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Classifying Alzheimer's disease, Lewy body dementia, and normal controls using 3D texture analysis in magnetic resonance images

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ABSTRACT

Dementia is an evolving challenge in society and early intervention is important. The ability to distinguish between different dementia and non-dementia early in course may be essential for successful patient care. Magnetic resonance (MR) imaging may aid as a noninvasive method to increase prediction accuracy. In this work we explored the use of two different 3D local binary pattern (LBP) texture features extracted from T1 MR images of the brain combined with a random forest classifier in an attempt to discern patients with Alzheimer's disease (AD), Lewy body dementia (LBD), and normal controls (NC). Analysis were conducted in areas with white matter lesions (WML) and normal appearing white matter (NAWM). We also calculated correlations between texture features and cognition measured by mini mental state examination (MMSE) controlling for age. Additionally, two different methods for handling the imbalanced data problem were tested, namely cost-sensitive classification and resampling of the data using the synthetic minority oversampling technique (SMOTE). Four different classification tasks were extensively tested, a three-class problem: AD vs. LBD vs. NC, a two-class problem: NC vs. AD, a two-class problem NC vs. LBD, and a two-class problem: AD vs. LBD. Results from 10 folds nested cross validation are reported as mean accuracy, precision, and recall with standard deviation in brackets. The two-class problems NC vs. AD and NC vs. LBD, show encouraging results with total accuracy of 0.97 (0.07) and 0.97 (0.06) respectively. The three-class problem and the two-class problem AD vs. LBD are not equally encouraging but shows higher accuracy than clinical diagnosis with a total accuracy of 0.79 (0.07) and 0.79 (0.15) respectively. Possible explanations may be that the AD- and LBD group are too similar concerning LBP texture analysis and that the LBD group is too small. Most of the texture features calculated for the AD subjects in the NAWM region were significantly correlated with cognition. Together with the positive classification results from the NAWM region this may suggest that the NAWM region is an important area for studying AD. Both cost-sensitive classification and resampling using SMOTE proved useful and improved the results considerably in many of the tests.

1. Introduction

The World Alzheimer Report 2010 [1] states that worldwide health care costs related to dementia were estimated to $604 billion and only set to rise. The 2014 edition of the yearly updated report states that the number of people living with dementia worldwide today is estimated to 44 million and that the strongest causal associations with dementia are those of low education in early life, hypertension in midlife, and smoking and diabetes across the life course. A great challenge in the global society is the increasing age in the population, since age is the primary marker for developing dementia. 50–60% of people with dementia have developed Alzheimer's disease (AD) which makes it the most common neurogenerative dementia [2]. Amyloid plaques and neurofibrillary tangles are the classical neuropathological findings of AD [3]. Lewy body pathology in brain stem, forebrain, and limbic and cortical structures are the defining pathological features for Dementia with Lewy bodies (DLB). Together with dementia associated with Parkinson's disease (PDD) DLB account for 15–20% of people with neurodegenerative dementia [2]. The DLB and PDD

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are often combined into a Lewy body dementia group (LBD) [4,5]. Clinical symptoms in LBD do not inherit a strong relationship with regional distribution and frequency of Lewy bodies [6]. This could suggest a possible link between LBD and other neurodegenerative dementia such as AD. Pathology and vascular brain changes related to AD, which also are common in the elderly, may contribute to the clinical presentation of LBD as well. Thanvi et al. [7] points out that vascular changes in the basal ganglia are common in the elderly and may cause parkinsonism and cognitive impairment. AD and LBD lack established diagnostic biomarkers. The neurological changes related to typical symptoms in neurodegenerative dementia are difficult to understand and make them challenging to prevent, delay, or cure. As in many other chronic diseases, the main approach towards these patient groups is helping patients maintain an acceptable mental functioning, managing typical behavioral changes, and slowing symptom progression. There exists important evidence that a reduced dementia risk can be achieved through reduction in tobacco use, increasing the ability to detect and control hypertension and diabetes as well as cardiovascular risk factors. To achieve this early intervention is important. The ability to distinguish between AD and normal controls (NC) as well as LBD and NC early in course may be essential for successful patient care. Differentiating between AD and LBD is also important since they differ in prognosis and response to drug treatment, but may be difficult to discern clinically early in the disease course. s The amyloid hypothesis for AD, with accumulation of peptide amyloid beta (Aβ) in the brain, have been a prevailing motivation for research activity for years. A critical reappraisal was given by Hardy in [8]. The efficient transmission of neural activity provided by the white matter (WM) complements information processing in the gray matter (GM). In his review paper [9], Bartzokis proposes a hypothesis where aging myelin is exposed to a host of insults and may initiate a cascade of events ending in dementia. From this perspective plaque and tangle formation are secondary and a result of failed myelin repair. Others have also pointed to the importance of studying WM in dementia [10,11]. White matter lesions (WML) can be seen as hyperintense areas on T2-weighted MR images and especially FLAIR MR images. WML is typically seen in Periventricular areas of the brain, but can also be found in deep white matter. With increasing age, healthy subjects can develop WML [12], but AD [13] and other dementia [14,15] have been shown to be associated with WML. Cortical changes developed as a consequence of WML might lead to cognitive decline and dementia [16]. Mild cognitive impairment (MCI), poor episodic memory, and late-life depression are associated with cerebral thinning and WML [17]. Disintegration of the normal appearing white matter (NAWM), which is the part of WM that is not affected by WML, is strongly related to the severity of WML [18]. This could indicate that WML as well as NAWM is important in dementia research.

Neuroimaging is an important tool for studying dementia and other diseases where cognitive degradation is an important symptom [19–22]. High statistical power and the ability to detect neurodegenerative changes early and non-invasively is some of the benefits. Computer aided diagnosis (CAD) is a branch in the neuroimaging field where the aim is to aid in diagnosis early in the disease course in a cost-effective manner and unbiased to human inconsistencies [23]. Even though many have put focus on AD and MCI [24–27], little effort has been put into developing CAD systems for LBD [28]. Clinical diagnosis of LBD depends on dopamine transporter scan and postmortem histology. The application of texture analysis in a machine learning (ML) environment has shown success in discerning MCI, different dementia as well as NC [29–32]. As of the authors knowledge, the only paper considering texture analysis as an approach to distinguish AD, LBD, and NC is [33].

Local binary pattern (LBP) was introduced as a texture descriptor by Ojala et al. [34,35] and Unay et al. [36] showed that the rotation invariant LBP is invariant to some common MRI artifacts which makes it a robust texture feature when used in brain MR image analysis. Even though 2D slice by slice approaches are successful, 3D texture features have shown to be an important step towards better discrimination in machine learning systems, especially when the images are intrinsic three dimensional like many MR modalities are [37]. Zhao and Pietikäinen [38] developed the volume LBP (VLBP) texture feature and demonstrated its robustness in dynamic images. In the same paper, the authors suggest to calculate the LBP values in all three orthogonal directions as an option for 3D texture feature calculation, calling it LBP three orthogonal planes, LBP-TOP.

Earlier we have shown that there neither were significant differences in WML volume between patients with AD and patients with LBD nor between patients with dementia and NC in [39]. In [40], we showed that regional WML volume used as features in a maximum likelihood classifier can distinguish between patients with dementia and NC to some degree, but that LBP features calculated in the WML area of fluid attenuated inversion recovery (FLAIR) MR images gives higher accuracy. In our previous work [41], we found that the best classification performance was reached when textural features were calculated from the T1 MR images rather than the FLAIR images. Part of the reason may be that the FLAIR MR images are prone to noise and have low image resolution in the interslice direction. WML segmentation can be challenging, however, high quality WM segmentation is readily available through many software packages such as FSL [42], SPM [43], and Freesurfer [44]. Therefore, we compared the classification performance between features extracted from WML regions to all of WM, and found only small differences. Additionally, since the data set was imbalanced, we applied the synthetic minority oversampling technique (SMOTE) [45] and found that upsampling of the data increased the classification performance in most of the tests.

T1 MR images are 3D images with the same resolution in all directions. A natural question is if features calculated using a 3D neighborhood rather than a 2D slice-wise approach, would increase the classification accuracy. To the authors' knowledge no other papers exist doing 3D textural feature extraction from MR images for classification of LBD subjects from subjects with other dementias and NC. In this paper a 3D approach is taken using the T1 MR images to classify different dementia types and normal controls. Two different ways of calculating 3D textural features are investigated. With the ambition to investigate whether the status of brain tissue health plays a role, features calculated from two different 3D regions of the brain are compared. In addition to applying 3D texture analysis to WML regions, features from regions of healthy white matter are used as well. In addition to performing classification on the original data and using SMOTE to handle the imbalanced data problem, we also applied cost sensitive classification. Finally, the clinical relevance of the 3D LBP features is investigated by calculating the correlation between texture features and cognition.

The paper is organized as follows: Section 2 describes the data material, Section 3 the image preprocessing and image processing methods, and Section 4 the proposed method and experimental setup. Section 5 reveals the results and the paper ends with a discussion 6.

2. Material

2.1. Subjects

The data material for this study were MR images of dementia subjects drawn from the DemWest cohort, Stavanger, Norway and MR images of the NC subjects from the ParkWest cohort, Stavanger, Norway. Criteria for inclusion- and exclusion can be found in [2] and [46] respectively. The dementia- and NC subjects were matched for sex, age, and years of education.