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Abstract

This paper investigates the assessment of brain stroke susceptibility using human movement analyses. It is supported by the knowledge that 1) many stroke risk factors are correlated with human movement characteristics and 2) the anecdotal reports of motor control disturbance (e.g. in handwritten signatures and handwriting) prior to some cerebrovascular accidents. Thus, to investigate the potential plus-value of human movement information for the development of tools dedicated to stroke prevention, we analyzed the relationship between human motor control and brain stroke risk factors. Hundred and twenty subjects with or without stoke risk factors have performed a neuromuscular test battery. The kinematic of the movements was analyzed using a computational neuromuscular model and predictive characteristics were extracted. Logistic regression and linear discriminant analysis with leave-one-out cross-validation was used to infer, from movements characteristics, the probability of presence of brain stroke risk factors. The clinical potential value of movement information for stroke prevention was assessed by computing area under the receiver operating characteristic curve (AUC) for the diagnostic of risk factors based on motion analysis. AUC mostly varying between 0.6-0.9 are obtained, depending on the neuromuscular test and the risk factor investigated (obesity, diabetes, hypertension, hypercholesterolemia, cigarette smoking, and cardiac disease). Our results support the feasibility of the proposed methodology and its potential application for the development of brain stroke prevention tools. Considering the novelty of this topic, these results are promising. Further research is needed to improve this methodology and its outcome.

1. Introduction

A brain stroke, or cerebrovascular accident, is the sudden loss of brain functions caused by an interruption of the blood supply to the brain or by the rupture of blood vessels in the brain. Each years, 50 000 Canadians and 795 000 Americans are victims of this disease. In Canada and United-States, it is the third cause of mortality, causing direct and indirect costs of Can$ 3.6 billion (evaluated in 2000) and US$ 68.9 billion (evaluated in 2009) (Fondation des maladies du coeur, 2012; Lloyd-Jones et al., 2009). For surviving patients, the consequences can be various. Among subjects of 65 years old or more of the Framingham Study cohort, six month post-stroke, 50% were suffering from hemiparesis, 30% were unable to walk without assistance, 26% needed assistance for the daily activities and 26% were institutionalized. Also, aphasia, depression, incontinence, sensitive deficits, social integration difficulties, and hemianopsis were frequent symptoms (between 15 % and 40 %) (Kelly-Hayes et al., 2003).

Although brain strokes are unexpected events which strikes suddenly, anecdotal reports of patients who can track motor control deterioration (e.g. handwriting or handwritten signature distortion) prior to their cerebrovascular accident has been unofficially reported. Moreover, some events are known to happen significantly more often before brain strokes such as transient ischemic attack (Hankey, 1996), silent brain infarction (Bokura et al., 2006; Kobayashi, Okada, Koide, Bokura, & Yamaguchi, 1997),

and pre-stroke dementia (Klimkowicz et al., 2004). These may be indicative of a particular pre-stroke state of the cerebrovascular system. Also, brain stroke risk factors can be associated with the deterioration of many cognitive and psychomotor characteristics (O'Reilly & Plamondon, 2011). Covert and overt responses to psychomotor tests can therefore be expected to correlate with the brain stroke susceptibility and possibly be used for prevention.

In this context, it might be interesting to look at the motor control for pre-stroke markers. Although such an investigation would require important resources to conduct the necessary prospective study, a feasibility study may check the potential of this approach by studying the possibility of assessing the brain stroke susceptibility through motion analysis. In this line of thoughts, we have gathered a transversal database of 120 subjects who have performed a variety of neuromuscular tests. In this paper, we present a summary of the outcome of our research program in terms of area under the receiver operating characteristic curve (AUC) for the classification of brain stroke risk factors as a demonstration of the level of clinical potential of human movement information for the development of brain stroke prevention tools.

2. Methods

2.1. Sample

One hundred and twenty volunteers recruited within the École Polytechnique community and from the patients of a rehabilitation hospital (Hôpital De Réadaptation Villa Medica) participated in the experiment. They were taken from a wide age range (25 to 85 years old) and from both genders (68 women, 52 men). Height participants had a stroke in the past and 63 were having some of the following modifiable health risk factors (abbreviation; number of subjects affected): diabetes mellitus (DM; 15), obesity (OB; 10), hypertension (HT; 40), hypercholesterolemia (HC; 28), cardiac disease (CD; 24), and cigarette smoking (CS; 13). The other 57 were free of these risk factors and were considered healthy. Risk factors were evaluated from a medical form processed by a neurologist (L.-H. Lebrun) for the subjects from community of the École Polytechnique, whereas, for the hospital patients, this information was collected by the same neurologist from the medical record of the patients. The experimenter was kept blind in regard of the presence of stroke risk factors in the subjects.

From our sample, 112 participants reported themselves as right-handed, seven as left-handed and one as ambidextrous. Each subject performed the experiment with his/her dominant hand (the ambidextrous subject performed the experiment with his right hand) and the left-handed were given reversed guiding sheets to mitigate the effect of the hand used in the experiment (O'Reilly & Plamondon, 2011).

Every participant in this experiment has given an informed written consent and the experimental protocol has been approved by the ethics board of the École Polytechnique de Montréal and of the Hôpital de Réadaptation Villa Medica.

2.2. Neuromuscular testing

Every participant was submitted to a battery of tests including well-known psychophysical tasks such as the simple reaction time (SRT) and choice reaction time (CRT) protocols (Luce, 1986) applied to reaching motion initiated on a visual or an auditory stimulus, speed-accuracy trade-off tasks (SAT, also known as Fitts' task (Fitts, 1954; Fitts & Peterson, 1964)), oscillatory motions (well-studied in the context of handwriting (Stelmach & Teulings, 1987; Teulings & Maarse, 1984)) and some tests less commonly used for psychophysical evaluation such as triangular movements and handwritten signatures. The complete description of the battery can be found in (O'Reilly, 2012; O'Reilly & Plamondon, 2013).

2.3. Material

The layout of the neuromuscular tests (e.g. stating point, target zone) was specified on guiding sheets placed under the transparent plastic surface of a Wacom Intuos2 digitizing tablets. The pen tip of the participant stylus was tracked by the tablet at 200 Hz with a 100 line per millimeter spatial resolution. A custom made stimulator was used to generate, with a millisecond precision, a visual stimulus (a green flash for visual SRT or a green arrow for visual CRT, both displayed on a 8 X 10 array of light-emitting diodes) or an auditory stimulus (1 kHz beep of a 500-milliseconds duration). The hardware components were managed through an in-house software named Sign@médic.

2.4. Movement kinematics modeling

Collected movements have been modeled with the Kinematic Theory of Rapid Human Movement (Plamondon, 1995a, 1995b) used in numerous motor control studies in the last 15 years. This framework proposes that movements are controlled by a series of motor commands dispatched through the neuromuscular system, each command resulting in a lognormal contribution to the observed speed profile. As example, for the simplest movements analyzed here (i.e. the fast reaching motions associated with the reaction time tests), the resulting movement is considered as being the synergetic result of two neuromuscular systems. The first one, the agonist, pushes the end-effector (the pen tip) toward its target. The second one, the antagonist, has a directly opposed contribution and is mainly used to break the motion, although it can also be useful in stabilising the movement and increasing its precision (Lestienne, 1979). Both neuromuscular systems are triggered at the same time t_0 by a command of amplitude D_1 and D_2, respectively. These commands propagate through the neuromuscular systems and produce the lognormal impulse responses Λ_1 and Λ_2, respectively. With this modeling, the observed speed profile can be represented by the delta-lognormal curve which is expressed by

$$\Delta\Lambda = D_1\Lambda_1 - D_2\Lambda_2 \qquad (1)$$

with the Λ_i terms being time-shifted lognormals

$$\Lambda_i = \frac{1}{\sigma_i(t-t_0)\sqrt{2\pi}} exp\left(\frac{(\ln(t-t_0)-\mu_i)^2}{2\sigma_i^2}\right) \quad (2)$$

The μ_i and σ_i parameters associated with the lognormal components represent the time delay and the response spread (both on a logarithmic time scale) of the neuromuscular systems whereas the t_0 and the D_i parameters are the command parameters.

The lognormal patterns of this model are naturally emerging from an application of the central limit theorem to a system modeling of the neuromuscular system. This representation considers a neuromuscular system as composed of a complex arrangement of subsystems which reaction to a motor command is cascaded such that they produce outputs which have cumulative time delays following a law of proportionate effects (Plamondon, 1995a). This methodology has been validated, in other things, by the observation of an event-related potential (ERP) occurring at time t_0 (O'Reilly, Plamondon, Landou, & Stemmer, 2012) and by the experimental observation of a law of proportionate effects in EMG recordings (Plamondon, Djioua, & Mathieu, 2012).

This modeling scheme can be generalized to model arbitrarily complex movements, such as handwritten signatures for example. To that end, a vectorial version of the previous representation is used. Such a data description is known as the sigma-lognormal modeling (O'Reilly & Plamondon, 2009; Plamondon & Djioua, 2006) and proposes a time superposition of lognormal neuromuscular components acting around circle-arc trajectories.

2.5. Statistical analysis

Various characteristics where defined to represent the neuromuscular health of the participants. The most important are the central tendency (evaluated as the median) and the spread (evaluated as the median of the absolute deviation from the median) of the lognormal parameters (t_0, D_i, μ_i, and σ_i) and of the most frequently studied experimental measurements (e.g. reaction time, movement duration, amplitude and occurrence of the maximum speed, etc.). The exact set of characteristics varied from a neuromuscular test to the other given the different characteristics of the motion associated with these different tests (see O'Reilly (2012) for more details).

For each test, about 20 of these features were computed. Computation and evaluation of a large number of features has been avoided to reduce the probability of overfitting. The best subset of a maximum of six features was defined using a semi-exhaustive selection algorithm (O'Reilly, 2012). A probability for the subjects to have the different brain stroke risk factors was evaluated using two techniques commonly used for medical diagnosis: the logistic regression and the a posteriori probability associated with the linear discriminant analysis (Tabachnick & Fidell, 2007). A leave-one-subject-out cross-validation was applied to get unbiased predictions from the logistic and the discriminant analysis. All statistical analyses were performed using the R statistical software.

Instead of using statistical significance and p-values computed from ANOVAs, AUC measures of classification performance has been considered to evaluate, beyond

statistical significance, the discriminative potential for clinical applications of the information available through motion analysis. A more complete description of our methodology can be found in (O'Reilly, 2012; O'Reilly & Plamondon, 2012).

3. Results

Table 1 reports the quality of risk factors classification based only on the movement information. The results are measured using the AUC, a statistic corresponding to the probability of classifying correctly two subjects, knowing that one is having the risk factor and one is free of it. Scores of 0.5 and 1.0 are associated with a random and a perfect classification, respectively. A rule of thumb used in clinical settings makes a parallel with the traditional academic point system to qualify the quality of the AUC associated with a diagnostic test: 0.9-1.0 is excellent, 0.8-0.9 is good, 0.7-0.8 is fair, and 0.6-0.7 is poor (Tape, 2012). Although such a qualitative assessment depends on the problem at hand, this rule of thumb can be used as a starting point when no previous data are available to compare the AUC reached in a study with previously established results.

Table 1. AUC for risk factors classification for the different neuromuscular tests.

Risk factor	SRT (visual)	SRT (auditory)	CRT (visual)	SAT	Triangles	Signatures	oscillations	mean
DM	0.85	0.82	0.89	0.85	0.82	0.82	0.76	0.84
HT	0.76	0.76	0.76	0.74	0.80	0.76	0.77	0.77
HC	0.81	0.78	0.73	0.75	0.73	0.69	0.66	0.75
CS	0.69	0.82	0.72	0.71	0.70	0.34	0.60	0.67
CD	0.81	0.82	0.85	0.80	0.81	0.82	0.74	0.81
OB	0.78	0.88	0.85	0.73	0.68	0.73	0.75	0.78
mean	0.78	0.81	0.80	0.76	0.76	0.71	0.69	0.77

Abreviations: DM: diabetes mellitus, HT: hypertension, HC: hypercholesterolemia, CS: ciragette smoking, CD: cardiac disease, OB: obesity, SRT: simple reaction time, CRT: choice reaction time, SAT: speed-accuracy tradeoff

In Table 1, the results for each neuromuscular test are shown in the different columns whereas the risk factors are associated with the rows. Mean AUC are given for each test (last row) and for each risk factor (last column). The cell at the bottom right corner of the table gives the overall average.

AUC varying mostly between 0.6 and 0.9 have been obtained, the majority (83%) of these being over 0.7 and 35% being over 0.8. This is quite satisfactory for this exploratory study. Looking at Table 1 in more details, a few key observations must be pointed out. As can be seen in its rows, the best results are achieved for the discrimination of the diabetes and the cardiac disease with a mean AUC of 0.85 and 0.81, respectively. Hypertension, hypercholesterolemia, and obesity seem to be a little more difficult to assess using this methodology although the mean AUC of 0.77, 0.75, and 0.78 nevertheless indicates a significant relationship. Cigarette smoking is the least well characterised risk factor with a mean AUC of 0.61.

In looking at the columns of Table 1, we can see that some tests seem more discriminative than others. In general, better results have been obtained with simpler task (e.g. mean AUC between 0.78 and 0.81 for the SRT and CRT tests) than for complex ones (e.g. signatures with a mean AUC of 0.71).

4. Discussion

In the results previously presented, we noticed a lower discriminability of the cigarette smoking. This might be the result of the opposing effects of long-term cigarette smoking and of short-term presence of nicotine in the blood stream. Whereas the first one has detrimental effects on the motion (Hill, 1989; Kalmijn, van Boxtel, Verschuren, Jolles, & Launer, 2002), the second one has positive effects such as reduced reaction time (Davranche & Audiffren, 2002; Hahn et al., 2009) and increased vigilance (Ernst, Heishman, Spurgeon, & London, 2001; Griesar, Zajdel, & Oken, 2002). However, as neither the duration between the last cigarette consumption and the experiment nor the history of cigarette smoking have been controlled or registered in this experiment, it is not possible, here, to discriminate between these two separate and opposite effects using a *post hoc* analysis.

It has previously been pointed out that simpler task seem to be more predictive. However, it should be noticed that more repetitions have been collected for the simpler tasks (e.g. 15 for SRT and 30 for CRT) than for the complex ones (e.g. 5 for the signatures). Hence, it is not clear if the better results are to be attributed to the simplicity of the task or to the availability of more repetitions. Moreover, tasks requiring significantly more information processing could be expected to be more discriminant for some risk factors, as it seem to be the case for nicotine abstinence (Marzilli & Shea, 2000).

It is also worth noticing that, in one hand, the consistency of the results across the different tests for some risk factors (e.g. the high AUC of the DM factor, the low AUC for the CS factor) seems to support the validity of the AUC obtained for these risk factors. In the other hand, the variability of the results for some other factors (e.g. the AUC for the OB factor vary between 0.68 and 0.88, depending on the test) may indicate that the tests are differentially assessing these risk factors from one another. However, in some case, the observed variability could also be a statistical artefact due, for example, to the relatively small number of subjects being affected by some of the analyzed risk factors. Our experiment will have to be duplicated to validate the reproducibility of these patterns before a decisive conclusion can be reached on that matter.

Given the novelty of the approach proposed in this paper, there is no previous literature to compare directly these results to. However, considering the statistical interpretation of the AUC, there is definitely a significant amount of information in the characteristics of human movements that is correlated with the brain stroke susceptibility. Of course, as of now, not all the information about the brain stroke risk factors can be extracted from motion analysis. As these results are obtained for a new trend of research, they should be taken as a first outcome on which we can estimate the potential of this new approach. As more work will be done in this direction, the methodology will be enhanced and we can expect to improve these initial results to be in good position to rule on the final

clinical utility of the movement analysis for the development of brain stroke prevention tools.

Two general remarks can be made from the outcome of our investigations to improve future studies on this topic. Firstly, the human motor control is a process which has an important variability and which needs a large number of repetitions in order to achieve a good statistical characterisation. Therefore, future studies should consider many repetitions by experimental condition. About 30 valid trials seem an adequate number when possible (i.e. for ethical reasons, it might be difficult to get that many repetitions from very young, very old, or severely diseased participants).

Secondly, the previous discussion on the short versus long-term effects of the cigarette smoking can be widened to the other risk factors. This highlights an important possible methodological enhancement: In the planning of the experiment, the investigators should discriminate between the long and short term effects by controlling or recording the appropriate variables.

5. Conclusion

To conclude, encouraging results have been obtained showing how the characteristics of human movements can be used as biomarkers for assessing the brain stroke susceptibility. This research trends aims, in the long run, at providing an adequate analysis framework for the inclusion of movement biosignals within new brain stroke prevention tools.

It should be emphasized that the objectives of our research program in general – and of this study in particular – is not in itself the diagnostic of brain stroke risk factors as there is already efficient tests for this purpose. It has to be seen in the wider perspective of studying the relationships that the brain stroke susceptibility and that a possible pre-stroke state both share with the characteristics of the motor control, keeping in mind the long-term goal of developing better ways to assess the risk of suffering from a stroke. This first investigation is an important step toward an eventual prospective study incorporating the tools we propose herein. In a final application, the movement information might be collected through the evermore ubiquitous movement tracking devices (computer mouse, camera, handheld devices) and integrated with other information such as the doctor's knowledge of the patient risk factors.

Further investigation will be necessary to better define the potential and the limitations of the proposed approach. These will have to corroborate the results reported herein and examine the properties of this measurement methodology, properties such as validity, specificity, and test-retest reliability. More attention will also have to be paid to 1) the pathophysiology linking the motor control to the brain stroke susceptibility, 2) the short versus long-term effects of the risk factor on the movements, and 3) the possible complementariness versus redundancy of the different neuromuscular tests used in our battery. Nevertheless, the results obtained so far are promising and will hopefully bring more attention to this innovative approach.

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