

# Digital Picture Co-occurrence Texture Characteristics Discriminate between Patients with Early Dementia of Alzheimer's Type and Cognitive Healthy Subjects

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**Abstract:** Gray level co-occurrence texture characteristics of digital drawings were compared between persons with early dementia of Alzheimer's disease and healthy controls. It was hypothesized that texture characteristics contribute to the differentiation between these subject groups. The study population consisted of 67 healthy subjects and 56 patients with early dementia of Alzheimer's type. Between subject groups comparisons of texture entropy, homogeneity, correlation and image size were conducted with Mann-Whitney-U tests. The diagnostic power of combining all texture features as explanatory variables was analysed with a logistic regression model and the area under curve (AUC) of the corresponding receiver operating control (ROC) curve was calculated. The gray level co-occurrence characteristics differed significantly between healthy and demented subjects and the logistic regression model resulted in an AUC of 0.86 (95% CI [0.80, 0.93], sensitivity=.80, specificity=.79).

## 1 INTRODUCTION

Alzheimer's disease (AD) is the most common form of dementia and with the further development of disease modifying therapies, the screening of early symptoms becomes increasingly important.

Symptoms in the early stage include forgetting recently learned information, difficulty in completing familiar tasks at work or in household, or troubles in following a conversation. Apart from these symptoms occurring in daily life, early symptoms also include problems in the handling of visual images and spatial relationships. This manifests in perceptual difficulties, i.e., in reading, but also in processing difficulties, i.e., in writing or drawing (Alzheimer's Association, 2017; Trojano and Gainotti, 2016). In particular, as the process of drawing involves the interaction of several cognitive mechanisms, drawing deficits may be used as a diagnostic tool in detecting psychological or cognitive impairment.

This idea was operationalized in the development of projective tests in the very early 20<sup>th</sup> century. Originating from childrens drawings, Goodenough (Goodenough,1936) developed the first idea of using drawings as a tool for psychological assessment for intelligence. In parallel Emil Jucker, a swiss occupational counselor in 1298 initiated the idea of using the picture of a tree for counseling (Koch, 1949). The interpretation of tree drawings was not that intuitive, as a variety of parameters were considered to have a diagnostic validity, such as hight of the trunk, skewness, line thickness or the percentage of paper place used for the drawing.

Within the last two decades, several authors have used projective drawing tests in clinical diagnostics and have developed evaluation schemes (Pintea et al., 2013). Although these approaches seem to be promising, a clinical validation with respect to their relevance on the diagnosis of dementia still is lacking.

Actually several drawing tests are applied in the screening of dementia which are often included in

test batteries. In particular, the clock drawing test (Shulman et al., 1993) has been considered as a tool for detection of mental impairments related to dementia, as it shows a high sensitivity and specificity (Shulman et al., 2000). The paper drawings of common screening tests are usually analysed and scored by specialists after the drawing process.

Another line of research has come across using more drawing related topics such as colourfulness by means of computer aided image analysis (Heymann et al., 2018). An innovative approach in this respect is given by the use of digital media. Instead of drawing the picture on a paper sheet, a digital pad is used. Using this digital equipment, analysis of drawing process itself with parameters such as line drawing speed and on-air-movements during the whole drawing process can be obtained and have been subject to previous research (Müller et al., 2017; Souillard-Mandar et al., 2016).

The current study examined if texture features derived from digital tree drawings were able to discriminate between cognitive healthy subjects and patients with early dementia of Alzheimer's disease (early AD). Sixty-seven healthy subjects and 56 patients diagnosed with early AD painted a tree from their memory on a digitizing tablet with a pressure-sensitive pen. Besides several drawing features, the texture parameters homogeneity, entropy and correlation extracted from the gray-level co-occurrence matrix (GLCM) (Haralick et al., 1973) and the picture size were computed. The gray-level co-occurrence matrix is a statistical method of texture analysis, which takes into account the spatial relationship of image pixels. Its application is studied in different clinical settings, e.g. in the differentiation of healthy from pathological tissues in mammography (Pratiwi et al., 2015), the identification of bone lesions to assess the risk of fractures (Shirvaikar et al., 2016) or in the detection of skin diseases (Parekh et al., 2011).

It was hypothesized that texture features contribute to the differentiation between cognitive healthy and early demented subjects.

## 2 MATERIAL AND METHODS

Subjects were recruited from the Memory Clinic of the University Hospital of Tübingen, Germany and the study was approved by the local ethical committee. All subjects were right-handed, had normal or corrected-to-normal visual acuity, no severe hearing impairments and no physical restrictions to perform drawings. The subjects

underwent clinic interviews and neuropsychological tests. In case of suspected cognitive deficits further examinations, e.g. brain images and special laboratory tests were made. Fifty-six patients (40 women, 16 men, mean age =  $66 \pm 10$  years) were diagnosed with early AD, according to the National Institute of Neurological and Communicative Disorders and Stroke Alzheimer's Disease and Related Disorders Association (McKhann et al., 1984).

Sixty-seven persons (25 women, 42 men, mean age =  $70 \pm 11$  years) had no signs of cognitive impairment confirmed by a clinical interview and neuropsychological tests. They formed the healthy control group.

The drawing task was first introduced by Heymann (Heymann et al., 2018). All subjects were told to draw a tree by memory without time restrictions on a tablet with a digital pen. Whereas at Heymann's study the resulting pictures were analysed per view by dementia specialized art therapists, drawing characteristics were calculated in the current study with a software program from attendra GmbH, Tübingen. The drawing program allowed choosing between 12 different colours and 3 line widths. The software recorded several variables, e.g. the total numbers of colours and line widths and the number of colour or line width changes, the pressure, the velocity, the pen-up / pen-down relations and the texture features.

The digital device was a multi-touch Surface Pro 3 tablet with a digital stylus (Figure 1). Windows 8.1 Pro software was implemented and the tablet had an Intel Core i7-4650U processor with 1.7 to 3.3 GHz. The screen had a 3:2 aspect ratio with a display area of 25.4cm x 16.9cm and a resolution of 2160 x 1440.

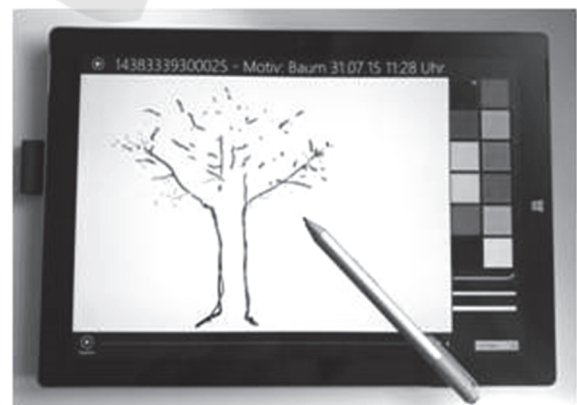


Figure 1: Digital device with drawing program.

Texture characteristics based on Haralick's GLCM (Haralick et al., 1973) describe visual

patterns of an image, regarding its structural surface arrangement. The GLCM is a square matrix where the number of rows and columns is equal to the number of different gray levels in the image. Each GLCM matrix element (i,j) represents the frequency a pixel with gray level value i is adjacent to a pixel of value j for a given distance d and angle θ, which defines the direction of the spatial relationship between both intensities i and j. GLCM texture features are extracted using the nearest neighbor distance d=1 and the four angles θ=0° (horizontal), θ=90° (vertical), θ=45° (right-diagonal) and θ=135° (left-diagonal).

For example we look at an image with window size four and four gray levels:

Table 1: Example of a 4x4 image matrix with four gray tones.

0	1	1	3
0	0	2	3
1	2	3	0
2	3	3	2

The corresponding GLCM at distance d=1 and angle θ=0° is then defined as:

Table 2: Gray-level co-occurrence matrix of example image with distance=1 and angle=0°.

	j=0	1	2	3
i=0	1	1	1	0
1	0	1	1	1
2	0	0	0	3
3	1	0	1	1

By dividing each GLCM element (i,j) by the total sum of the matrix elements, the resulting elements P(i,j) of the normalized GLCM can be considered as the probabilities of finding the specific spatial relationship. Haralick proposed several scalar texture measures which are extracted from the normalized GLCM. With

P(i,j) = Element ij of the normalized GLCM  
 N = Number of gray levels in the image

$$\mu = \sum_{i,j=0}^{N-1} i P(i,j)$$

$$\sigma^2 = \sum_{i,j=0}^{N-1} P(i,j) (i - \mu)^2$$

the following texture features were calculated:

- **Entropy:** Measures the local variations in the GLCM. The entropy is small when the image is texturally uniform.

$$entropy = \sum_{i,j=0}^{N-1} -\ln P(i,j) P(i,j) \quad (1)$$

- **Correlation:** Measures the gray level linear dependence between the pixels at the specified positions relative to each other.

$$correlation = \sum_{i,j=0}^{N-1} P(i,j) \frac{(i - \mu)(j - \mu)}{\sigma^2} \quad (2)$$

- **Homogeneity:** Large homogeneity values indicate that the image contains only few gray levels.

$$homogeneity = \sum_{i,j=0}^{N-1} \frac{P(i,j)}{1 + (i - j)^2} \quad (3)$$

- **Format full frame:** The area covered by tree image pixels in relation to the available display area.

All statistical calculations were done using SAS (Version 9.4) and p-values < .05 were considered to be significant.

### 3 RESULTS

**Entropy:** Frequency polygon charts of entropy data separated by subject groups (Figure 2a) revealed a much more right skewed distribution of demented patients than the distribution of the healthy subjects. These indicated smaller entropies, i.e., more uniform images, in the early AD group. Median comparisons with Mann-Whitney-U-Tests supported this by significant differences between healthy and early demented subjects with a p-value < .0001 (Figure 2b).

**Correlation:** Both distributions of texture correlation were left skewed but with a smaller peak for the early AD group, revealing smaller texture correlations for the demented (Figure 3a). Median comparisons of texture correlation supported this by showing significant differences between both subject groups (p<.05) (Figure 3b).

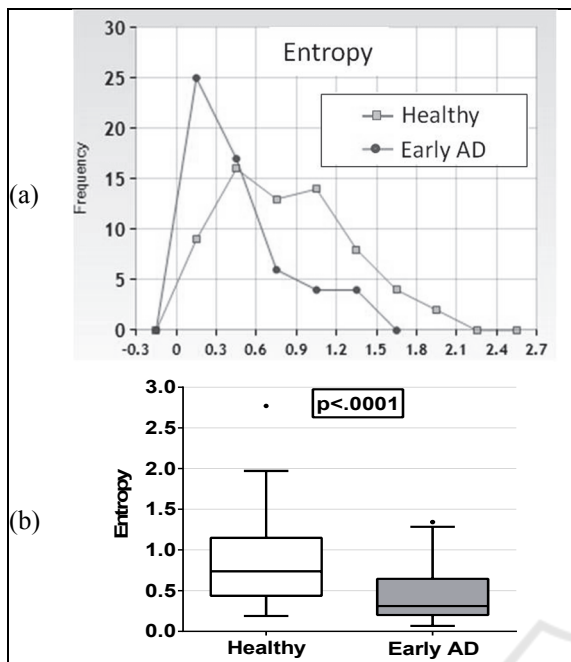


Figure 2: Frequency polygon charts (a) and boxplots (b) of GLCM texture entropy separately for healthy subjects (n=67) and patients with early AD (n=56).

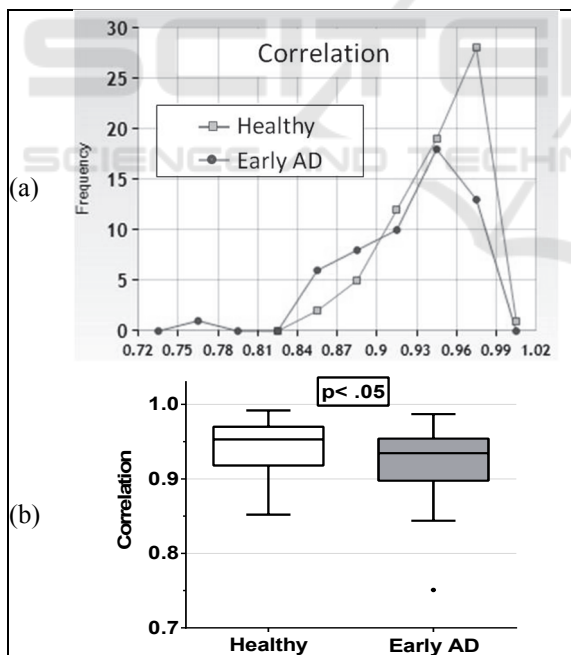


Figure 3: Frequency polygon charts (a) and boxplots (b) of GLCM texture correlation separately for healthy subjects (n=67) and patients with earlyAD (n=56).

**Homogeneity:** The left skewed distribution of the demented was, compared to the healthy group, more shifted to the right, indicating more homogenous

images for them (Figure 4a). This was supported by a significant larger median in the early AD group (p-value < .0001) (Figure 4b).

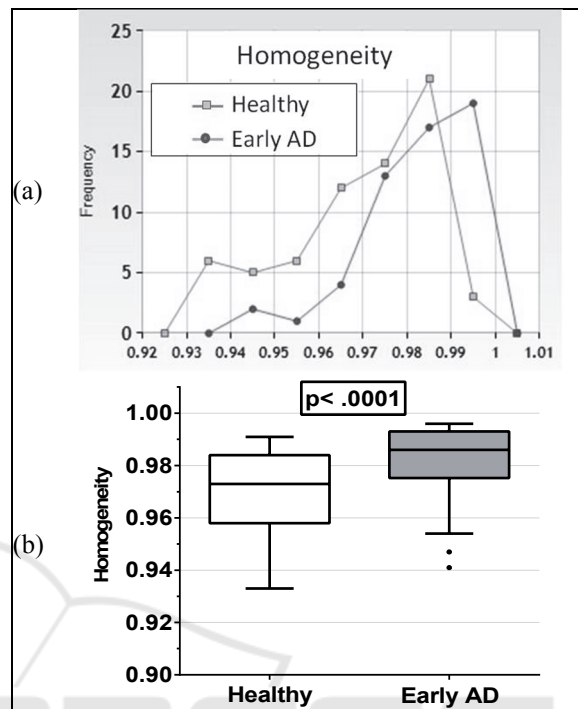


Figure 4: Frequency polygon charts (a) and boxplots (b) of GLCM texture homogeneity separately for healthy subjects (n=67) and patients with earlyAD (n=56).

**Format full frame:** The distribution of the early AD group was nearly symmetric compared to a left skewed distribution of the healthy group (Figure 5a). The images of the cognitive impaired subjects were significant smaller than those of the cognitive healthy ones (Mann-Whitney-U test, p-value < .0001) (Figure 5b).

A **ROC-curve analysis** was performed to evaluate if a combination of the texture characteristics was able to discriminate well between cognitive healthy and subjects with early dementia. The ROC-Curve was calculated with a gender-, education- and age-adjusted logistic regression model. All four texture feature entropy, correlation, homogeneity and format full frame were included as factors (Figure 6). The corresponding AUC was equal 0.864 with a 95% confidence interval of [0.799; 0.929]. The Youden-Index calculation resulted in a sensitivity of 0.804 and a specificity of 0.788.

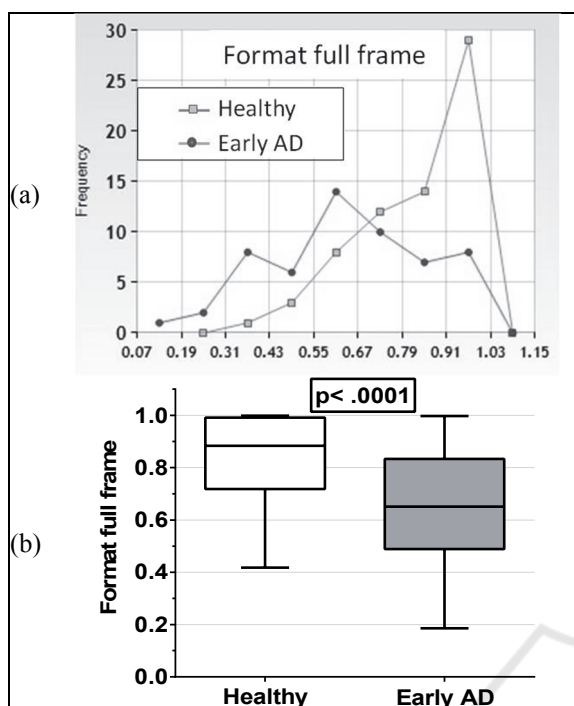


Figure 5: Frequency polygon charts (a) and boxplots (b) of the picture size (format full frame) separately for healthy subjects (n=67) and patients with earlyAD (n=56).

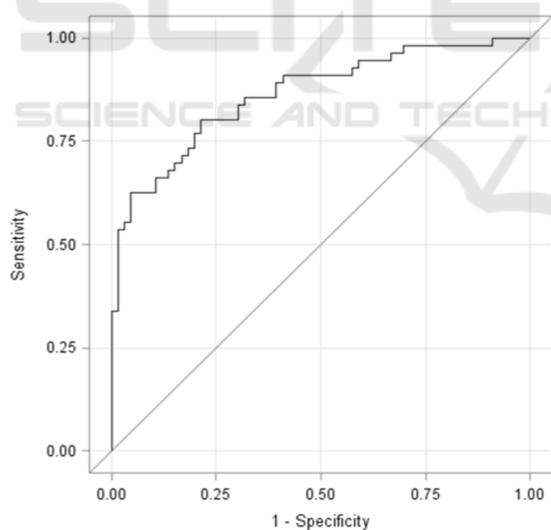


Figure 6: ROC curve for discrimination of healthy subjects (n=67) from patients with early AD (n=56).The logistic regression model was adjusted for gender, age and education level and texture variables entropy, correlation, homogeneity and format full frame were includes as factors.

## 4 CONCLUSIONS

The study investigated if gray-level co-occurrence texture features of digital drawings can contribute to the differentiation between cognitive healthy and mildly demented patients. Subjects in an early stage of Alzheimer’s dementia showed significant differences in texture features compared to cognitive healthy subjects. A reduction in entropy, correlation and picture size and an increase in homogeneity were observed for the early demented group. In line with these findings, characteristic drawing disorders of AD patients have been reported in literature as omissions, simplifications, and impaired perspective and spatial relations (Gragnaniello et al., 1998; Kirk and Kertesz, 1991; Trojano and Gainotti, 2016). The ROC-Curve, with all texture characteristics included, separated cognitive healthy and early demented subjects very good with an AUC of 0.86.

Essential requirements to a dementia screening tool are a high sensitivity and specificity and a fast and easy handling procedure with a good patient acceptance. Our obtained results indicate that the analysis of texture features in a digital drawing test might be a reasonable approach to discriminate between healthy and early demented subjects as it results in a sensitivity and specificity of about 80%. The creative procedure of drawing a tree without performance pressure and time restrictions is furthermore less stressful than for example memory tests, where the patient is confronted with his cognitive deficits. This leads to a good patient’s acceptance. Using a digital device instead of paper allows for an objective evaluation of drawing features and the images don’t have to be rated by a trained specialist.

Although the study results are very promising, further analysis and validation is needed, especially with a larger sample size and the inclusion of persons with amnesic mild cognitive impairment, who are more likely to develop AD than people without it (Petersen, 2004).

Our future aim is to automatically calculate a decision-value from the linear combination of the texture features adjusted for age, gender and education and to provide a cut-off value for healthcare professionals to support their decision whether the patient needs further clinical examinations or not.

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