# Analysis of Effects of Parkinson's Disease on the Somatosensory System via CM-4 Tactile Stimulator

Olcay Kursun, Betul Erdogdu Sakar, M. Erdem Isenkul, C. Okan Sakar, Fikret Gurgen, Sakir Delil, Hulya Apaydin, Mark Tommerdahl and Oleg V. Favorov*

***Abstract*—Patients with Parkinson's disease (PD), in addition to motor disorders, such as tremor, hypokinesia, rigidity, and postural instability, also suffer from somatosensory abnormalities. Abnormal central processing of somatosensory signals occurs in PD as a result of dopamine deficit. The findings of recent studies show that cortical excitability could be involved in changes in somatosensory integration in PD depending upon dopamine lack or treatment. Accordingly, examining the state of somatosensory system might be helpful the diagnosis and treatment of PD. This work presents a study of PD patients with a portable tactile stimulator called Cortical Metrics 4 (CM-4) device, which was developed to examine the effects of various neurological disorders on the individual's somatosensory cortex. PD patients and healthy subjects were evaluated in Department of Neurology in Cerrahpaşa Faculty of Medicine, Istanbul University on vibrotactile stimulus amplitude discrimination and the duration discrimination tests using CM-4. The performance values of each patient were used as features and were fed to Support Vector Machines and k–Nearest Neighbor classifiers, which were trained to distinguish between control and PD subjects. The results show that these two CM tests can discriminate PD and controls with around 74% accuracy, further suggesting that these tests can be used as a measure of the disturbance of the somatosensory system due to PD.**

## I. Introduction

Parkinson's disease (PD) is a neurodegenerative motor system disease that affects motor reflexes, speaking, behavior, mental capacities and other neural functions [1]. PD is the second – after Alzheimer – most common disease seen in people over 60 [2]. An "early onset" PD can start before the age of 60 [3]. Symptoms include depression, difficulty in speaking, and motor disorders, such as tremor, hypokinesia, rigidity, and postural instability caused by sensory abnormalities [4]. PD may arise from a genetic reason, head trauma, environmental factors, some other diseases or use of some drugs [5]. There is no definite cure for PD [6] [7] [8]. The existing treatments are designed to suppress or remedy the symptoms and are mainly based on drug therapies that try to balance the dopamine level.

The diagnosis of PD is made by a neurologist based on a physical examination, which makes the evaluation subjective. In addition to subjectivity, diagnosis and monitoring of the disease are also troublesome because it is difficult for patients to come to clinic in the advanced stages of the disease. There are several studies on non-invasive diagnosis and monitoring of PD using voice and handwriting samples, aimed at addressing these issues [7] [8] [9]. Quantitative testing of somatosensory functions affected by PD can also, in principle, be used as an objective means of evaluating the progression of PD in a given patient and/or the effectiveness of attempted treatments. Such quantitative testing can be readily performed using the Cortical Metrics 4 (CM-4) vibrotactile stimulator device, which was designed for the purposes of examining an individual's somatosensory perceptual capacities impaired by various neurological disorders [10]. To date, CM-4 has been used successfully to diagnose patients with autism spectrum disorder, migraine, and vulvodynia [11] [12] [13].

A potential complication of interpreting the results of somatosensory tests performed on individuals varying significantly in age might be that skin sensitivity decreases with aging [14]. However, a number of tests using CM-4 measuring the processing speed, sensitivity (thresholds), discriminative capacity, and adaptation metrics of subjects ranging in age from 18 to 70 showed that although reaction speed and sensory thresholds do change with age, discriminative capacity and adaptation metrics do not [15]. In the present study, we used CM-4 to apply Amplitude Discrimination (AD) and Duration Dual Site Sequential Discrimination (DDSSD) tests to human subjects with PD and to neurologically healthy subjects in the Department of Neurology in Cerrahpaşa Faculty of Medicine, Istanbul University.

The rest of the paper is organized as follows. To evaluate the discriminability of PD vs. controls using these two tests, subjects' performance values on the tests were given as features to the Support Vector Machines (SVM) and k–Nearest Neighbor (k-NN) classifiers, as will be explained in Section II. The protocol is given in Section III. Experimental results and conclusions are given in Sections IV and V, respectively.

*Corresponding Author (e-mail: favorov@bme.unc.edu).
Olcay Kursun is with the Department of Computer Engineering, Istanbul University, Istanbul, Turkey (email: okursun@istanbul.edu.tr)
Betul Erdogdu Sakar is with the Department of Computer Engineering, Bahcesehir University, Istanbul, Turkey (email: berdogdu@bahcesehir.edu.tr)
M. Erdem Isenkul is with the Department of Computer Engineering, Istanbul University, Istanbul, Turkey (email: eisenkul@istanbul.edu.tr)
C. Okan Sakar is with the Department of Computer Engineering, Bogazici University and Bahcesehir University, Istanbul, Turkey (email: okan.sakar@bahcesehir.edu.tr)
Fikret Gurgen is with the Department of Computer Engineering, Bogazici University, Istanbul, Turkey (email: gurgen@boun.edu.tr)
Sakir Delil is with the Department of Neurology, Istanbul University, Istanbul, Turkey (email: okursun@istanbul.edu.tr)
Hulya Apaydin is with the Department of Neurology, Istanbul University, Istanbul, Turkey (email: okursun@istanbul.edu.tr)
Mark Tommerdahl is with the Joint Department of Biomedical Engineering, University of North Carolina and North Carolina State University, NC, USA (email: mark_tommerdahl@med.unc.edu)
Oleg V. Favorov is with the Joint Department of Biomedical Engineering, University of North Carolina and North Carolina State University, NC, USA (email: favorov@bme.unc.edu)

## II. Materials and Methods

CM-4, shown in Figure 1, is a device that can be used to investigate effects of various neurological disorders and other conditions on a person's somatosensory cortex [10]. It was designed by a research team at the University of North Carolina at Chapel Hill. This device offers non-invasive and fast examination of neurological changes [16] with outstanding sensitivity, which can be crucial for the diagnosis and monitoring of the neurological disorders.

Figure 1. CM-4 tactile stimulator [16]

The data were gathered from twenty six PD patients (13 males and 13 females) with ages ranging from 40 to 84 (65.1±10.5) and sixteen healthy subjects (11 males and 5 females) with ages ranging from 29 to 84 (47.5±15.4) in Department of Neurology in Cerrahpaşa Faculty of Medicine, Istanbul University. After the physician's examination, subjects were asked to take two tests on CM-4. All the subjects were informed about the tests and attended the tests voluntarily with the permission of ethical committee of Cerrahpaşa Faculty of Medicine, Istanbul University.

The subjects were seated comfortably in a chair and their preferred hand was placed on the detachable hand unit [10]. The index and middle fingers were placed in mechanical contact with two probes [15], which could deliver sinusoidal vertical skin displacement vibratory stimuli to the contacted fingertips of various amplitudes, frequencies, and durations, specified by the selected test protocol. The subject was asked to compare the sensations evoked on each fingertip along a specified perceptual dimension and press the right or left computer mouse button to indicate which finger was more impacted by stimulation. The visualization was provided by the software [10] that prior to the testing session asks the subject some information like demographics, medical history, etc. As a training phase, before starting the data acquisition on each test, the subject had to give three correct answers in a row to test stimuli. Feedback was given to the subject to inform whether the response was correct after each stimulus in the trial stage. The real data acquisition phase consisted of 20 stimulation trials and the subject was informed about the accuracy of his/her responses not after each trial, but after every 5 trials.

## III. Protocols

A large repertoire of test protocols has been developed for CM-4 vibrotactile stimulator. Two of these protocols were used in this study: the Amplitude Discrimination (AD) protocol and the Duration Dual Site Sequential Discrimination (DDSSD) protocol. These tests examine the ability of a subject is able to discriminate between two vibrotactile stimuli that differ either in their amplitude (AD) or duration (DDSSD). In the AD protocol, a stimulus of the "standard" amplitude (0.3mm peak-to-peak) is applied to one fingertip (chosen at random on each trial), while the amplitude of the "test" stimulus applied to the other fingertip varies from one trial to the next. The subject is asked to indicate which fingertip felt stronger vibration. At the start of the test, the amplitude of the test stimulus is set at easily distinguishable amplitude of 0.6mm. If the subject correctly identified the stronger stimulus on two successive trials, the amplitude of the test stimulus on the next trial was reduced by 0.03mm. If the subject failed to correctly identify the stronger stimulus on one trial, the amplitude of the test stimulus on the next trial was raised by 0.03mm. The entire test consisted of 20 trials, in a course of which the amplitude of the test stimulus was tracked down to a steady level. The amplitude difference limen (i.e., the difference in the amplitudes of the two stimuli at which the subject correctly identified the stronger stimulus with 67% accuracy) was computed as the difference between the average of the test amplitudes of the last 5 trials and the amplitude of the standard stimulus (i.e., 0.3mm).

In the DDSSD protocol, a stimulus of the "standard" duration (0.5s) is applied to one fingertip (chosen at random on each trial), while the duration of the "test" stimulus applied to the other fingertip varies from one trial to the next. The subject is asked to indicate which fingertip felt longer vibration. At the start of the test, the duration of the test stimulus is set at easily distinguishable duration of 0.75s. If the subject correctly identified the longer stimulus on two successive trials, the duration of the test stimulus on the next trial was reduced by 0.025s. If the subject failed to correctly identify the longer stimulus on one trial, the duration of the test stimulus on the next trial was raised by 0.025s. The entire test consisted of 20 trials, in a course of which the duration of the test stimulus was tracked down to a steady level. The duration difference limen (i.e., the difference in the durations of the two stimuli at which the subject correctly identified the longer stimulus with 67% accuracy) was computed as the difference between the average of the test durations of the last 5 trials and the duration of the standard stimulus (i.e., 0.5s).

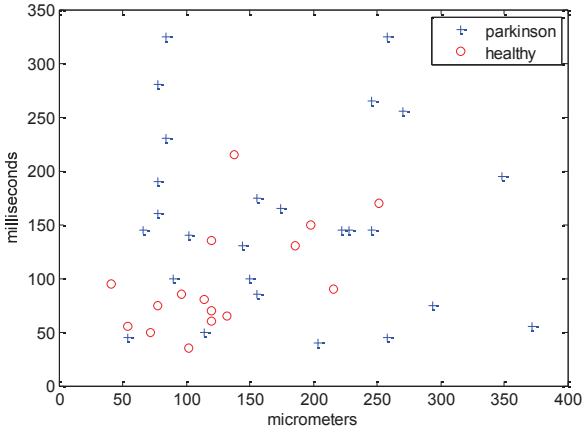


Figure 2. Amplitude difference limen (in micrometers) vs duration difference limen (in milliseconds)

## IV. Experimental Results

The AD and DDSSD tests were applied to the subjects using CM-4 tactile stimulator. The performance of all the studied subjects on these tests is shown graphically in Figure 2. This plot shows that the difference limen values of AD and DDSSD tests obtained from PD patients and from healthy subjects overlap only partially. The mean amplitude difference limen for control subjects is 0.127(±0.059) mm, while for PD patients it is 0.175(±0.092) mm. The mean duration difference limen for control subjects is 0.098(±0.049) sec, while for PD patients it is 0.154(±0.085) sec. Both difference are statistically significant at $p = 0.047$ for AD test and $p = 0.009$ for DDSSD test (using Walsh's difference of the means test).

The difference limen values of AD and DDSSD tests were treated as features of our dataset that we used for pattern discrimination. In our experiments we used leave-one-out cross validation technique [8]. The difference limen values of the tests were fed to *k*-NN classifier with Euclidean distance and SVM classifier with linear, Radial Basis Function (RBF), and polynomial kernels. The accuracy, sensitivity and specificity values for the *k*-NN classifier for 1, 3, 5, and 7 are shown in Table I. The highest accuracy (73.81%) is obtained with *1*-NN. The *1*-NN classifier also produced the highest sensitivity value (80.77%).

TABLE I. K-NN CLASSIFICATION ACCURACIES (%)

| | Accuracy | Sensitivity | Specificity |
|---|---|---|---|
| k = 1 | 73.81 | 80.77 | 62.50 |
| k = 3 | 71.43 | 76.92 | 62.50 |
| k = 5 | 64.29 | 65.38 | 62.50 |
| k = 7 | 61.90 | 61.54 | 62.50 |

The LIBSVM [17] implementation of SVM was used with the linear, polynomial and radial basis function (RBF) kernels along with cost value (c) parameter of one and kernel width (g) of 0.5 (default values). The SVM results are shown in Table II. It must be noted that the same results with *1*-NN are obtained with the RBF kernel SVM; however the results with the linear kernel are also very close. To put it in a different way, the linear kernel is also good at distinguishing the PD and the healthy subjects. However, the highest SVM classification accuracy is obtained with RBF kernel. In Figure 3, support vectors and class separation with SVM RBF kernel are shown. This SVM model is obtained using 70% of the samples for training and the rest for test.

TABLE II. SVM CLASSIFICATION ACCURACIES (%)

| | Accuracy | Sensitivity | Specificity |
|---|---|---|---|
| linear | 71.43 | 76.92 | 62.50 |
| polynomial | 64.29 | 92.31 | 18.75 |
| rbf | 73.81 | 80.77 | 62.50 |

## V. Conclusions

There is a growing interest in non-invasive diagnosis and monitoring of PD. The current studies in this field mostly aim at discriminating the PD from healthy subjects by examining the motor system disorders such as speech or handwritings. In this study, taking into account that the somatosensory system of PD is affected by the disease, we aimed to discriminate the PD from healthy subjects using the CM-4 portable tactile stimulator, a device that can be used in clinical research of neurological disorders. Since it was obvious that the response time of the subjects would have an obvious association with the disease, we focused instead on other aspects of somatosensory perception. For this task, we used the amplitude discrimination and the duration discrimination tests of CM-4. A dataset has been collected by applying these two tests to the healthy subjects and PD patients. The test results were fed to classifiers, such as Support Vector Machines and k–Nearest Neighbor classifiers. We obtained 73.81% classification accuracy (80.77% sensitivity and 62.50% specificity) using leave-one-out cross validation technique. These results indicate that PD significantly impacts even very basic functions of somatosensory perception. Collecting data from more subjects and using other CM-4 tests, such as temporal order judgment and adaptation tests, would help increase the classification accuracy of the system and explore other effects of Parkinsonism on the somatosensory cortex.

Apart from modeling a decision support system based on tracking neurological changes in somatosensory system of PD, this dataset also offers an opportunity of building a multi-view dataset for PD. Actually this study is a part of a project that aims to collect and analyze a multi-view dataset, including CM-4 test results and both voice and handwriting samples, to develop a more robust decision support system. Another future research direction is to analyze and extract the correlated variates between the motor and sensory system disorders seen in PD (Figure 4). In such a multi-view dataset, the views may be composed of groups of subviews such as motor system measurements with speech and handwritten subviews and somatosensory system measurements such as those of amplitude and duration discrimination.

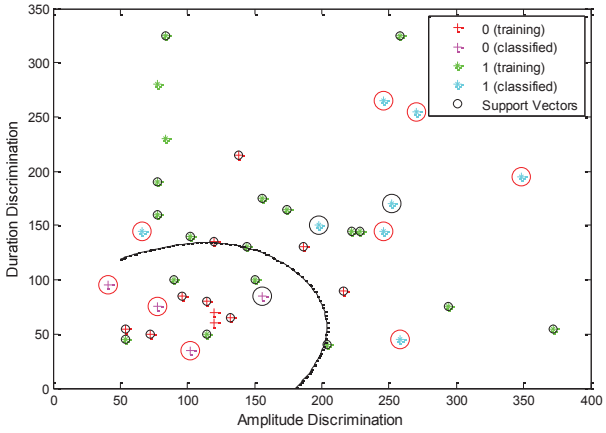


Figure 3. Support vectors and class separation using SVM with the RBF kernel (70% of the dataset for training set and 30% for the test set). Correctly classified test samples are shown in red circles, and the incorrectly classified samples in black.

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## REFERENCES

[1]J. Jankovic, "Parkinson's disease: clinical features and diagnosis," *Journal of Neurology, Neurosurgery and Psychiatry*, vol. 79, no. 4, pp. 368-376, 2007.
[2]L. M. de Lau and M. M. Breteler, "Epidemiology of Parkinson's disease," *The Lancet Neurology*, vol. 5, no. 6, pp. 525-535, 2006.
[3]The Michael Stern - Parkinson's Research Foundation. [Online]. http://www.parkinsoninfo.org/about-parkinsons-disease/who-gets-parkinsons-disease/ [last access date: 13 July 2013].
[4]G. Rigas et al., "Assessment of Tremor Activity in the Parkinson's Disease Using a Set of Wearable Sensors," *IEEE Transactions on Information Technology in Biomedicine*, vol. 16, no. 3, pp. 478-487 , 2012.
[5]W. Dauer and S. Przedborski, "Parkinson's Disease: Mechanisms and Models," *Neuron*, vol. 39, pp. 889-909, 2003.
[6]N. Singh, Vi. Pillay, and Y. E. Choonara, "Advances in the treatment of Parkinson's disease," *Progress in Neurobiology*, vol. 81, no. 1, pp. 29-44, 2007.
[7]M. A. Little, P. E. McSharry, E. J. Hunter, J. Spielman, and L. O. Ramig, "Suitability of dysphonia measurements for telemonitoring of Parkinson's disease," *IEEE Transactions on Biomedical Engineering*, vol. 56, no. 4, pp. 1010-1022, 2009.
[8]B. E. Sakar, M. E. Isenkul, C. O. Sakar, A. Sertbas, F. Gurgen, Ş. Delil, H. Apaydin, and O. Kursun, "Collection and analysis of a Parkinson speech dataset with multiple types of sound recordings", *IEEE Journal of* Biomedical and Health Informatics, vol. 17, no. 4, pp. 828-834, 2013.
[9] C.O. Sakar and O. Kursun, "Telediagnosis of Parkinson's Disease Using Measurements of Dysphonia", *Journal of Medical Systems*, vol. 34, no. 4, pp. 591-599, 2010.
[10] J. K. Holden et al., "A novel device for the study of somatosensory information processing," *Journal of Neuroscience Methods*, vol. 204, no. 2, pp. 215-220, 2012.
[11] M. Tommerdahl, V. Tannan, C. J. Cascio, G. T. Baranek, and B. L Whitsel, "Vibrotactile adaptation fails to enhance spatial localization in adults with autism," Brain Research, vol. 1154, 116-123. 2007.
[12] R.H. Nguyen, S. Ford, A.H. Calhoun, R.H. Gracely and M. Tommerdahl, "Neurosensory assessments of migraine", Brain Research, vol. 1498, pp. 50-58, 1 March 2013.
[13] Z. Zhang, D.A. Zolnoun, E.M. Francisco, J.K. Holden, R.G. Dennis, M. Tommerdahl, "Altered Central Sensitization in Subgroups of Women With Vulvodynia", Clin J Pain, 17 May 2011.
[14] K. L. Minaker, "*Common clinical sequelae of aging*", in Goldman's Cecil Medicine, 24th ed. Philadelphia: Elsevier Saunders, 2011, ch. 24.
[15] Z. Zhang, E. M. Francisco, J. K. Holden, R.G. Dennis, and M. Tommerdahl, "Somatosensory information processing in the aging population," *Frontiers in Aging Neuroscience*, vol. 3, no. 18, 2011.
[16] Cortical Metrics. [Online]. http://www.corticalmetrics.com/ [last access date: 13 July 2013].
[17] C. W. Hsu and C. J. Lin, "A Comparison of Methods for Multiclass Support Vector Machines," *IEEE Transactions On Neural Networks*, vol. 13, no. 2, pp. 415-425, 2002.

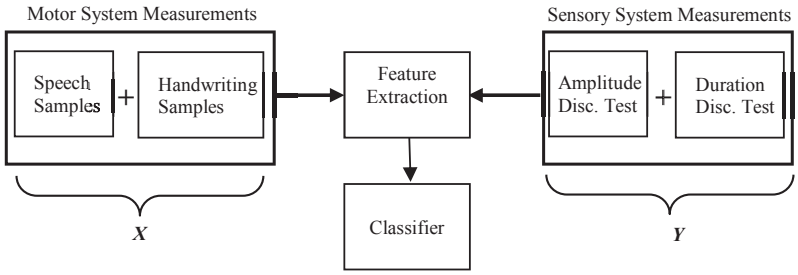


Figure 4. Two groups of multi-view data, X and Y used to extract features