Multi-contrast z-score comparison discriminates patients with psychiatric disorders from controls

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Target Audience Image analysts, psychiatrists, neuroscientists, psychologists, physicists.

Purpose: Developing a neuroimaging tool that can determine the normalcy of a multi-contrast MR examination will be useful in clinical practice. In a given radiology department, close to 50% of all MRI examinations are read as normal by the staff radiologists. Here, we describe a z-score based method[1,2] which reduces the entire MRI examination to a single number, which can be used to determine the disease state. We have applied this methodology to two groups of patients (schizophrenia[3] and bipolar disease) and two groups of matched healthy controls. We show that although the clinical MR imaging was not diagnostic, we can separate the patient group from controls using this method.

Methods: We studied 48 schizophrenia subjects, 40 bipolar subjects, and age-matched 106 healthy controls. The healthy controls were divided into two independent groups of 53 subjects. One control group was only used to determine the normative values for each pixel. The second control group and the patients groups were then compared. Patients were scanned using a 3T clinical magnet. MR imaging included, T1w, T2w, DTI, FLAIR imaging. FMRIB software library (www.fmrib.ox.ac.uk/fsl) was used to preprocess all images which included brain extraction and registration to the MNI template, and eddy current correction for DTI images. DTI analysis produced FA, MD, DWI and b=0 maps. Four DTI derived contrasts and three clinical MR contrast images were used in the analysis. Below, *s* refers to a given subject; *s'* refers to normal subjects; $n_{s'}$ is the number of normal subjects; *i ,j, k* refer to pixel coordinates in MNI template; *c* is an MR contrast volume (T1w, T2w, etc). For subject *s*, and contrast *c*, the normalized MRI signal intensity at pixel *i, j, k* after pre-processing is: $I(s,c,i,j,k)$. Following pre-processing, for each MRI contrast and for each pixel, we calculated a mean (μ) and standard deviation (σ) of the MRI signal intensity *I* at each contrast using the control subjects: $\mu(c,i,j,k) = \frac{1}{n_{s'}}\sum_{s'} I(s',c,i,j,k)$ and $\sigma(c,i,j,k) = \sqrt{\frac{1}{n_{s'}}\sum_{s'}(I(s',c,i,j,k) - \mu(c,i,j,k))^2}$ where *s'* refers to normal subjects only. We then calculated a Z-score for each pixel in each contrast for every subject using the above calculated means and standard deviations: $Z\_score(s,c,i,j,k) = \frac{I(s,c,i,j,k) - \mu(c,i,j,k)}{\sigma(c,i,j,k)}$. Using all Z-scores for each contrast (T1w, T2w, FLAIR, FA, MD, DWI, b=0) we defined a multivariate total Z-score, *ZT_score(s,i,j,k)* for all image contrasts as: $ZT\_score(s,i,j,k) = \mathrm{Sqrt}(\sum_c Z\_score(s,c,i,j,k)^2)$ which was summed over all image contrasts for each pixel. We then defined a cumulative multivariate Z-score for each subject *s* as: $CZT\_score(s) = \sum_{i,j,k} ZT\_score(s,i,j,k)$ calculated by summing multivariate Z-scores over each subject's brain volume. The *CZT_score(s)* for each subject was then used to determine the normalcy of a given subject's MRI exam. This data reduction technique reduces the entire MRI exam including many image volumes into a single number by calculating how far off each pixel's intensity is from the normal mean in the units of standard deviations in each pixel and then combining the distance in a multivariate way for each image contrast, and then determining overall distance for the entire volume.

Results: Figure 1 shows the independent control group and two groups of patients listed according to their cumulative z-scores. While both patient groups' data overlapped with each other, there was a clear separation between the patients and the controls (Student t-test, p<0.0001).

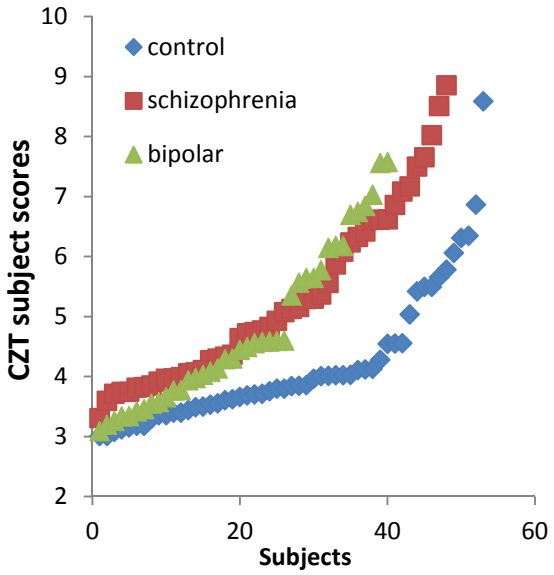

Fig. 1 The CZT scores of all subjects are shown. The z-scores were calculated using an independent control group. Although the patient groups cannot be separated from each other, patients and controls were separated (p<0.0001).

Discussion/Conclusions: In this study we have calculated a multi-contrast z-score using different MR image contrasts for each subject. We than computed a total score for each subject. This way entire MR study with all different contrasts was reduced into a single number. While the two patient groups were not separable from each other (p>0.05), we were able to separate the patient group from the control group with high significance (p<0.0001).

References: (1) Watts R *et al*. Radiology 272 (1), 217-223 (2014). (2) Lipton ML *et al.* Brain Imaging and Behavior 6. 329-342 (2012). (3) White T *et al.* Psychiatry Research: Neuroimaging 174, 110-115 (2009).

Acknowledgments This work was supported in part by a grant from TUBITAK 2236 Co-circulation Program and grants from NARSAD, the National Institutes of Health R01 MH076995, R01 MH060004, M01 RR018535, P30 MH090590, P50 MH080173, R01 MH79800.