BAYESIAN-BASED EARLY DETECTION OF COGNITIVE IMPAIRMENT IN ELDERLY USING fNIRS SIGNALS DURING COGNITIVE TESTS

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Abstract: This paper presents a new trial approach to early detection of dementia in the elderly with the use of functional brain imaging during cognitive tests. We have developed a non-invasive screening system of the elderly with cognitive impairment. In addition of our previous research of speech-prosody based data-mining approach, we had started the measurement of functional brain imaging for patient having a cognitive test by using functional near-infrared spectroscopy (fNIRS). We had collected 42 CHs fNIRS signals on frontal and right and left temporal areas from 50 elderly participants (18 males and 32 females between ages of 64 to 92) during cognitive tests in a specialized medical institute. We propose a Bayesian classifier, which can discriminate among elderly individuals with three clinical groups: normal cognitive abilities (NL), patients with mild cognitive impairment (MCI), and Alzheimer's disease (AD). The Bayesian classifier has two phases on the assumption of screening process, that firstly checks whether a suspicion of the cognitive impairment (CI) or not (NL) from given fNIRS signals; if any, and then secondly judges the degree of the impairment: MCI or AD. This paper also reports the examination of the detection performance by cross-validation, and discusses the effectiveness of this study for early detection of cognitive impairment in elderly subjects. Consequently, empirical results that both the accuracy rate of AD and the predictive value of NL are equal to or more than 90%. This suggests that proposed approach is adequate practical to screen the elderly with cognitive impairment.

1 INTRODUCTION

It is no doubt about abrupt increase in elderly patients with dementia due to growing super-aging society in developed countries. Research and development of new dementia medications is accelerated. Development of the early detection methods for dementia that are both sensitive and specific is also very important as a diagnostic tool.

To screen for dementia and cognitive impairment, a questionnaire test such as Mini-Mental State Examination (MMSE) (Folstein et al., 1975), Revised Hasegawa's Dementia Scale (HDS-R) (Imai and Hasegawa, 1994), Clinical Dementia Rating (CDR) (Morris, 1993), and Memory Impairment Screen (MIS) (Buschke et al., 1999), is commonly used in addition to a neurophysiological test (Zhang et al., 2011) (e.g., using MRI (de Leon et al., 2004), FDG-PET (Mosconi et al., 2010), and CSF biomarkers (de Leon et al., 2007)). Questionnaire tests have some disadvantages and their use is limited in the clinic. The MMSE, HDS-R, and CDR are more time-consuming than a general practitioner's consultation. In general, the questionnaire cannot completely dismiss the influence of education, social class, and gender difference on the results. In addition, there is a possibility that practitioner subjectivity may affect the scoring. Thus, we believe that the development of a simple, non-invasive examination that is objective and combined with a physiological test could enables the early detection of dementia in a broad population.

In our previous study, we have studied a novel approach to the early detection of cognitive impairment in the elderly (Kato et al., 2011), in which we focused on the prosodic features of speech sound during the subject's answers to the questionnaire. The method had an advantage that enables everyone to check his/her own cognitive ability anywhere because

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Table 1: A Breakdown list of participants (N=50).

Age	64-70	71-75	76-80	81-85	86-92	Total
Male	3(2,0,1)	2(1,1,0)	4(3,1,0)	7(1,4,2)	2(0,0,2)	18(7,6,5)
Female	7(4,2,1)	7(5,2,0)	8(2,5,1)	6(2,1,3)	4(1,3,0)	32(14,13,5)
Subtotal	10(6,2,2)	9(6,3,0)	12(5,6,1)	13(3,5,5)	6(1,3,2)	50(21,19,10)

Value in bracket means the number of subjects in NL, MCI, AD clinical groups.

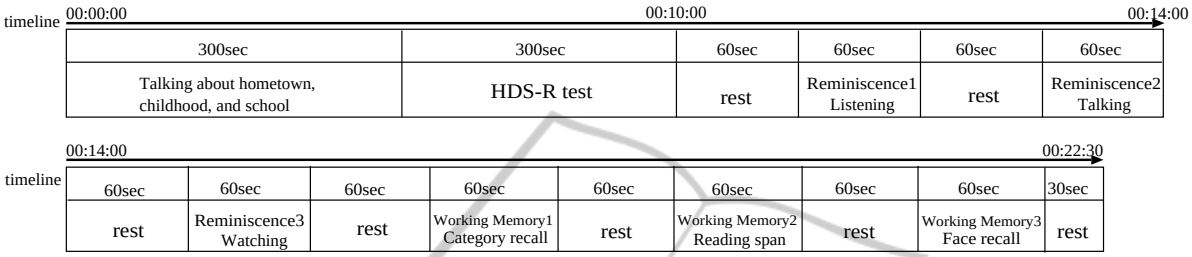


Figure 1: Block design task of cognitive tests.

of using speech signals only. The method is effective for the first step of screening for dementia, but, however, it has limitations of the reliability because the method does not measure brain function. On the other hand, a neurophysiological test, such as using MRI, FDG-PET, and CSF biomarkers, imposes severe constraint on a subject, for instance, pain at obtaining cerebral spinal fluid, radiation exposure, physical restraint and so on. This is a disadvantage in early screening, which should covers all elderlies.

In this study, we focus on functional near-infrared spectroscopy (fNIRS) as a brain function measurement system, which can eliminate physical restraint from a subject by non-invasive procedures, and develop a prototype for computer-aided diagnosis of cognitive impairment in the elderly with the use of fNIRS signals during cognitive tests. In this paper, we present signal processing technique of feature extraction and selection for hyper-dimensional time series data of fNIRS signals, and propose the two-phase Bayesian classifier for discriminating among elderly individuals with three clinical groups. In addition, we addressed the effectiveness of proposed method in discriminating among elderly individuals with normal cognitive abilities (NL), patients with mild cognitive impairment (MCI), and Alzheimer's disease (AD)

2 METHOD

2.1 Participants

Fifty Japanese subjects (18 males and 32 females between the ages of 64 and 92 years) participated in this study. Table 1 shows the breakdown list of participants. In this study, all participants are clinically conditioned that CDR of a participant in MCI group and AD group corresponds to 0.5 and 1, respectively.

2.2 Cognitive Tests

To measure brain function of an elderly during various cognitive tests including HDS-R, we have made a block designed task shown in Fig. 1, and then conducted simultaneous voice-fNIRS measurement during cognitive tests. Firstly a participant talks about the topics of hometown and childhood and answers for an HDS-R questionnaire test for ten minutes. And then, he/she does three reminiscence tasks (1. listening, 2. talking, 3. watching) and three working memory tasks (1. category recall, 2. reading span, 3. face recall) for twelve minutes. These six tasks are done for 60 seconds after rest gazing at a single point on the display for 60 seconds interval.

2.3 fNIRS Measurement

Functional near-infrared spectroscopy (fNIRS) can measure neural activity of the cerebral cortex using infrared rays that are safe to living organisms (Villringer and Chance, 1997). fNIRS monitors regional relative changes of oxy/deoxygenated hemoglobin concentration to measure cortical activation utilizing the tight coupling between neural activity and regional cerebral blood flow (Villringer and Firnafl, 1995). This measurement method requires only compact experimental systems and can eliminate physical restraint from a subject by non-invasive procedures (Fig. 2).

We used the fNIRS topography system FOIRE-3000 Near-Infrared Brain Function Imaging System

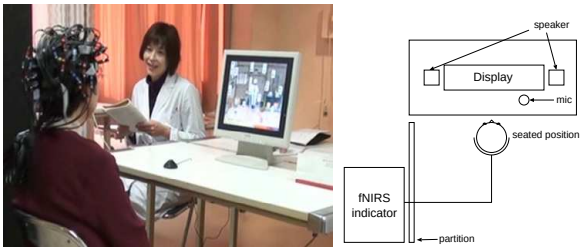


Figure 2: Snapshot of fNIRS measurement of an elderly participant having a cognitive test.

(Shimadzu, Kyoto, Japan), which uses near-infrared light with wavelengths of 780, 805, and 830 nm. We set 16 illuminators and 15 detectors in lattice pattern to form 42 channels (CHs) (22 CHs on frontal lobe, 10 CHs on right parietal and temporal lobe, 10 CHs on left parietal and temporal lobe) shown in Fig. 3.

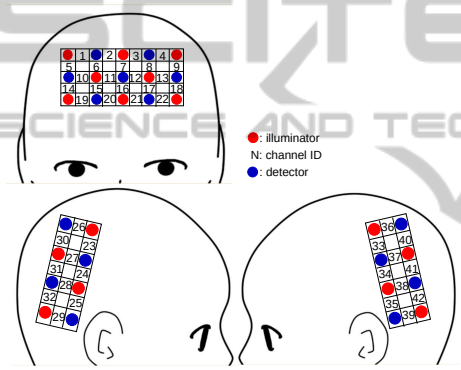
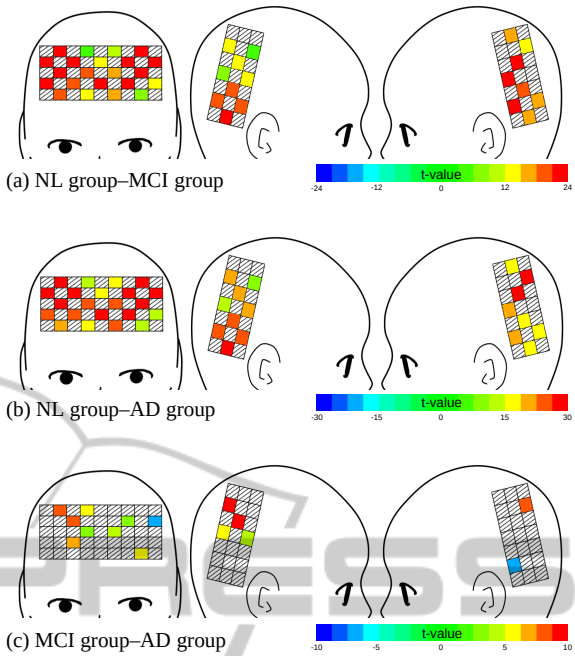


Figure 3: Channel arrangement of fNIRS measurement.

2.4 Statistical Tests of fNIRS Signals

Preliminary to development of the screening tool, we have conduct statistical tests of between-group significant differences using fNIRS signals of oxy-Hb during working memory task (1. category recall). We used two-tailed t-test with significance level of ($P < 0.001$) after applying Bonferroni's adjustment (1/42). Fig. 4 shows the results of t-test for significant differences in channel-wise fNIRS signals between any single pair from NL, MCI, and AD groups. The CHs that exhibited significant oxy-Hb increase are colored according to the t-values, as shown in the color bar, while those below the threshold are indicated in gray. The results indicate the significant difference of fNIRS signals during cognitive test between normal group and disease groups. This suggests that fNIRS signals during cognitive test have potential for detection of cognitive impairment in elderly patients. Additionally, for fNIRs signals during rest, there are no CHs with significant difference between any single pair from NL, MCI, and AD groups.



(a) NL group–MCI group

(b) NL group–AD group

(c) MCI group–AD group

Figure 4: Results of t-test for significant differences in channel-wise fNIRS signals between any single pair from NL, MCI, and AD groups.

3 CLASSIFICATION OF NL, MCI, AD GROUPS

The section describes a Bayesian classifier, which can discriminate among elderly individuals with three clinical groups: normal cognitive abilities (NL), patients with mild cognitive impairment (MCI), and Alzheimer's disease (AD). To design algorithm for computer-aided diagnosis of cognitive impairment in the elderly, we consider the screening process by a specialist in geriatrics. We thus propose a two-phase Bayesian classifier shown in Fig. 5 on the assumption of screening process, that firstly checks whether a suspicion of the cognitive impairment (CI) or not (NL) from given fNIRS signals; if any, and then secondly judges the degree of the impairment: MCI or AD.

3.1 Primitive Analysis of fNIRS Signals

In advance of Bayesian classification, we make a primitive signal processing fNIRS signals shown in Fig. 6. Firstly, we make five fNIRS signals every channels such that noise is reduced by channel-wise smoothing through three low-pass filters and difference filters (Fig. 7).

F1 (cutoff freq. 1.92[Hz]): to remove noise arisen from

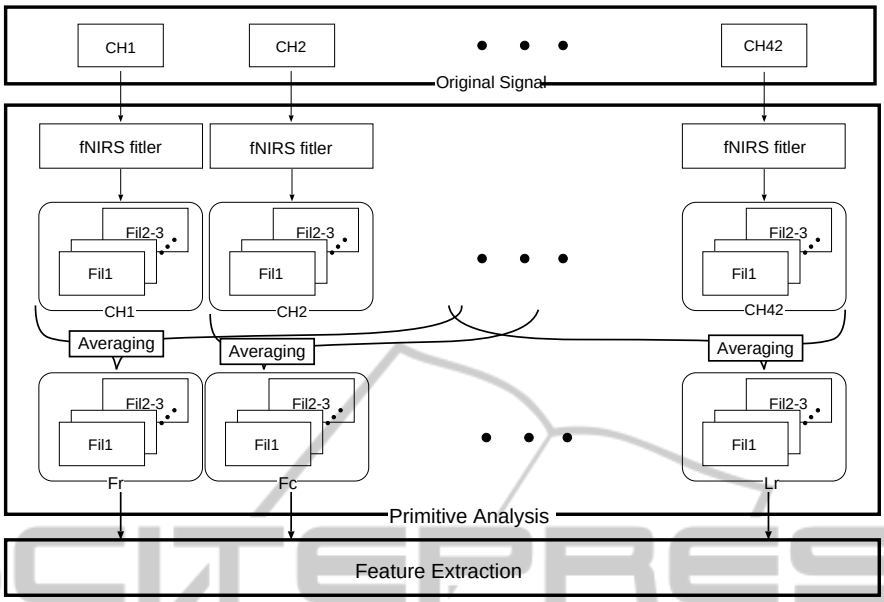


Figure 6: The outline of primitive analysis of fNIRS signals.

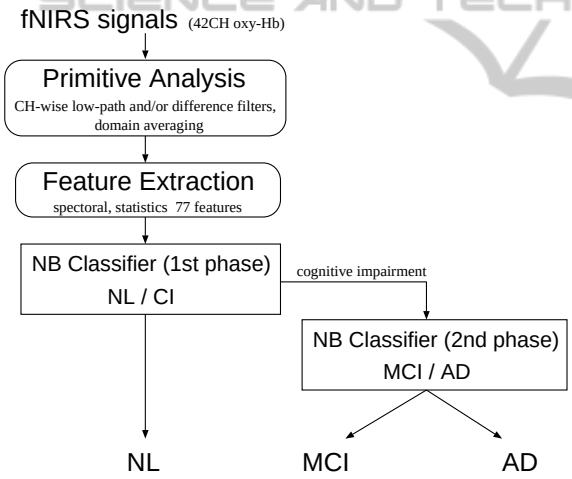


Figure 5: Classification of NL/MCI/AD by two-phase Bayesian Classifier.

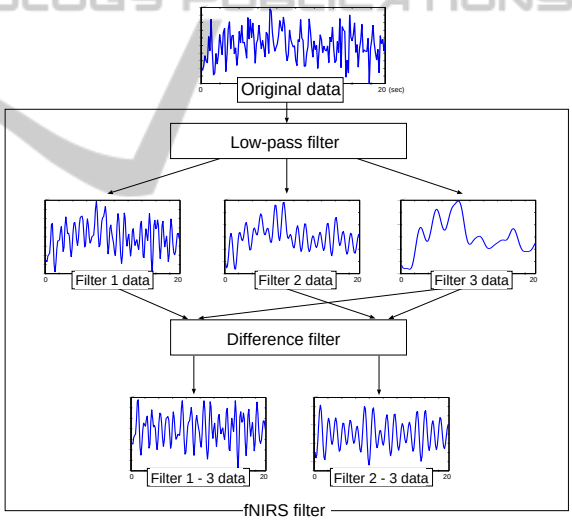


Figure 7: A filter design in fNIRS primitive analysis.

environmental light.

F2 (cutoff freq. 0.96[Hz]): to remove background noise arisen from biosignal such as pulse wave and blood pressure.

F3 (cutoff freq. 0.48[Hz]): to remove noise arisen from body movement such as jaw, eye, neck and so on.

F1-F3: to subtract F3 from F1.

F2-F3: to subtract F3 from F2.

Secondly, we segregate 42 CHs into the following seven brain areas and then make signal averaging that integrates fNIRS signals within each of the areas.

Fr: 7 CHs on the right side of frontal lobe (CH: 1,5,6,10,14,15,19).

Fc: 8 CHs on the central part of frontal lobe (CH: 2,3,7,11,12,16,20,21).

Fl: 7 CHs on the left side of frontal lobe (CH: 4,8,9,13,17,18,22).

Rf: 5 CHs on the front of right parietal lobe (CH: 23,24,26,27,30).

Rr: 5 CHs on the rear of right temporal lobe (CH: 25,28,29,31,32).

Lf: 5 CHs on the front of left parietal lobe (CH: 33,34,36,37,40).

Lr: 5 CHs on the rear of left temporal lobe (CH: 35,38,39,41,42).

Table 2: fNIRS feature candidates.

fNIRS filtered	Feature / Statistics
Filter 1 (F1)	Mean value (mean)
	Fundamental Frequency (f0)
	Centroidal Frequency (fc)
Filter 3 (F3)	Maximum value (max)
	Minimum value (min)
	Variance (var)
	Mean value (mean)
	Fundamental Frequency (f0)
	Gradient of the linear regression line (gr)
Filter1-3 (F1-3)	Variance (var)
Filter2-3 (F2-3)	Variance (var)

3.2 Extraction of fNIRS Features

We enumerate features that represents fluctuations of regional cerebral blood flow if it is the slightest effective in detection of cognitive impairment, and extract 11 features shown in Table 2 from fNIRS signals in each of the seven brain areas.

3.3 Bayesian Classifier

In this paper, we adopted naive Bayes classifier (NB), (Langley et al., 1992) which is a simple Bayesian classifier with strong independence assumption of attributes (Domingos and Pazzani, 1996). We construct two classifiers: $NB_{NL/CI}$, which checks whether a suspicion of the cognitive impairment (CI) or not (NL) at the first phase, if any suspicion, and $NB_{MCI/AD}$, which judges the degree of the impairment (MCI or AD) at the second phase.

In our strategy for feature extraction, all of the 77 fNIRS features described above may not be equally useful and important for discrimination among NL, MCI, and AD. In this study, we conduct systematic feature selection by using the forward stepwise (FSW) method (Draper and Smith, 1998), which is the most popular form of feature selection in statistics and consists of a combination of the forward selection and backward elimination methods. FSW is a greedy algorithm that adds the best feature (or deletes the worst feature) during each round. We make a model selection method based on the criterion of accuracy rate of the classification.

4 CLASSIFICATION ASSESSMENT

We have examined discrimination performance by modeling two-phase Bayesian classifiers for discriminating among elderly individuals with NL, MCI, and AD, by using fNIRS signals of oxy-Hb during working memory task (1. category recall) (see Fig. 1) collected from 50 participants (see Table 1). Table 3 shows the selected fNIRS features by each of NB classifiers. To evaluate detection performance, we adopted leave-one-out cross-validation.

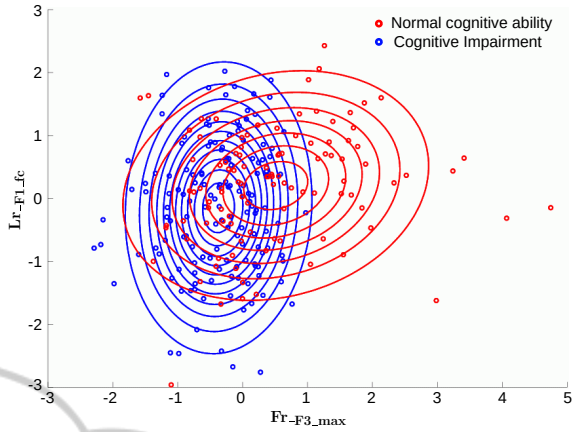


Figure 8: Distributions of NL/CI estimated by classifier $NB_{NL/CI}$.

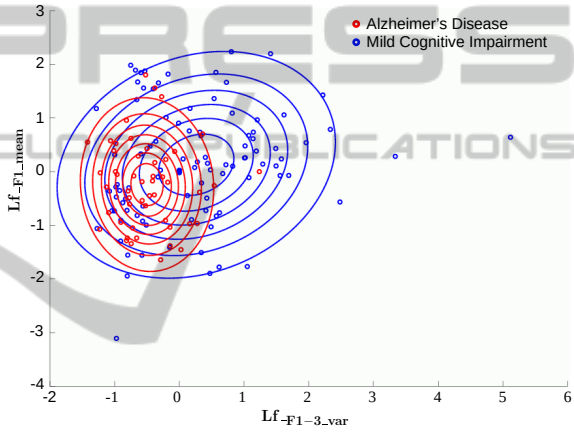


Figure 9: Distributions of MCI/AD estimated by classifier $NB_{MCI/AD}$.

Table 3: Selected fNIRS features.

Classifier	Selected Feature
$NB_{NL/CI}$	Fr_F3_max, Lr_F1_fc
$NB_{MCI/AD}$	Lf_F1-3_var, Lf_F1_mean, Fc_F1-3_var

Fig. 8 and Fig. 9 show the distributions of NL group / CI group and MCI group / AD group by classifiers $NB_{NL/CI}$ and $NB_{MCI/AD}$, respectively. In the figures, 250 samples (145 samples in Fig. 9), such that fNIRS signals are analyzed after divided into five spans, are plotted. fNIRS features are mean and vari-

Table 4: Classification results.

detection / clinical	NL	MCI	AD	accuracy
NL	11	7	3	52.4%
MCI	1	14	4	73.7%
AD	0	1	9	90.0%
predictive value	91.7%	63.6%	56.3	68.0%

ance normalize in each variable.

Table 4 shows the confusion matrices and the statistics of classification results using two-phase classifiers consist of $NB_{NL/CI}$ and $NB_{MCI/AD}$. The results indicate that both the accuracy rate of AD and the predictive value of NL are equal to or more than 90%. This means that no subject in AD groups are misclassified into NL group (only one is misclassified into MCI group), and that subjects classified into NL group are not all patient with AD (only one should be in MCI group). This suggests that proposed approach is adequate practical to screen the elderly with cognitive impairment. The results that the accuracy rate of MCI is 73.7% and that most of subjects misclassified are classified into AD group are both relative acceptable performance for screening tool.

5 CONCLUSIONS

We developed a new technology for early detection of cognitive impairment in the elderly, focusing on the brain activity during cognitive task. The detection method is based on the data mining approach using Bayesian classification and is simple and non-invasive procedure using functional near-infrared spectroscopy (fNIRS). We proposed a Bayesian classifier using fNIRS signals, which can discriminate among elderly individuals with three clinical groups: normal cognitive abilities (NL), patients with mild cognitive impairment (MCI), and Alzheimer's disease (AD). This paper also reported the examination of the detection performance by cross-validation, and the results that both the accuracy rate of AD and the predictive value of NL are equal to or more than 90%. Consequently, the empirical results suggested that proposed approach is adequate practical to screen the elderly with cognitive impairment.

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REFERENCES

Buschke, H., Kuslansky, G., Katz, M., Stewart, W. F., Sliwinski, M. J., Eckholdt, H. M., and Lipton, R. B. (1999). Screening for dementia with the Memory Impairment Screen. *Neurology*, 52(2):231–238.

de Leon, M. J., DeSanti, S., Zinkowski, R., Mehta, P. D., Pratico, D., Segal, S., Clark, C., Kerkman, D., DeBernardis, J., Li, J., Lair, L., Reisberg, B., Tsui, W., and Rusinek, H. (2004). Mri and csf studies in the early diagnosis of alzheimer's disease. *Journal of Internal Medicine*, 256(3):205–223.

de Leon, M. J., Mosconi, L., De Santi, K. B. S., Zinkowski, R., Mehta, P. D., Pratico, D., Tsui, W., Saint Louis, L. A., Sobanska, L., Brys, M., Li, Y., Rich, K., Rinne, J., and Rusinek, H. (2007). Imaging and CSF studies in the preclinical diagnosis of Alzheimer's disease. *Annals of New York Academy of Sciences*, 1097:114–145.

Domingos, P. and Pazzani, M. (1996). Beyond Independence: Conditions for the Optimality of the Simple Bayesian Classifier. In *Proc. of International Conference on Machine Learning*, pages 105–112.

Draper, N. and Smith, H. (1998). *Applied Regression Analysis (3rd edition)*. John Wiley & Sons.

Folstein, M. F., Folstein, S. E., and McHugh, P. R. (1975). "Mini-Mental State": A practical method for grading the cognitive state of patients for the clinician. *J. Psychiat. Res*, 12(3):189–198.

Imai, Y. and Hasegawa, K. (1994). The revised Hasegawa's Dementia Scale (HDS-R): evaluation of its usefulness as a screening test for dementia. *J. Hong Kong Coll. Psychiatr.*, 4(SP2):20–24.

Kato, S., Suzuki, Y., Kobayashi, A., Kojima, T., Itoh, H., and Homma, A. (2011). Statistical analysis of the signal and prosodic sign of cognitive impairment in elderly-speech: a preliminary study. In *Proc. of 5th International Jount Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2011)*, pages 322–327.

Langley, P., Iba, W., and Thompson, K. (1992). An analysis of Bayesian classifiers. In *Proc. of The Tenth National Conference on Artificial Intelligence (AAAI-92)*, pages 223–228.

Morris, J. C. (1993). The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology*, 43(11):2412–2414.

Mosconi, L., Berti, V., Glodzik, L., Pupi, A., De Santi, S., and de Leon, M. J. (2010). Pre-clinical detection of Alzheimer's disease using FDG-PET, with or without amyloid imaging. *Journal of Alzheimers' Disease*, 20(3):843–854.

Villringer, A. and Chance, B. (1997). Non-invasive optical spectroscopy and imaging of human brain function. *Trends Nurosci.*, 20:435–442.

Villringer, A. and Firnafl, U. (1995). Coupling of brain activity and cerebral blood flow: basis of functional nuroimaging. *Cerebrovasc. Brain Metab. Rev.*, 7:240–276.

Zhang, D., Wang, Y., Zhou, L., Yuan, H., Shen, D., and the Alzheimer's Disease Neuroimaging Initiative (2011). Multimodal classification of alzheimer's disease and mild cognitive impairment. *Journal of Neuroimage*, 55(3):856–867.