Analysis of the Use of Colour for Early Detection of Dementia

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Abstract: Cognitive visuo-constructive impairments, which can be detected by drawing tasks are early signs of Alzheimer's disease (AD). Additionally, several studies revealed deficits in colour perception for patients with AD. In a former analysis of the impact of digital tree-drawing parameters on the screening of early dementia, a logistic regression revealed the number of colours together with the drawing velocity and the number of line widths changes as discrimination characteristics (ROC AUC=0.90, sensitivity=.86, specificity=0.82). To analyse the diagnostic importance of colour variations in drawings, a reanalysis of these data was done with 67 healthy subjects (25 females, mean age 66 ± 10 yrs.) and 56 subjects with early AD (40 females, mean age 73 ± 9 yrs.). The exclusion of colour variables resulted in a good discrimination of healthy and AD (ROC AUC=0.89, specificity=0.89) but in a reduction of sensitivity to .77 compared to the former model. This suggest that the analysis of colour variations in drawings has an important diagnostic impact.

1 INTRODUCTION

Although the neurodegenerative process of AD cannot be stopped yet, an early diagnosis allows for the application of symptomatic therapies which can temporally reduce symptoms and maintain the patient's level of life quality and functioning (Alzheimer's Association, 2018).

Several drawing tests, such as Shulman's clock drawing test (Shulman, Gold, Cohen, & Zucchero, 1993) or the Rey–Osterrieth complex figure test (Shin, Park, Park, Seol, & Kwon, 2006), have been established to screen for dementia in assessing several cognitive functions, e.g. the eye-hand coordination, concentration, visuospatial and planning skills, and short-term memory (Freedman et al., 1994). These screening tests all have in common that the patient draws with a pen or pencil on a paper sheet and that the resulting picture is analysed by dementia specialists.

Actual studies suggest that the digital assessment of the total drawing process, including time and kinematic variables as well as texture features, provides additional prognostic information in detecting mild cognitive impairment and early AD. (Muller, Preische, Heymann, Elbing, & Laske, 2017; Robens, Heymann, et al., 2019; Robens, Ostermann, et al., 2019; Souillard-Mandar et al., 2016).

In the digital tree-drawing test (dTDT), which was firstly introduced by Heyman et al. (Heymann et al., 2018), patients drew a tree from memory with a digital pen on a Microsoft Surface Pro 3 digitizer without time restrictions and optionally 12 colours and 3 line widths. The dTDT analysis of digitally recorded grey-level texture features revealed significant differences between cognitive healthy subjects and patients with early AD, indicating more homogeneity and less contrast in the pictures of the dementia patients (Robens, Ostermann, et al., 2019). Furthermore a current study on the dTDT analysed 19 dTDT characteristics with stepwise logistic regression models and identified the average painting velocity in combination with the variation in the use of colours and line widths as significant predictors for early AD (Robens, Heymann, et al., 2019). These results are in accordance with neuropsychological findings on colour vision deficiencies in AD patients (Safar & Press, 2011; Wijk, Berg, Sivik, & Steen,

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1999) and case reports on artists' drawings before and with AD (Lee, Tsai, & Chen, 2015; Maurer & Prvulovic, 2004).

As nearly all actual screening drawing tasks are based on pencil-paper drawings, the main question of the current analysis is, whether the exclusion of colour variables in a digital tree drawing task does influence the test's sensitivity.

2 MATERIAL AND METHODS

The participants came to the clinical ambulance of the Memory Clinic at the University Hospital of Tübingen from July 2015 to July 2016 in order to check their cognitive skills. All participants underwent neuropsychological testing. The healthy control subjects had no signs of cognitive impairments besides normal cognitive aging. Participants fulfilled the inclusion criteria of normal or corrected-to-normal visual acuity, of no severe hearing impairments and had the ability to perform tests and drawings without physical restrictions. The study was approved by the local ethical committee of the University Hospital of Tübingen and all participants signed an informed consent form after receiving a detailed explanation of the study.

The diagnostic criteria for early dementia of Alzheimer's type (eAD) were defined according to the National Institute of Neurological and Communicative Disorders and Stroke Alzheimer's Disease and Related Disorders Association (McKhann et al., 1984). All 56 patients diagnosed with eAD had a score of 3 or 4 on the Global Deterioration Scale (Reisberg, Ferris, de Leon, & Crook, 1982).

In addition to the conventional neuropsychological tests, participants performed the dTDT (Heymann et al., 2018). They were asked to draw a tree from their memory with a digital pen on a Microsoft Surface Pro 3 digitizer with no time limit for painting. Windows 8.1 Pro software was implemented on this multi-touch digital device with an Intel Core i7-4650U processor (1.7 - 3.3 GHz). The size of the display area was 25.4 times 16.9 cm with a resolution of 2160 x 1440. The participants could hold the display upright or crosswise by drawing and were able to choose between 3 lines widths and 12 different colours. The participants became familiar with the device in drawing one sample-tree before the actual test started.

The impact of dTDT variables was analysed using logistic regression models adjusted for age, education level and gender. Receiver operating characteristic (ROC) curves of the logistic models and areas under curves (AUCs) were calculated and compared. Sensitivities and specificities of different models based on Youden-index cut-points were calculated. All statistical calculations were done using SAS (Version 9.4) and p-values < .05 were considered significant.

3 RESULTS

The study population included 67 cognitive healthy subjects (Controls; mean age 65.9 ± 10.3 years; 25 females) and 56 patients with early Alzheimer's disease (early AD; mean age 72.7 ± 9.2 years; 40 females).

The years of education were on average 3 years lower in the early AD (11 years) compared to control (14 years). The percentage of females was higher in the group of early AD (71%) compared to the control group (37%) and early AD subjects were on average 6.8 years older. These demographic differences suggest an adjustment in the logistic model analysis for age, gender and education. A brief summary of the subjects' characteristics is given in Table 1.

Table 1: Means, standard deviations (SD), median (Med) and interquartile range (IQR) of clinical and demographic characteristics.

	N	Mean	SD	Med	IQR
Control					
Male/female	42/25				
Age (yrs.)	67	65.9	10.3	65	[59, 74]
Education (yrs.)	66	14.1	3.0	15	[12, 17]
GDS	67	2.1	2.0	1	[0, 4]
MMSE	67	29.3	0.8	29	[29, 30]
CDT	67	1.2	0.6	1	[1, 1]
Early AD					
Male/female	16/40				
Age (yrs.)	56	72.7	9.2	74	[67, 80]
Education (yrs.)	56	11.1	2.9	11	[8, 13]
GDS	56	3.1	2.2	3	[2, 4.5]
MMSE	55	22.3	2.9	22	[20, 25]
CDT	56	2.8	0.9	3	[3, 3]

GDS=Geriatric Depression Scale; MMSE=Mini Mental State Examination; CDT=Clock Drawing Test.

Figure 1 illustrates examples of tree drawings from two subjects of the control group, and two subjects from the early AD group. As can be seen, the pictures clearly differ in their use of colours. However, there are also obvious differences in the shaping and the complexity of the pictures.

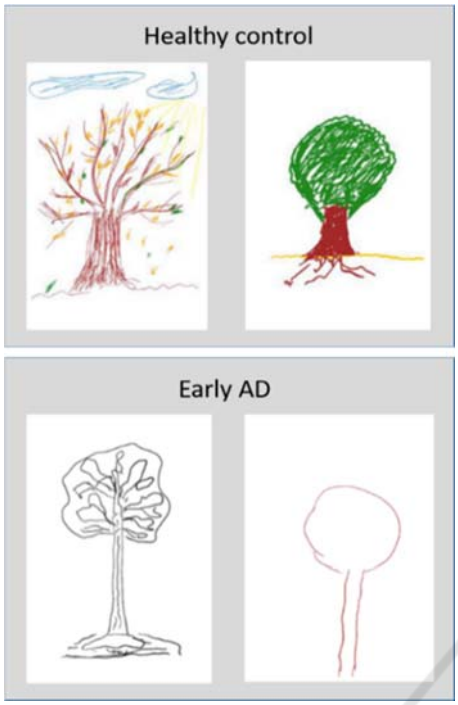

Figure 1: Examples of digital tree drawings of two healthy controls and two early AD participants.

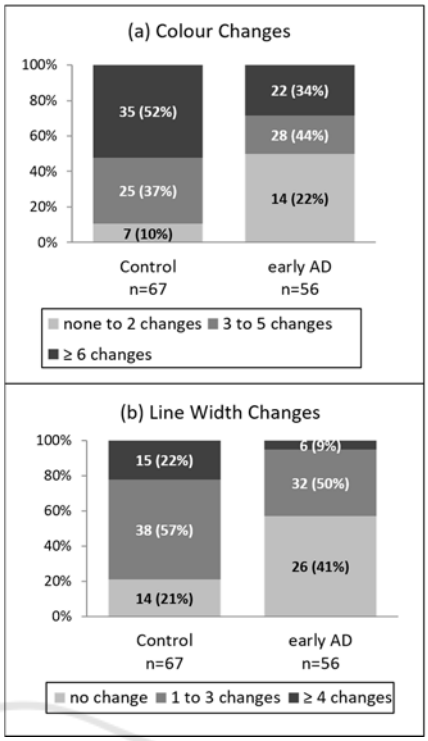

Figure 2: Number and percentages (in brackets) of subjects with number of colour and line width changes during the drawing process.

Number of Colour- and Line Width Changes

There were significant differences in the number of line width and colour changes during the painting process between the subject groups (Figure 2, all p-values of chi-square test < .0001) with less colour and line width changes in cognitive impaired patients compared to healthy subjects. Fifty percent of the patients with early AD only used one colour compared to 10% in the control group.

Number of Different Colours and Line Widths

In both subject groups, the most used colours were green and brown, followed by yellow-orange. Except for black, all colours were more often used by healthy subjects (Figure 3).

There was a significant difference in the mean number of used colours and line widths between healthy and early AD subjects (Table 2, p-values <.001), indicating less colour and line width variations in cognitive impaired individuals.

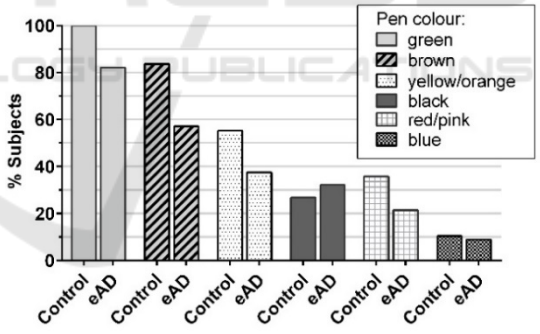

Figure 3: Percentage of subjects using a specific colour, grouped by healthy control and early AD (eAD).

Table 2: Means, standard deviations (SD), median (Med) and interquartile range (IQR) of dTDT characteristics.

	Mean	SD	Med	IQR
Control				
No. of colours	4.6	1.8	4	[3, 6]
No. of line widths	2.2	0.8	2	[2, 3]
Early AD				
No. of colours	3.3	1.6	3	[2.5, 4]
No. of line widths	1.6	0.7	1	[1, 2]

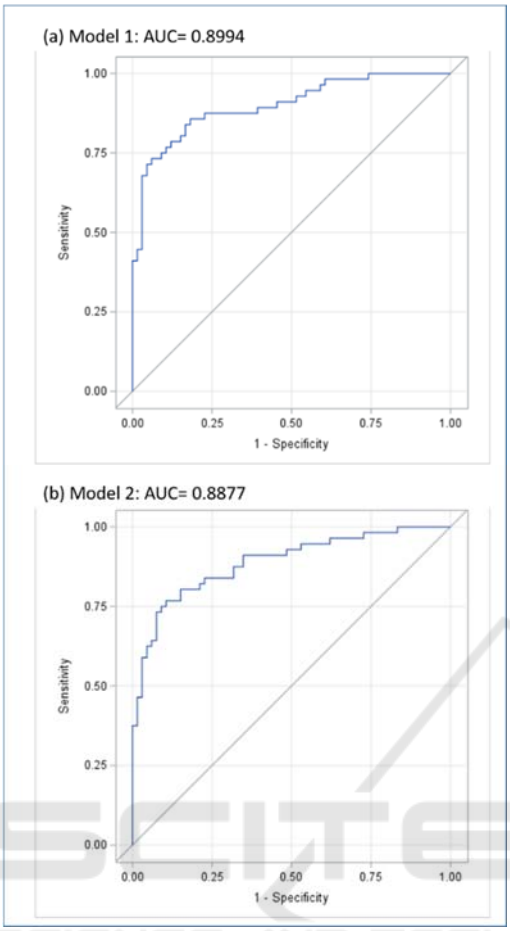

Figure 4: ROC-curves of model 1 (a) with number of colours, number of line widths and average velocity as factors and model 2 (b) with number of line widths and average velocity as factors. Both models were adjusted for age, gender and years of education.

Table 3 summarizes the results of the two logistic regression models with and without colour variables included (model 1 and model 2, respectively). Both models were adjusted by age, gender and education level by including these variables as covariates. In both models, the number of used line widths is a significant and stable predictor with ORs of 0.328 (model 1) and 0.283 (model 2). The same stability holds for the average velocity of the strokes, which is quite comparable within both models (ORs of 0.840 and 0.850). The AUC's of the ROC-curves based on both logistic regression models (figure 4) ranged between 0.89 (model 2, without colours) and 0.90 (model 1), indicating only a slight loss of discrimination power for model 2. Youden-Index calculations resulted in sensitivities of 86% (model 1) and 77% (model 2) and in specificities of 82% (model 1) and 89% (model 2).

Table 3: Results of logistic regression of healthy controls (n=67) versus patients with early AD (n=56). Models adjusted for gender, age and education.

Model	AUC	Spec. %	Sens. %	Variable	OR	95% CI_{OR}
1	.90	82	86	**Colours**	0.67	[0.47, 0.97]
				Line widths	0.33	[0.17, 0.64]
				Velocity	0.84	[0.74, 0.96]
2	.89	89	77	**Line widths**	0.28	[0.15, 0.54]
				Velocity	0.85	[0.74, 0.97]

AUC: Area under curve of receiver operating curve, ß: Estimated logistic regression coefficient, OR: Odds ratio, CI_{OR}: Confidence Interval of odds ratio; Specificity (Spec.) and Sensitivity (Sens.) are based on Youden-Index calculations.

4 CONCLUSIONS

In accordance with the literature we observed reduced colour variations in the images of early AD patients and found a good separation of healthy from early AD subjects by combining the number of used colours with the average painting velocity and the number of line width changes (ROC AUC=0.90).

After omitting the colour information from the logistic regression the corresponding AUC was still good and only slightly smaller (AUC= 0.89), but the Youden-index calculation revealed a reduction in sensitivity (0.77).

Several drawing deficits have been reported with early stages of AD, e.g. image simplifications, reduced image sizes and disorders of spatial relations and perspectives (Gragnaniello, Kessler, Bley, & Mielke, 1998; Heymann et al., 2018; Trojano & Gainotti, 2016). Paintings of AD patients have been described as a reduction in colour variations with a preference to yellow-red in early stages and a tendency to darker colours in later stages (Lee et al., 2015; Maurer & Prvulovic, 2004). Results of Wijk et al. (Wijk et al., 1999) and Pache et al. (Pache et al., 2003) suggest colour vision deficiencies in AD patients with difficulties in discriminating between blue-green colours.

One limitation of the current study is its small sample size and the results have to be validated in larger clinical settings. The differences concerning demographic parameters as age, gender, and education level, indicated an adjustment in the logistic regression model. With larger sample sizes, pre analysis matching of subjects can be applied to avoid demographic differences between subject groups.

In further analyses, the percentage composition of colours should be examined, too, as this might be an important characteristic for identifying patients with early AD.

Our results suggest that the number of colours used in a free tree-drawing task has an impact on discriminating healthy subjects from patients with early AD. Nevertheless, a good separation of both subject groups was also achieved by only including the average velocity and the number of stroke changes in the ROC-curve analysis.

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