We hope to encourage developers of qEEG to be more accurate in describing sample parameters and diagnosing fat-tailedness in their datasets and users to demand this information before employing qEEG in research and diagnostics in the future.

**Statement of Ethics** 

422

428

The present research only contains numerical simulations based on reference kurtosis and skewness data publicly available in the scientific literature (<a href="http://dx.doi.org/10.1300/J184v02n04\_02">http://dx.doi.org/10.1300/J184v02n04\_02</a>, Table 2.2, p. 16 and <a href="http://dx.doi.org/10.1300/J184v07n03\_05">http://dx.doi.org/10.1300/J184v07n03\_05</a>, Table 1, p. 101). All issues of this journal (terminated in 2013) are available online for free download (<a href="https://www.isnr-jnt.org/issue/archive">https://www.isnr-jnt.org/issue/archive</a>). Therefore, no ethics approval was collected.

**Conflict of Interest Statement** 

430 "The authors have no conflicts of interest to declare."

# **Funding Sources**

This research was not funded by any agency.

# **Author Contributions**

- 434 GW wrote the programming code for the numerical simulations and parts of the text of the
- 435 manuscript. KW. Provided statistical expertise to guide the interpretation of the results and wrote
- parts of the manuscript. JWK wrote parts of the manuscript. SEK provided relevant literature for
- setting up the numerical simulations and wrote parts of the manuscript.

# **Data Availability Statement**

- The script used to generate the data and figures is available as electronic supplementary material
- 441 ESM.

429

431

432

433

438

439

# References

- 1 Johnstone J, Gunkelman J. (2003). Use of databases in QEEG evaluation. *Journal of Neurotherapy* 7(3-4), 31-52.
- 2 Thatcher, R. W., & Lubar, J. F. (2009). History of the scientific standards of QEEG normative databases. *Introduction to quantitative EEG and neurofeedback: Advanced theory and applications*, 2, 29-59.
- 3 Gruzelier, J. H. (2014). EEG-neurofeedback for optimising performance. III: a review of methodological and theoretical considerations. *Neuroscience & Biobehavioral Reviews*, 44, 159-182.
- 4 Kropotov J. *Quantitative EEG, event-related potentials and neurotherapy*. Academic Press; 2010 Jul 28.
- 5 Thompson Jr, W. A., & Endriss, J. (1961). The required sample size when estimating variances. *The American Statistician*, 15(3), 22-23.
- 6 Thatcher, R. W. (1998). Normative EEG databases and EEG biofeedback. *Journal of Neurotherapy*, 2(4), 8-39.
- 7 Thatcher, R. W., Walker, R. A., Biver, C. J., North, D. N., & Curtin, R. (2003). Quantitative EEG normative databases: Validation and clinical correlation. *Journal of Neurotherapy*, 7(3-4), 87-121.
- 8 Gasser, T., Bächer, P., & Möcks, J. (1982). Transformations towards the normal distribution of broad band spectral parameters of the EEG. *Electroencephalography and clinical neurophysiology*, *53(1)*, 119-124.
- 9 Taleb, N. N. (2020). Statistical consequences of fat tails: Real world preasymptotics, epistemology, and applications. *arXiv* preprint *arXiv*:2001.10488.
- 10 van Albada, S. J., & Robinson, P. A. (2007). Transformation of arbitrary distributions to the normal distribution with application to EEG test–retest reliability. *Journal of neuroscience methods,* 161(2), 205-211.
- 11 Roberts, A. M., Fillmore, P., & Decker, S. L. (2016). Clinical applicability of the test-retest reliability of qEEG coherence. *NeuroRegulation*, *3*(1), 7-7.

- 12 Salinsky, M. C., Oken, B. S., & Morehead, L. (1991). Test-retest reliability in EEG frequency analysis. *Electroencephalography and clinical neurophysiology*, *79*(5), 382-392.
- 13 Thatcher, R. W. (2010). Validity and reliability of quantitative electroencephalography. *Journal of Neurotherapy*, 14(2), 122-152.
- 14 Salkind, N. J. (Ed.). (2010). Encyclopedia of research design (Vol. 1). sage.
- 15 Huber HP. Psychometrische einzelfalldiagnostik. Beltz; 1973.
- 16 Breusch, T. S., & Pagan, A. R. (1979). A simple test for heteroscedasticity and random coefficient variation. *Econometrica: Journal of the econometric society*, 1287-1294.
- 17 Breusch, T. S., & Pagan, A. R. (1980). The Lagrange multiplier test and its applications to model specification in econometrics. *The review of economic studies, 47(1),* 239-253.
- 18 Team, R. C. (2013). R: A language and environment for statistical computing.
- 19 John, L. K., Loewenstein, G., & Prelec, D. (2012). Measuring the prevalence of questionable research practices with incentives for truth telling. *Psychological science*, *23(5)*, 524-532.
- 20 Ali, S. S., Lifshitz, M., & Raz, A. (2014). Empirical neuroenchantment: from reading minds to thinking critically. *Frontiers in human neuroscience*, *8*, 357.
- 21 George D. SPSS for windows step by step: A simple study guide and reference, 17.0 update, 10/e.

  Pearson Education India; 2011.
- 22 Tabachnick BG, Fidell LS. Using multivariate statistics, 6th edn Boston. Ma: Pearson. 2013.
- 23 Nuwer, M. R., Hovda, D. A., Schrader, L. M., & Vespa, P. M. (2005). Routine and quantitative EEG in mild traumatic brain injury. *Clinical Neurophysiology*, *116*(9), 2001-2025.
- 24 Hamilton-Bruce, M. A., Boundy, K. L., & Purdie, G. H. (1991). Interoperator variability in quantitative electroencephalography. *Clinical and experimental neurology*, 28, 219-224.
- 25 Shapiro, S.S.; Wilk, M.B. (1965). "An analysis of variance test for normality (complete samples)". *Biometrika*. **52** (3–4): 591–611.
- 26 Sijtsma K. (2016). Playing with data—or how to discourage questionable research practices and stimulate researchers to do things right. *Psychometrika* 81(1):1-5.

- 27 Box GE, Cox DR. (1964). An Analysis of Transformations," *Journal of the Royal Statistical Society, Series B, 26,* 211-243.
- 28 Morozova M, Koschutnig K, Klein E, Wood G. (2016). Monotonic non-linear transformations as a tool to investigate age-related effects on brain white matter integrity: A Box–Cox investigation. *NeuroImage 125*: 1119-1130.
- 29 Ros T, Enriquez-Geppert S, Zotev V, Young KD, Wood G, Whitfield-Gabrieli S, Wan F, Vuilleumier P, Vialatte F, Van De Ville D, Todder D. (2020). Consensus on the reporting and experimental design of clinical and cognitive-behavioural neurofeedback studies (CRED-nf checklist). *Brain* 43(6): 1674-1685. doi: 10.1093/brain/awaa009
- 30 Marzbani, H., Marateb, H. R., & Mansourian, M. (2016). Neurofeedback: a comprehensive review on system design, methodology and clinical applications. Basic and clinical neuroscience, 7(2), 143. doi: 10.15412/J.BCN.03070208
- 31 Thibault, R. T., MacPherson, A., Lifshitz, M., Roth, R. R., & Raz, A. (2018). Neurofeedback with fMRI: A critical systematic review. Neuroimage, 172, 786-807.https://doi.org/10.1016/j.neuroimage.2017.12.071
- 32 Kalokairinou, L., Choi, R., Nagappan, A., & Wexler, A. (2022). Opportunity Cost or Opportunity Lost: An Empirical Assessment of Ethical Concerns and Attitudes of EEG Neurofeedback Users. Neuroethics, 15(3), 28. https://doi.org/10.1007/s12152-022-09506-x
- 33 Wakefield, J. C. (2015). Psychological justice: DSM-5, false positive diagnosis, and fair equality of opportunity. Public Affairs Quarterly, 29(1), 32-75. <a href="https://www.jstor.org/stable/43574514">https://www.jstor.org/stable/43574514</a>
- 34 Wakefield, J. C. (2010). Misdiagnosing normality: Psychiatry's failure to address the problem of false positive diagnoses of mental disorder in a changing professional environment. Journal of Mental Health, 19(4), 337-351. https://doi.org/10.3109/09638237.2010.492418
- 35 Newson, J. J., & Thiagarajan, T. C. (2019). EEG frequency bands in psychiatric disorders: a review of resting state studies. Frontiers in human neuroscience, 12, 521. https://doi.org/10.3389/fnhum.2018.00521

#### **Figure Legends**

Figure 1. Comparison of the densities of the Gaussian distribution (black line) and lognormal distributions, the latter with increasing variances. Note that at very small variance values the lognormal is indistinguishable from the Gaussian, but small increases in variance lead to large deviations at the tails.

Figure 2. Inflation of the number of positive observations more extreme than cut-off values. The y-axis represents the proportion of values in EEG data exceeding the cut-off value divided by the expected frequency of a Gaussian distribution. In this simulation the cut-off values were set at 1.5, 2, 2.5 and  $3\sigma$ .

Figure 3. The curvature in the normal Q-Q plot highlights the disagreement between the simulated data and the Gaussian model.