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Using Upper Limb Kinematics to Assess Cognitive Deficits in People Living with Both HIV and Stroke

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Abstract

In this study, we aim to explore ways to objectively assess cognitive deficits in the stroke and HIV/stroke populations, where cognitive and motor impairments can be hard to separate. Using an upper limb rehabilitation robot called the Haptic TheraDrive, we collect performance error scores and motor learning data on the impaired and unimpaired limb during a trajectory tracking task. We compare these data to clinical cognitive scores. The preliminary results suggest a possible relationship between unimpaired upper limb performance error and visuospatial/executive function cognitive domains, but more work needs to be done to further investigate this. The potential of using robot-assisted technologies to measure unimpaired limb kinematics as a tool to assess cognitive deficits would be useful to inform more effective rehabilitation strategies for HIV, stroke, and HIV/stroke populations.

I. INTRODUCTION

Stroke and human immunodeficiency virus (HIV) are two of the leading causes of death and disability in the world [1]. 800,000 people suffer a stroke in the United States each year [2]. 40,000 new people are diagnosed with HIV each year and 1.2 million people live with HIV [3]. There is increasing evidence that HIV is an independent risk factor for stroke, giving way to an emerging HIV/stroke population on which little research has been conducted, particularly from a neurorehabilitation standpoint [4], [5], [6]. From 1997–2006, there was a 60 percent increase in stroke rates in the U.S. HIV population while stroke rates in the general population decreased by 17 percent [4]. This issue is magnified in low and middle income countries where stroke rates have increased by 100 percent and the prevalence of HIV is higher [5]. HIV and stroke can significantly impact a person's cognitive and motor abilities, thus affecting their quality of life. Although HIV and stroke are both associated with neurologic injury, stroke neurorehabilitation strategies have received far greater focus while there is a paucity of neurorehabilitation successes in HIV populations, who are in dire need of such strategies[7], [8]. The impetus for rehabilitation strategies tailored to the HIV population stems from research showing that upwards of 80 percent of people living with

HIV deal with an impairment, activity limitation, or social participation restriction [9]. Particularly in resource-limited settings, access to rehabilitation services requires innovative approaches that can be taken outside of a hospital setting [10].

HIV can lead to stroke in various ways. Antiretroviral therapy (ART) has transformed HIV from a life-threatening disease into a manageable chronic disease. The life expectancy of someone with HIV in the U.S. has increased from under 40 years in 1996 to 73.1 years in 2011 [11]. This is still about 13 years below the general populations life expectancy, but the increased lifespan naturally exposes the HIV population to conventional stroke risk factors. However, other causes for stroke have been directly attributed to HIV, such as opportunistic infection, HIV-associated vasculopathy, cardioembolism, chronic inflammation, and the neurotoxicity of ART itself [5]. ART has been an overwhelmingly positive development in the treatment of HIV, but there are problems that have yet to be addressed.

While ART has decreased the prevalence of HIV-associated dementia (HAD), the prevalence of less severe HIV-associated neurocognitive diseases (HAND) – asymptomatic neurocognitive impairment (ANI) and minor neurocognitive disorder (MND) – remains at around 50 percent of the HIV population [12]. HAND can lead to problems with adhering to medication, while MND and HAD in particular can affect a persons ability to perform activities of daily living [13]. However, accurately diagnosing the milder forms of HAND remains difficult. The three subtypes of HAND are defined by the Frascati criteria and can be diagnosed via an extensive neuropsychological battery, but brief screening tools are more desirable because an in-depth test cannot always be performed in the clinic [14]. Both the HIV Dementia Scale (HDS) and Montreal Cognitive Assessment (MoCA) have been used as screening tests, but neither performs well in distinguishing the milder forms of HAND [15]. HIV is also associated with motor deficits and physical disability[16], [17]. The HIV Dementia Motor Scale (HDMS), which is different from the HDS, measures motor abnormalities to predict cognitive impairment. A potential benefit of using motor function tests is that it is insensitive to population biases [18].

In HIV/stroke, a challenge arises when trying to assess the impact of each disease on the patient. For example, assessing the kinematics of the impaired limb in a HIV/stroke patient to determine the extent of motor and cognitive deficits would result in many confounding factors. Being able to separate these contributions is important in developing better rehabilitation strategies that take into account the individual's cognitive and motor abilities. To most effectively do this, metrics are needed to objectively assess the motor and cognitive deficits in an individual that can be tracked over the course of therapy. To this end, robot-assisted technologies have been implemented and motor performance has been assessed by kinematic measures, such as deviation from the desired line, peak speed, mean speed, movement smoothness, movement duration, and mean jerk [19], [20]. In addition, cognition, executive function, and attention have been shown to be correlated to motor recovery [21]. Motor learning principles have been used to develop rehabilitation strategies for stroke, such as impairment-oriented training, constraint-induced movement therapy, electromyogram-triggered neuromuscular stimulation, interactive robotic therapy, and virtual reality-based rehabilitation [22]. Of particular interest is interactive robotic therapy, which allows for more quantitative assessment during the rehabilitation process. This approach can provide user-

specific therapy across a wide range of impairment levels, and has been shown to be more effective than conventional therapy [23].

A component of motor learning that may have relevance to recovery in HIV/stroke is explicit versus implicit learning strategies. Implicit motor learning involves acquiring a motor skill without explicit knowledge of the learning of that particular task [24]. This reduces the cognitive load on patients and provides a potential strategy to improve motor recovery in cognitively impaired patients [25]. Given the prevalence of HAND, there is a high possibility that cognitive impairment is present prior to stroke in people with both HIV and stroke. Stroke can result in additional cognitive impairment. Regardless of the source, cognitive impairment can be a rate limiting factor in motor recovery, and this is not always taken into account when implementing rehabilitation regimens.

In this paper, we report preliminary data to assess and compare both cognitive and motor deficits in people with stroke and HIV/stroke using a robot-assisted paradigm involving the Haptic TheraDrive, a one degree-of-freedom, adaptive robot for upper limb stroke rehabilitation [26]. Given that cognitive and motor impairments can confound kinematic assessment of the impaired limb, we also examine the utility of assessing the unimpaired limb. Our hypothesis is that kinematic metrics of the unimpaired limb derived from task performance and motor learning can be used to assess cognitive impairments, providing a more objective alternative to current screening tests.

II. METHODS

A. Subject Population

8 subjects participated in this study: four healthy subjects, two stroke subjects, and two HIV/stroke subjects. A clinical evaluation was performed on the HIV/stroke and stroke subjects. Subjects were included in the stroke group if they met the following criteria: were more than six months after their most recent stroke and not currently receiving physical therapy. Subjects were included in the HIV/stroke group if they met the same criteria as the stroke group and also presented with HIV. All protocols were approved by the University of Pennsylvania Institutional Review Board. Informed consent was obtained prior to the start of the study from all participants.

B. Clinical Assessment

A clinical assessment was administered to the stroke and HIV/stroke subjects to evaluate cognitive and motor functions. Included in the clinical assessment were the Montreal Cognitive Assessment (MoCA), Beck's Depression Inventory (BDI), Upper Extremity Fugl-Meyer test (UE-FM), grip strength test, Box and Block test, and the Modified Ashworth Scale [27], [28], [29], [30]. These tests were performed by a single physical therapist who was blinded to the patient's HIV status. Of particular interest are the MoCA and UE-FM scores. The MoCA is a screening tool to detect impairment in various cognitive domains (visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall, and orientation) and reflects the degree of cognitive deficits in a subject. Of the cognitive domains, we focus on the visuospatial/executive and delayed recall domains because they

have been shown previously to play a more significant role in motor recovery than the other domains [21]. The UE-FM test is widely used to assess motor function of the impaired upper limb.

Table I includes the group, UE-FM score (max = 66), MoCA visuospatial subscore (max = 5), MoCA delayed recall subscore (max = 5), and total MoCA (max = 30) for each stroke and HIV/stroke subject. While the two stroke patients had both high motor and cognitive function, the two HIV/stroke patients both demonstrated mild cognitive impairments. Subject 3 demonstrated impairment in language and delayed recall domains, while Subject 4 demonstrated impairment in visuospatial ability, executive function, and delayed recall domains.

C. Haptic TheraDrive

Haptic TheraDrive (Fig. 1) is a one degree-of-freedom robot originally designed by Johnson and colleagues for upper limb stroke rehabilitation [26]. It includes an adaptive controller for user-specific therapy and haptic feedback to supply assistive or resistive forces. The user operates TheraDrive by manipulating a vertically mounted crank with a handle equipped with force sensors and an optical encoder. TheraDrive can operate in one of four different modes [31]. For this study, it is only run in zero-impedance mode. In this mode, the forces applied by the user's arm onto the end-effector – as measured by Takktile force sensors (Takktile LLC, Cambridge, MA) in the handle – are used to calculate the necessary response by the motor in order to give the sensation that there is no resistance when the user pushes or pulls on the handle. This is implemented using a force-dependent proportional-integral-derivative (PID) impedance controller.

D. Task Description

Each subject performed a set of trajectory tracking tasks on TheraDrive. A single task consists of the user moving the crank arm forward and backward to move a triangular cursor left and right on the screen, respectively, to follow a preprogrammed, pseudo-random sinusoidal path for 15 seconds (Fig. 1). The cursor can only move in a single dimension while the sinusoidal trajectory scrolls down the display. For visual feedback, there is a box that demonstrates an acceptable region to be in while following the trajectory. When the cursor is in this box, the cursor is green. Once outside of the box, the cursor becomes red. This task is repeated on the dominant/unimpaired and non-dominant/impaired side for all subjects. The displayed trajectory and handle's angular position data are recorded during each trial at a sampling rate of 150 Hz.

E. Performance Error

Performance on each tracking task was quantitatively assessed by calculating the root mean square error (RMSE) of angular position from the sinusoidal trajectory in degrees. RMSE has been previously shown to have a direct correlation to clinical measures of motor ability [32]. The RMSE for each trial was normalized by the RMSE resulting from the condition where no handle movement occurred during the task. The RMSE values are then used to calculate two different measures – a mean performance error score and the motor learning rate. For the first measure, the normalized RMSEs over the last 15 trials are averaged. The

last 15 trials are used in order to ignore any effects of learning that may be present at the beginning of the trial. All analysis was done using custom scripts in MATLAB 2016a (Mathworks, Natick, MA).

F. Motor Learning Rate

Motor learning was assessed by fitting an exponential curve to the normalized RMSE values over all the trials. For the healthy group, a single representative learning curve was generated for the dominant and non-dominant sides by averaging the RMSEs across all the healthy subjects and fitting an exponential curve to the averaged set. For the other subjects, individual motor learning curves were generated. An example of a motor learning curve fit to a healthy subject is shown in Fig. 2. The motor learning rate is extracted from the equation used to fit the curve and is represented as the constant b in Equation 1.

$$f(x) = a * e^{-bx} + c \quad (1)$$

G. Statistical Analysis

Using a Wilcoxon signed rank test, the average RMSE values and motor learning rates of the dominant hand were found to be not significantly different from the non-dominant hand for the healthy group ($p = 0.63$ and 0.875 , respectively). Given this, the dominant and non-dominant hand data were combined when comparing impaired and unimpaired data of stroke and HIV/stroke subjects to the healthy group.

To compare the individual stroke and HIV/stroke values to the healthy group, a z-score was calculated using the stroke or HIV/stroke subject's scores and the mean and standard deviation of the healthy group. The z-score is calculated using equation 2, where X is either of the kinematic metrics. A z-score greater than or equal to 2 or less than or equal to -2 , which corresponds to being 2 or more standard deviations away from the healthy population mean, was characterized as being abnormal.

$$z = (X_{subject} - \overline{X_{healthy}}) / S_{healthy} \quad (2)$$

Correlation coefficients between clinical scores and the taskderived metrics were assessed by calculating Spearman's rho, a nonparametric measure of rank correlation.

III. RESULTS

A. Mean Performance Error Results

Table II shows the mean performance error for each subject's impaired and unimpaired side along with the calculated z-score compared to the healthy group. Fig. 3 shows a visual representation of the averaged RMSE scores for the unimpaired and impaired sides compared to the healthy group. On the unimpaired side, Subjects 2, 3, and 4 demonstrated abnormal performance relative to the healthy population. On the impaired side, Subjects 1

through 4 demonstrated abnormal performance relative to the healthy population. Although not significant relative to an alpha level of 0.05, a strong negative correlation was found in the stroke and HIV/stroke data between the unimpaired limb performance error score and the visuospatial/executive function MoCA subscore ($\rho = -0.95$, $p = 0.17$). The relationship between impaired limb performance and visuospatial/executive function subscore was weaker and less significant ($\rho = -0.63$, $p = 0.5$).

B. Motor Learning Results

We show the general motor learning curves for the healthy group and the individual motor learning curves for the stroke and HIV/stroke subjects for the dominant/unimpaired (Fig. 5) and non-dominant/impaired (Fig. 5) sides. The shaded region shows the standard deviation of the healthy group over the course of the trials. Table III shows the motor learning rates for the dominant/unimpaired and non-dominant/impaired sides for all the subjects. On the unimpaired side, Subjects 1 and 2 demonstrated abnormal motor learning rates compared to the healthy population. On the impaired side, only Subject 4 demonstrated an abnormal learning rate.

C. Impaired vs. Unimpaired Performance Error Scores

Fig. 6 shows the performance error scores of the nondominant/impaired side plotted against the scores of the dominant/unimpaired side. There is a distinct cluster of the healthy subjects, the group with the highest cognitive and motor abilities. The two stroke subjects are also close together. Subject 3, whose Fugl-Meyer is close to the two stroke subjects' scores, is also nearby to the right. Subject 4, who has both motor and cognitive deficits, is farther away.

IV. DISCUSSION

We set out to assess the utility of using the Haptic Theradrive robot to measure performance error and motor learning rate of the impaired and unimpaired side for stroke and HIV/stroke subjects to assess cognitive impairments. Examining performance error seemed to match what we expected, in that the unimpaired hand performed better than the impaired hand, even if the unimpaired hand was abnormal compared to the healthy population. However, examining the motor learning rate did not seem to match. The two stroke subjects tested as abnormal on their unimpaired side while only one subject (Subject 4) tested abnormally on their impaired side. Thus, performance error was a more insightful metric compared to motor learning rate.

Motor learning rate can still be an insightful metric. In our case, our results indicate that our task may not be suitable in its current form to measure learning rate, but changes can be made in the future to more reliably extract a motor learning metric, such as using point-to-point tracking or another form of assessment. Given that we only tried to measure motor learning over a short period of time, there is still an opportunity to explore motor learning in more detail with a more relevant task and its relation to cognitive impairment.

Although not significant, we found a strong correlation between performance error on the unimpaired side and the visuospatial/executive function MoCA subscores. This relationship

was weaker when examining the impaired side. We plan to explore this relationship in more detail going forward with more subjects. Our preliminary findings of motor assessment being more correlated to visuospatial/executive function among the cognitive domains matches what has been found in literature [21]. The relationship between unimpaired limb metrics and cognitive impairment suggests that measuring kinematics of the unimpaired side may be a strategy to quantify cognitive deficits that play a role in motor recovery. A potential benefit to this approach is that it could more clearly assess cognitive deficits that would be confounded by other factors in the impaired limb. Being able to assess motor and cognitive deficits in a quantitative manner can potentially make the recovery process more effective as well as help identify the effect of HIV on stroke recovery. For example, someone who has high motor and cognitive capabilities might benefit from a task that is both mentally and physically challenging, while someone who has the same motor capabilities but more impaired cognitive abilities might require an alternative learning strategy, such as error-less learning. It was by chance that the two HIV/stroke subjects were both cognitively impaired while the two stroke subjects had high cognitive function, but it highlights that the HIV/stroke population does indeed present with both cognitive and motor deficits.

An important step going forward is determining how to best incorporate and represent impaired and unimpaired data to reflect the contributions of cognitive and motor deficits. One potential way to do this is shown in Fig. 6, where showing both the impaired and unimpaired performance scores together portrays a better sense of the contributions of cognitive and motor impairments in that clusters can form around distinct groups, such as high cognitive/high motor, high cognitive/low motor, etc. The distribution of the subjects matches what we would expect, in that there is a cluster of healthy subjects with the stroke subjects nearby due to their high cognitive/high motor status and the subject with both motor and cognitive impairments further away. Another consideration is how to distinguish the effects of bimanual motor deficits from cognitive deficits. In three of the four non-control subjects, the less impaired side still performed worse compared to the control group, but two had mild cognitive impairment according to their MoCA scores. A potential solution would be to explore the relationship between bimanual clinical scores - such as the Box-and-Block test - and the kinematic measures we collected.

The limitations of this study include small sample sizes, potential confounding factors such as fatigue – both physical and mental – or learning transfer, and having only high and moderate functioning subjects. More work needs to be done to further investigate the potential of this approach.

V. CONCLUSION

There is a need to more objectively assess cognitive deficits because of the difficulty of doing an extensive neuropsychological test, the lack of effective screening tests, and the unknown contributions of HIV to stroke recovery. The preliminary results show that there is potential utility in using unimpaired limb kinematics and robot-assisted technology as a tool to assess cognitive deficits, but more work needs to be done to assess the potential of this approach. Developing tools like this can lead to a better understanding of the interactions

between HIV and stroke, which will inform more effective rehabilitation strategies that are applicable to HIV, stroke, and HIV/stroke populations.

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Fig. 1.

Haptic TheraDrive (left) and screenshot of the tracking task (right) in which the user attempts to keep the cursor in the target box to follow the path. The box represents the acceptable error and moves along the path. When inside the box, the cursor is green. Outside of the box, the cursor becomes red. The user moves the crank arm forward and backward to move the cursor left and right, respectively. The horizontal line represents the starting line.

Fig. 2.

Example of the motor learning curve generated for Subject 7. An exponential curve is fit to the 25 data points.

Fig. 3.

Performance error scores for the healthy group and individual stroke and HIV/stroke subjects. The healthy group data contains both dominant and non-dominant scores, which were not significantly different from each other.

Fig. 4.

Unimpaired and dominant side motor learning curves. For the healthy group, the motor learning curve is fit to the performance scores generated by averaging over all healthy subjects. The standard deviation of the healthy scores is shown by the shaded gray region. The individual curves were then generated for the stroke and HIV/stroke subjects.

Fig. 5.

Motor learning curves for the impaired and non-dominant hand. For the healthy group, the motor learning curve is fit to the performance scores generated by averaging over all healthy subjects. The standard deviation of the scores is shown by the shaded gray region. The individual curves are then generated for the stroke and HIV/stroke subjects.

Fig. 6.
Impaired performance accuracy score plotted against unimpaired score.

Table I:

UE-FM, VISUOSPATIAL, DELAYED RECALL, TOTAL MOCA, AND NON-IMPAIRED AND IMPAIRED LIMB BOX-AND-BLOCK SCORES

Sub	Group	FM	VS	DR	MoCA	BB (NI)	BB (I)
1	stroke	51	5	4	29	59	44
2	stroke	58	5	4	29	41	31
3	HIV/stroke	61	4	0	22	24	26
4	HIV/stroke	45	3	3	24	40	15

Table II:

PERFORMANCE ERROR SCORE OF DOMINANT/UNIMPAIRED AND NON-DOMINANT/IMPAIRED HANDS FOR ALL SUBJECTS (Z-SCORES IN PARENTHESES)

Subject	Group	Dom/Unimpaired	Non-Dom/Impaired
1	stroke	0.19 (0.40)	0.36 (5.21)
2	stroke	0.25 (2.16)	0.26 (2.37)
3	HIV/stroke	0.27 (2.62)	0.33 (4.22)
4	HIV/stroke	0.66 (13.43)	0.96 (21.72)
5	healthy	0.18	0.17
6	healthy	0.19	0.21
7	healthy	0.11	0.13
8	healthy	0.21	0.20

Table III:

DOMINANT/UNIMPAIRED AND NON-DOMINANT/IMPAIRED MOTOR LEARNING RATE FOR ALL SUBJECTS (Z-SCORES IN PARANTHESES)

Subject	Group	Dom/Unimpaired	Non-Dom/Impaired
1	stroke	3.05 (4.37)	0.23 (−0.59)
2	stroke	5.20 (8.17)	0.0005 (−1.00)
3	HIV/stroke	1.32 (1.33)	0.21 (−0.64)
4	HIV/stroke	0.002 (−1.00)	15.86 (26.97)
5	healthy	0.12	1.67
6	healthy	0.60	0.93
7	healthy	0.27	0.11
8	healthy	0.86	0.0002
9	mean healthy	0.40	0.02