A human-machine-interface integrating low-cost sensors with a neuromuscular electrical stimulation system for post-stroke balance rehabilitation.
--Manuscript Draft--

Manuscript Number:	JoVE52394R5
Full Title:	A human-machine-interface integrating low-cost sensors with a neuromuscular electrical stimulation system for post-stroke balance rehabilitation.
Article Type:	Invited Methods Article - JoVE Produced Video
Keywords:	Stroke, Movement Rehabilitation, Low-cost device, Operant Conditioning, Biofeedback training, Neuroplasticity, Standing Balance.
Manuscript Classifications:	93.31.6: engineering (general)
Corresponding Author:	Anirban Dutta, Ph.D. INRIA, Université de Montpellier, CNRS Montpellier, FRANCE
Corresponding Author Secondary Information:	
Corresponding Author E-Mail:	adutta@ieee.org
Corresponding Author's Institution:	INRIA, Université de Montpellier, CNRS
Corresponding Author's Secondary Institution:	
First Author:	Deepesh Kumar
First Author Secondary Information:	
Other Authors:	Deepesh Kumar
	Abhijit Das, M.D., D.M.
	Uttama Lahiri, Ph.D.
Order of Authors Secondary Information:	
Abstract:	A stroke is caused when an artery carrying blood from heart to an area in the brain bursts or a clot obstructs the blood flow to brain thereby preventing delivery of oxygen and nutrients. About half of the stroke survivors are left with some degree of disability. Innovative methodologies for restorative neurorehabilitation are urgently required to reduce long-term disability. The ability of the nervous system to respond to intrinsic or extrinsic stimuli by reorganizing its structure, function and connections is called neuroplasticity. Neuroplasticity is involved in post-stroke functional disturbances, but also in rehabilitation. Beneficial neuroplastic changes may be facilitated with non-invasive electrotherapy, such as neuromuscular electrical stimulation (NMES). NMES involves coordinated electrical stimulation of nerves and muscles with continuous short pulses of electrical current leading to improvements in muscle strength and reduction in spasticity. Here, active cortical participation in rehabilitation procedures may be facilitated by driving the non-invasive electrotherapy with biosignals (electromyogram (EMG), electroencephalogram (EEG), electrooculogram (EOG)) that represent simultaneous active perception and volitional effort. To achieve this in a resource-poor setting, e.g., in low- and middle-income countries, we present a low-cost human-machine-interface (HMI) by leveraging recent advances in off-the-shelf video game sensor technology. In this paper, we discuss the open-source software interface that integrates low-cost off-the-shelf sensors with NMES to assist postural control for balance rehabilitation. We demonstrate the proof-of-concept on healthy volunteers.
Author Comments:	1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues. The JoVE editor will not copy-edit your manuscript and any errors in the submitted revision may be present in the published version. There remains many copy-editing errors throughout that significantly reduces

the clarity of the manuscript.
1. Thanks. We have tried to thoroughly proof-read the draft.

2. There continues to be textual overlap in the manuscript. This textual overlap should be revised to include original and novel language and failure to do so will prevent publication of the manuscript.
2. Sorry, we have revised the statements.

3. 3.3.2: How is the minimum baseline NMES level determined? What is clinically being observed and how do these observations determine the minimum baseline NMES level? Please provide a reference on how to do so.
3. Thanks. We have revised accordingly. "3.3.2. Set a minimum baseline NMES level (pulse-width and current level) necessary for upright standing according to clinical observation (i.e., zero body weight support)20. For setting the minimum baseline NMES level, one can set the stimulation frequency at 20Hz and then increase the pulse-width and/or current level until upright standing is achieved. Here, NMES of knee extensors is required to generate enough torque to prevent knee buckling."

4. 3.3.4: How is the calibration done? What steps are done with respect to the software? What is the "routine"?
4. The "routine" is the Matlab program that needs to be run. We have revised accordingly. "3.3.4. Run 'CalibSensors.m' program in Matlab to collect calibration data from Motion Capture Sensor, Balance Board, and EEG data acquisition systems while the subject performs various visually cued reach movements that affects center of mass (CoM) and center of pressure (CoP) location. The calibration program will identify subject-specific maximum EMG level (MEL) of the muscles and maximum excursions of CoM/CoP (CoMmax/CoPmax) during the reach movements."

5. 3.3.5: What is the calibration software routine? Please provide more explicit details, i.e, command lines?
5. The "routine" is the Matlab program that needs to be run.
6. 4.1: WHat is the CollectBaseline software routine? Please provide more explicit details, i.e, command lines?
6. The "routine" is the Matlab program that needs to be run. "5.1. Run 'CollectBaseline.m' program in Matlab to collect baseline resting-state eyes-open multi-sensor data by asking the subject to stand still for 2 minutes while looking straight at the CoP target on the PC monitor (see Figure 3a)."

7. Please include Representative Results that show the efficacy of the protocol. Previous revisions had these Representative Results but this most recent revision has removed it. Furthermore, please include how to analyze the data (either a reference on how to do so or explicit details in the protocol on how to do so) in the Protocol following step 4).
7. We apologize. We have now added the Representative Results in Figures 4 and 5. Figure 4. Top panel shows an illustrative figure of the smooth pursuit during horizontal movement. Bottom panel shows an illustrative figure of the smooth pursuit during vertical movement.
Figure 5. a) Changes in the ratio of fixation duration on the target and the fixation duration on the cursor - FDratio - extracted from electrooculogram during visuomotor balance task (VBT) trials. b) Changes in the baseline normalized mean squared error (MSEnorm) during VBT trials.

8. Please highlight 2.75 pages or less of the Protocol (including headings and spacing) that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol. The highlighted steps should form a cohesive narrative with a logical flow from one highlighted step to the next. Remember that non-highlighted Protocol steps will remain in the manuscript, and therefore will still be available to the reader.
8. Thanks. We have now highlighted 2.75 pages or less of the Protocol in grey for the video.

9. Please ensure that the highlighted steps form a cohesive narrative with a logical flow from one highlighted step to the next. Please highlight complete sentences (not parts of sentences). Please ensure that the highlighted part of the step includes at least one

	action that is written in imperative tense. 9. Yes, we have written the protocol in imperative tense.
Additional Information:	
Question	**Response**
If this article needs to be "in-press" by a certain date to satisfy grant requirements, please indicate the date below and explain in your cover letter.	
If this article needs to be filmed by a certain date to due to author/equipment/lab availability, please indicate the date below and explain in your cover letter.	May 31, 2014

1 **TITLE:**
2 A human-machine-interface integrating low-cost sensors with a neuromuscular electrical
3 stimulation system for post-stroke balance rehabilitation.
4
5 **AUTHORS:**
6 Kumar, Deepesh
7 Doctoral candidate of Electrical Engineering
8 Indian Institute of Technology Gandhinagar
9 Gandhinagar, India
10 deepesh.kumar@iitgn.ac.in
11
12 Das, Abhijit
13 Director of NeuroRehabilitation
14 Institute of Neurosciences Kolkata
15 Kolkata, India
16 abhijit.neuro@gmail.com
17
18 Lahiri, Uttama
19 Assistant Professor of Electrical Engineering
20 Indian Institute of Technology Gandhinagar
21 Gandhinagar, India
22 uttamalahiri@iitgn.ac.in
23
24 Dutta, Anirban
25 Institut national de recherche en informatique et en automatique-INRIA
26 Montpellier, France
27 anirban.dutta@inria.fr
28
29 **CORRESPONDING AUTHOR:**
30 Dutta, Anirban
31 Institut national de recherche en informatique et en automatique-INRIA
32 Montpellier, France
33 anirban.dutta@inria.fr
34
35 **KEYWORDS:**
36 Stroke, Movement Rehabilitation, Low-cost device, Operant Conditioning, Biofeedback training,
37 Neuroplasticity, Standing Balance.
38
39 **SHORT ABSTRACT:**
40 A novel low-cost human-machine interface for an interactive post-stroke balance rehabilitation
41 system is presented in this article. The system integrates off-the-shelf low-cost sensors towards
42 volitionally driven electrotherapy paradigm. The proof-of-concept software interface is
43 demonstrated on healthy volunteers.
44

LONG ABSTRACT:
A stroke is caused when an artery carrying blood from the heart to an area in the brain bursts or a clot obstructs the blood flow to the brain thereby preventing delivery of oxygen and nutrients. About half of the stroke survivors are left with some degree of disability. Innovative methodologies for restorative neurorehabilitation are urgently required to reduce long-term disability. The ability of the nervous system to reorganize its structure, function and connections as a response to intrinsic or extrinsic stimuli is called neuroplasticity. Neuroplasticity is involved in post-stroke functional disturbances, but also in rehabilitation. Beneficial neuroplastic changes may be facilitated with non-invasive electrotherapy, such as neuromuscular electrical stimulation (NMES). NMES involves coordinated electrical stimulation of nerves and muscles with continuous short pulses of electrical current leading to improvements in muscle strength and reduction in spasticity. Here, active cortical participation in rehabilitation procedures may be facilitated by driving the non-invasive electrotherapy with biosignals (electromyogram (EMG), electroencephalogram (EEG), electrooculogram (EOG)) that represent simultaneous active perception and volitional effort. To achieve this in a resource-poor setting, e.g., in low- and middle-income countries, we present a low-cost human-machine-interface (HMI) by leveraging recent advances in off-the-shelf video game sensor technology. In this paper, we discuss the open-source software interface that integrates low-cost off-the-shelf sensors with NMES to assist postural control for balance rehabilitation. We demonstrate the proof-of-concept on healthy volunteers.

INTRODUCTION:
An episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction is called a stroke[1]. Strokes are a global health problem and fourth leading cause of disability worldwide[1]. In countries like India and China, the two most populous nations of the world, neurologic disability due to stroke is being labeled as a hidden epidemic [2]. One of the most common medical complications after a stroke are falls with a reported incidence of up to 73% in the first year post-stroke [3]. The post-stroke fall is multifactorial and includes both spinal and supraspinal factors like balance and visuospatial neglect [4]. A review by Geurts and colleagues [5] identified multi-directionally impaired maximal weight shifting during bipedal standing, slow speed, directional imprecision, and small amplitudes of single and cyclic sub-maximal frontal plane weight shifts as the balance factors for fall risk. The consequent impact on activities of daily living can be significant since prior works have shown that balance is associated with ambulatory ability and independence in gross motor function [5,6]. Moreover, Geurts and colleagues [5] suggested that supraspinal multisensory integration (and muscle coordination [7]) in addition to muscle strength is critical for balance recovery which is lacking in current protocols. Towards multisensory integration, our hypothesis[8] on volitionally driven NMES is based on the results presented by Roby-Brami et al.[9] who demonstrated acquisition of adaptive behavior by the hemiparetic patients during a volitional hand reaching and grasping task. We further postulate[8] that this adaptive behavior will be facilitated with active perception of sensory inputs during NMES-assisted movement of the affected limb such that the brain can incorporate this feedback into subsequent movement output by recruiting alternate motor pathways[9], if needed.

89   To achieve volitionally driven NMES assisted balance training in a resource-poor setting, a low-
90   cost human-machine-interface (HMI) was developed by leveraging available open-source
91   software and recent advances in off-the-shelf video game sensor technology. NMES involves
92   coordinated electrical stimulation of nerves and muscles that has been shown to improve
93   muscle strength and reduce spasticity [10]. Here, the HMI will make possible sensory-motor
94   integration during interactive post-stroke balance therapy where volitionally-driven NMES for
95   the ankle muscles will act as a muscle amplifier to assist healthy ankle strategies [11,12] for upright
96   stance during postural sways. This is based on the hypothesis presented in Dutta et al. [8] that an
97   increased corticospinal excitability of relevant ankle muscles effected through NMES may lend
98   to an improved supraspinal modulation of ankle stiffness. Indeed, prior work has shown that
99   NMES elicits lasting changes in corticospinal excitability, possibly as a result of co-activating
100   motor and sensory fibers [13]. Moreover, Khaslavskaia and Sinkjaer [14] showed in humans that
101   concurrent motor cortical drive present at the time of NMES enhanced motor cortical
102   excitability. Therefore, volitionally-driven NMES may induce short-term neuroplasticity in spinal
103   reflexes (e.g., reciprocal Ia inhibition [14]) where corticospinal neurons that project via
104   descending pathways to a given motoneuron pool can inhibit the antagonistic motoneuron pool
105   via Ia-inhibitory interneurons in humans [15], as shown in Figure 1, towards an operant
106   conditioning paradigm (see Dutta et al. [8]).
107
108   [Place Figure 1 here]
109
110   The antero-posterior (A-P) displacements in center of mass (CoM) are performed by ankle
111   plantarflexors (such as medial gastrocnemius and soleus muscles) and dorsiflexors (such as the
112   anterior tibial muscle) while medio-lateral (M-L) displacements are performed by ankle
113   invertors (such as the anterior tibial muscle) and evertors (such as peroneus longus and brevis
114   muscles). Consequently, stroke-related ankle impairments including weakness of the ankle
115   dorsiflexor muscles and increased spasticity of the ankle plantarflexor muscles lead to impaired
116   postural control. Here, agility training programs[6] can be leveraged that challenge dynamic
117   balance where tasks are progressively increased in difficulty which may be more effective than
118   static stretching/weight-shifting exercise program in preventing falls [6]. For example, subjects
119   can perform volitionally driven NMES assisted A-P and M-L displacements during a dynamic
120   visuomotor balance task where the difficulty can be progressively increased to ameliorate post-
121   stroke ankle-specific control problems in weight shifting during bipedal standing. Towards
122   volitionally driven NMES assisted balance therapy in a resource-poor setting, we present a low-
123   cost HMI for Mobile Brain/Body Imaging (MoBI)[16], which can also be used for data collection
124   from low-cost sensors for offline data exploration in MoBILAB (see Ojeda et al.[17]).
125
126   **PROTOCOL:**
127
128   Note: The HMI software pipeline was developed based on freely available open-source
129   software and off-the-shelf low-cost video game sensors (details available at:
130   https://team.inria.fr/nphys4nrehab/software/). The HMI software pipeline is provided for data
131   collection during a modified functional reach task (mFRT)[18] for visuomotor balance therapy
132   (VBT)[8]. Figure 2a shows the diagnostic eye tracker setup where the gaze features are extracted

133   offline for the quantification of post-stroke residual function. Figure 2b shows the experimental
134   setup for VBT.
135
136   [Place Figure 2 here]
137
138   1. Software installation for Mobile Brain/Body Imaging during VBT
139
140   1.1. Installation of Psychtoolbox[19] in Windows for the visual biofeedback (installation
141   procedures for different operating systems are given at http://psychtoolbox.org/download/)
142
143   1.1.1. Download Subversion installer from http://www.sliksvn.com/en/download
144
145   1.1.2. Download the Psychtoolbox installer (DownloadPsychtoolbox) to your desktop from
146   https://raw.github.com/Psychtoolbox-3/Psychtoolbox-
147   3/master/Psychtoolbox/DownloadPsychtoolbox.m
148
149   1.1.3. Open the My Computer icon (it is either on the desktop or in the Start Menu).
150
151   1.1.4. Double-click on the C: drive icon.
152
153   1.1.5. Create a new folder called toolbox to install Psychtoolbox into that folder.
154
155   1.1.6. Move the Psychtoolbox installer (DownloadPsychtoolbox) from the Desktop to the new
156   toolbox folder - toolbox.
157
158   1.1.7. Open Matlab as administrative user and type the following in the command window:
159   >> cd C:\toolbox
160   >> DownloadPsychtoolbox('C:\toolbox')
161
162   1.2. Install drivers for the Motion Capture (installation procedures provided at
163   https://code.google.com/p/labstreaminglayer/wiki/KinectMocap)
164
165   1.2.1. Download and install Kinect Runtime from
166   http://go.microsoft.com/fwlink/?LinkId=253187. Do not plug in the motion Capture sensor into
167   any of the USB ports on the computer.
168
169   1.2.2. Plug in the powered Motion Capture Sensor into a USB port via the interface cable. The
170   drivers will load automatically.
171
172   1.3. Install drivers for the Eye Tracker Sensor (installation procedures provided at
173   https://github.com/esdalmaijer/EyeTribe-Toolbox-for-Matlab)
174

175   1.3.1. Download the software from http://theeyetribe.com, launch the application and install
176   the software (Eye Tracker sensor should not be plugged into any of the USB ports on the
177   computer).
178
179   1.3.2. Plug in the powered Eye Tracker Sensor and the drivers will load automatically.
180
181   1.3.3. Download and extract the Matlab toolbox from
182   https://github.com/esdalmaijer/EyeTribe-Toolbox-for-Matlab/archive/master.zip.
183
184   1.3.4. In Matlab, go to File -> Set Path -> Add folder, and add the EyeTribe_for_Matlab folder to
185   communicate with the Eye Tracker Sensor from Matlab.
186
187   1.4. Install drivers for the Balance Board (installation procedures provided at
188   http://www.colorado.edu/intphys/neuromechanics/cu_wii.html)
189
190   1.4.1. Download and extract CU_WiiBB.zip from
191   http://www.colorado.edu/intphys/neuromechanics/CU_WiiBB.zip
192
193   1.4.2. Copy the WiiLab folder to Microsoft Window operating system's standard Program Files
194   directory.
195
196   1.4.3. Open the WiiLab folder in the Program Files directory and run as an administrator the
197   InstallWiiLab.bat file to install the Balance Board.
198
199   1.5. Install drivers for EEG (installation procedures provided at http://openvibe.inria.fr/how-to-
200   connect-emotiv-epoc-with-openvibe/)
201
202   1.5.1. Download and install Emotiv SDK from http://www.emotiv.com/apps/sdk/209/
203
204   1.6. Download and install OpenViBE Acquisition Server with labstreaminglayer (LSL) from
205   https://code.google.com/p/labstreaminglayer/downloads/detail?name=OVAS-withLSL-0.14.3-
206   3350-svn.zip for distributed multi-sensor signal transport, time synchronization and data
207   collection system (installation procedures provided at
208   https://code.google.com/p/labstreaminglayer/).
209
210   ==2. Low-cost sensor placement for Mobile Brain/Body Imaging (MoBI)==
211
212   Note: The open-source HMI software pipeline provides Mobile Brain/Body Imaging (MoBI) [16]
213   with low-cost off-the-shelf sensors (see Figure 2b) which can be adapted for other agility
214   training programs.
215
216   ==2.1. Visual Feedback for MoBI:==
217

218 2.1.1. Place the personal computer (PC) monitor (recommended 0.6 m) for visual biofeedback
219 at the one end of the room on an adjustable stand. Adjust the height such that the center of
220 the screen is roughly at the eye-level of the subject.
221
222 2.2. Motion Capture for MoBI:
223
224 2.2.1. Place the Motion Capture Sensor in front of the PC monitor such that it is aimed at the
225 volume of motion capture. Confirm that the volume of motion capture is 1.5 m to 2.4 m in the
226 front of the Motion Capture Sensor.
227
228 2.3. Balance Board placement for MoBI:
229
230 2.4.1. Place the Balance Board on the floor, roughly 2.0 m away from the PC monitor stand.
231 Make sure that there is enough space around the Balance Board for full-body movement (i.e.,
232 during modified functional reach task[18]).
233
234 2.5. EEG/EMG/EOG sensor placement for MoBI
235
236 2.5.1. Ask the subject to sit on a chair facing the Motion Capture and with their feet on the
237 Balance Board.
238
239 2.5.2. Place the recording (EMG) cum stimulation (NMES) electrodes bilaterally on the Medial
240 Gastrocnemius (MG) and Tibialis Anterior (TA) muscles of the subject. Then, connect them to
241 the wireless NMES stimulator system.
242
243 2.5.3. Place the electroencephalogram (EEG) cap on the subjects head following the
244 International 10–20 system. Then, place the EEG active electrodes with conductive paste at —
245 Fz, C3, Cz, C4, P3, Pz, P4, PO7, Oz, PO8 — before connecting them to the wireless EEG headset.
246
247 2.5.4. Place two EEG passive electrodes with conductive paste above and below one of eyes for
248 vertical EOG and put two electrodes with conductive paste at the outer canthus of each eye for
249 horizontal EOG.
250
251 2.5.5. Place two EEG passive electrodes on earlobes as EEG reference electrodes.
252
253 3. NMES-assisted visuomotor balance therapy (VBT) under MoBI
254
255 3.1. Install the drivers for the commercial NMES stimulator (details at
256 http://www.vivaltis.com/gammes/phenix/phenix-usb-neo-50-554-1.html#content).
257
258 3.2. Connect all the sensors to PC (see Figure 2).
259

260 3.2.1. Make sure that the Eye Tracker sensor is powered on, connected to computer, and that it
261 has fully booted. Start the Eye Tracker server - EyeTribe.exe and EyeTribe_Matlab_server.exe -
262 applications available in the Eye Tracker driver folder (see steps 1.3).
263
264 3.2.2. Make sure that the Motion Capture sensor is powered on, connected to the computer
265 and that it has fully booted (there is a green LED on the front). Start the KinectMocap
266 application available in the LSL folder (see steps 1.6) which will automatically link itself to the
267 LSL and start streaming Motion Capture sensor data.
268
269 3.2.3. Make sure that the Balance Board sensor is powered on. Then, right-click on the
270 Bluetooth icon in the task bar and select "Add a Device". Press and release the Button of the
271 Balance Board sensor, which makes the remote discoverable. The device should show up in the
272 list of discovered devices. Add this device and click "pair without using a code." Then, start the
273 Wiimote application available in the LSL folder (see steps 1.6) which will automatically link itself
274 to the LSL and start streaming Balance Board sensor data.
275
276 3.2.4. Make sure that the EEG/EOG data acquisition systems are powered on. Then, double-
277 click on the openvibe-acquisition-server-withlsl.cmd available in the LSL folder (see steps 1.6).
278 From the menu, select the respective sensor hardware (i.e., Emotiv EPOC for EEG/EOG) and
279 configure the module, if necessary, by clicking on the "Driver Properties". Then, click on
280 "Connect", and then click on "Play" to start the acquisition server.
281
282 3.3. Calibrate the sensors for VBT
283
284 3.3.1. Ask the subject to stand on the Balance Board with safety harness (and partial body
285 weight support, if necessary).
286
287 3.3.2. Set a minimum baseline NMES level (pulse-width and current level) necessary for upright
288 standing according to clinical observation (i.e., zero body weight support)[20]. For setting the
289 minimum baseline NMES level, set the stimulation frequency at 20 Hz and then increase the
290 pulse-width and/or current level until upright standing is achieved. Here, NMES of knee
291 extensors is required to generate enough torque to prevent knee buckling.
292
293 3.3.3. Ask the subject to perform various reach movements that affects CoM and CoP location
294 as cued by the visual feedback.
295
296 3.3.4. Run 'CalibSensors.m' program in Matlab to collect calibration data from Motion Capture
297 Sensor, Balance Board, and EEG data acquisition systems while the subject performs various
298 visually cued reach movements that affects center of mass (CoM) and center of pressure (CoP)
299 location. The calibration program will identify subject-specific maximum EMG level (MEL) of the
300 muscles and maximum excursions of CoM/CoP (CoM_{max}/CoP_{max}) during the reach movements.
301
302 4. Eye Tracker based evaluation of post-stroke pursuit eye movements
303

304   4.1. Ask the subject to sit with the chin resting comfortably on the height-adjustable Chin-Rest.
305   Then, raise the computer monitor to a convenient height such that the eyes are roughly facing
306   the center of the computer monitor (see Figure 2a).

308   4.2. Place the Eye Tracker roughly 50 cm from the Chin-Rest and ask the subject to look straight
309   at the computer monitor for visual cues.

311   4.3. Run EyeTribeWinUI.exe in the Eye Tracker driver folder to calibrate the Eye Tracker sensor.
312   The subject will be asked to look at various targets on the PC monitor for roughly 2 seconds
313   each. A typical user calibration process takes approximately 20 seconds to complete. The (x, y)
314   coordinates of the subject's gaze point are recorded for different cued targets for calibration.

316   4.4. Run 'EyeTrack' program while asking the subject to pursue the moving dot on the computer
317   monitor. This data will be used for the evaluation of post-stroke pursuit eye movement.

319   [Place Figure 3 here]

321   5. Multi-sensor data collection from low-cost sensors during VBT (see Figure 2b)

323   5.1. Run 'CollectBaseline.m' program in Matlab to collect baseline resting-state eyes-open
324   multi-sensor data by asking the subject to stand still for 2 minutes while looking straight at the
325   CoP target on the PC monitor (see Figure 3a).

327   5.2. Run 'CollectVBT.m' program in Matlab to collect sensor data during VBT.

329   5.2.1. From upright standing, called the 'Central hold' phase, ask the subject to steer the cursor,
330   driven by the CoP, as fast as possible towards randomly presented peripheral target as cued by
331   visual feedback (see Figure 3b).

333   5.2.2. Following this 'Move' phase, ask the subject to hold the cursor at the target location for 1
334   sec during the 'Peripheral hold' phase.

336   5.2.3. Following the 'Peripheral hold' phase, the cursor will 'Reset' back to the center when the
337   subject needs to return back to upright standing - the 'Central hold' position. NMES is triggered
338   for the muscle when its EMG level goes above a certain target level (set as a percent of MEL) to
339   assist the volitional effort to return the CoP to the 'Central hold' position.

341   Note: The difficulty of the mFRT can be increased by decreasing the gain, ε, or increasing the
342   noise variance, $\eta = N(0, \sigma = 0.1s^{-2})$, within subject-specific feasible range:

343   $$\begin{bmatrix} x \\ y \end{bmatrix}_{Cur}^{t} = \varepsilon \begin{bmatrix} x \\ y \end{bmatrix}_{CoP}^{t} + \eta$$

344 where the CoP excursions, $\begin{bmatrix} x \\ y \end{bmatrix}_{CoP}$, drive the computer cursor, $\begin{bmatrix} x \\ y \end{bmatrix}_{Cur}$, in discretized time, t,

345 with time-step, dt.

346

347 **REPRESENTATIVE RESULTS:**

348 Figure 4 shows the eye gaze features that were extracted offline for the quantification of an

349 able-bodied performance during a smooth pursuit task. The following features were extracted

350 as shown in Table 1:

351 Feature1= percentage deviation between target stimulus position and the centroid of

352 participant's fixation points when the stimulus is changing position in the horizontal direction.

353 Feature2= percentage deviation between target stimulus position and centroid of participant's

354 fixation points when the stimulus is changing position in the vertical direction.

355 Feature3 = blink per minute

356 Feature4 = percentage of time the participant is looking (eye was detected by eye tracker) at

357 the stimulus.

358 Feature5 = percentage of time the participant is not looking (eye was detected by eye tracker)

359 at the stimulus. (Note: Feature 5= 100-Feature 4)

360 Feature6 = percentage Smooth Pursuit Length (SPL) overshoot made by the participant, i.e.,

361 $$\% SPL\ Overshoot = \left(\frac{SPL - SML}{SML} \right) \times 100$$

362 where SPL=Smooth Pursuit Length is the length (in pixels) covered by participant to track the

363 moving stimulus, SML= Stimulus Movement Length (in pixel), i.e., actual length of the path in

364 which the stimulus moves.

365

366 [Place Figure 4 here]

367

368 A proof-of-concept VBT study (without NMES) was conducted on 10 able-bodied subjects (5

369 right-leg dominant males and 5 right-leg dominant females aged between 22 to 46 years) under

370 a modified functional reach task (mFRT) paradigm (see Figure 3c). The mFRT is proposed to

371 quantify the subjects' ability to volitionally shift their CoP position as quickly as possible without

372 losing balance while cued with CoP visual biofeedback. During mFRT, multi-sensor data was

373 collected for mobile brain/body imaging (MoBI)[16]. MOBI data was processed offline to

374 determine the overall postural sway from CoP (from Balance Board) and CoM (from Motion

375 Capture Sensor) trajectories. Also, the features were extracted from biosignals that were

376 recorded simultaneously along with the gaze behavior (e.g., blink rate, saccadic direction from

377 electrooculogram). The results from this proof-of-concept study was presented in Dutta et al.[8]

378 where alpha event-related desynchronization (aERD%) was found primarily in the parietal and

379 occipital EEG electrodes. Moreover, the mean squared error (MSE) normalized by the baseline

380 value trended towards a decrease, the blink rate trended towards an increase, and the saccadic

381 direction relative to the cursor acceleration trended towards zero during learning of the

382 visuomotor task. Based on the data from Dutta et al.[8], the EOG data showed that the ratio of

383 fixation duration on the target and the fixation duration on the cursor before the initiation of

384 the motor response (i.e., EMG onset) - FD_{ratio} - increased (see Figure 5a) while the baseline

385   normalized mean squared error (MSEnorm) decreased (see Figure 5b) during VBT trials.
386
387   [Place Figure 5 here]
388
389   Figure 1. The concept (details at Dutta et al.[21]) underlying interactive human machine interface
390   (HMI) to drive the center of pressure (CoP) cursor to the cued target to improve ankle muscle
391   coordination under volitionally driven neuromuscular electrical stimulation (NMES)-assisted
392   visuomotor balance therapy. EEG: electroencephalography, MN: α-motoneuron, IN: Ia-
393   inhibitory interneuron, EMG: electromyogram, DRG: dorsal root ganglion.
394
395   Figure 2. a) Schematic of the human-machine-interface for the evaluation of post-stroke pursuit
396   eye movements. b) Schematic of the human-machine-interface where the software interface
397   integrates biosignal sensors and motion capture to record mobile brain/body imaging data with
398   a neuromuscular electrical stimulation system (NMES) for post-stroke NMES-assisted
399   visuomotor balance therapy. NMES: Neuromuscular Electrical Stimulation, EMG:
400   Electromyogram, EEG: Electroencephalogram, EOG: Electrooculogram, CoP: Center of Pressure,
401   PC: Personal Computer.
402
403   Figure 3. a) Cursor representing the center of pressure (CoP) which needs to be volitionally
404   driven to the cued target during visuomotor balance therapy , b) Visuomotor balance therapy
405   protocol where the subject steers the computer cursor to a peripheral target driven by
406   volitionally generated CoP excursions. The Reset can be assisted with Neuromuscular Electrical
407   Stimulation (NMES), c) Experimental setup for visually-cued visuomotor balance therapy.
408
409   Figure 4. Top panel shows an illustrative figure of the smooth pursuit during horizontal
410   movement. Bottom panel shows an illustrative figure of the smooth pursuit during vertical
411   movement.
412
413   Figure 5. a) Changes in the ratio of fixation duration on the target and the fixation duration on
414   the cursor - FDratio - extracted from electrooculogram during visuomotor balance task (VBT)
415   trials. b) Changes in the baseline normalized mean squared error (MSEnorm) during VBT trials.
416
417   Figure 6. Left panel shows the joint labels for the skeleton model data from the Motion Capture
418   Sensor which can be analyzed offline using a reduced dimension biped model (right panel) for
419   capturing the posture. (see Banerjee et al. [22]). RMP: Reaction Mass Pendulum, CoP: Center of
420   Pressure, CoM: Center of Mass, GRF: Ground reaction force vector.
421
422   Table 1. Eye Gaze Feature
423
424   **DISCUSSION:**
425   A simple-to-use, clinically valid low-cost tool for movement and balance therapy will be a
426   paradigm shift for neurorehabilitation in a low-resource setting. It is likely to have a very high
427   societal impact since neurological disorders like stroke will dramatically increase in future due
428   to aging world population [2]. There is, therefore, a pressing need to leverage cyber physical

429 systems where the ability to customize, monitor, and support neuro-rehabilitation at remote
430 sites has recently become possible with the integrations of computation, networking, and
431 physical processes via telecommunications. Towards that overarching goal, the low-cost Eye
432 Tracker based evaluation of post-stroke pursuit eye movements can not only provide home-
433 based diagnosis but also therapy where smooth pursuit eye movement training promoted
434 recovery from auditory and visual neglect[23]. Here, the latency of the smooth-pursuit in healthy
435 subjects has been found to be very consistent for targets moving 5 degrees/s or faster with a
436 mean latency of 100±5 ms[24].
437
438 Moreover, the proposed human-machine-interface (HMI) for volitionally driven neuromuscular
439 electrical stimulation (NMES) for post-stroke balance therapy integrated biosignal sensors and
440 motion capture with NMES for post-stroke balance rehabilitation, which has the potential[25][26]
441 as a home-based intervention to post-stroke improve standing balance. The novel part of the
442 HMI is the software interface that integrates multiple off-the-shelf low-cost sensors to record
443 mobile brain/body imaging data during NMES assisted visuomotor balance therapy (VBT).
444 Based on healthy subject results from the proof-of-concept study (without NMES), we propose
445 that the multi-sensor information can be fused to estimate the state of motor learning during
446 post-stroke VBT, and therefore the difficulty can be adapted online for mFRT. For example,
447 smooth pursuit eye movement training [23] can be integrated with myoelectrically driven NMES-
448 assisted visuomotor task, as presented in Dutta et al.[8], where alpha event-related
449 desynchronization at the parietal and occipital EEG electrodes may predict the normalized
450 mean square error (MSE) in reaching the peripheral targets. Therefore, based on the evaluation
451 of post-stroke pursuit eye movements as well as the gaze behavior during VBT task, we can
452 objectively analyze and monitor eye-related problems contributing to balance disability. The
453 residual function can be reconditioned with a gradual increase in the intensity (number of hours
454 per day) and frequency (number of days per week) of VBT thereby providing a higher level as
455 they improve their function [27]. Moreover, gaze behavior (e.g. blink rate, saccades) can be used
456 to monitor user engagement during motor learning [28].
457
458 The motor learning during VBT can be analyzed using a reduced dimension reaction mass
459 pendulum (RMP) biped model that is presented in Dutta et al.[22]. The reduced dimension RMP
460 model[22] can be constructed offline from skeleton tracking data (which is the joint data that is
461 streamed out of the Motion Capture sensor in the skeleton stream, see Figure 6). Significance
462 of RMP model over traditional point-mass pendulum model was during occasional arm swinging
463 in healthy to regain balance at the limits of stability during mFRT where the RMP model
464 augmented the traditional point-mass pendulum model by capturing the shape, size and
465 orientation of the aggregate rotational centroidal inertia. In our prior work [18] we concluded that
466 the CoM-CoP lean-line could be used for posture feedback and monitoring during tDCS therapy
467 in conjunction with balance training exercises. Also, we have shown the relevance of whole
468 body normalized centroidal angular momentum during stand-to-walk transition in post-stroke
469 gait[22]. Indeed, angular momentum is tightly regulated with segment-to-segment cancellations
470 of angular momentum during human walking[29] and possibly in all coordinated human
471 movement including mFRT to prevent falls. Based on these prior works, it can be postulated
472 that stroke survivors with muscle weakness and coordination deficits will take it longer to

473 regulate CAM when compared to age-matched able-bodied subjects. This is currently under
474 investigation using the reduced dimension RMP model[22].
475
476 [Place Figure 6 here]
477
478 The grand challenge is to develop and clinically validate advanced cyber physical systems for
479 teleneurorehabilitation that is based on the manipulation of environmental, behavioral, and
480 pharmacologic contexts. The future applications of the HMI include a teleneurorehabilitation
481 paradigm in a home-based setup where identification and monitoring of visuomotor
482 deficits/learning from gaze-behavior may lend to an operant conditioning paradigm which will
483 enforce volitional use of relevant residual function. For example, the HMI can be augmented
484 with two Wii BB (one for the paretic and one for the non-paretic limb) which can be positioned
485 side by side without touching (i.e., <1 mm apart). Following the experimental protocol of
486 Mansfield and colleagues [7], the subjects could stand with one foot on each Wii BB in a standard
487 position (feet oriented at 14° with 7° rotation of each foot with an inter-malleoli distance equal
488 to 8% of the height), with each foot equidistant from the midline between both Wii BBs. During
489 mFRT, both the paretic and non-paretic limbs will contribute to the CoP position where the
490 operant conditioning can be implemented by providing positive reinforcement to the residual
491 function of the paretic limb and negative reinforcement for the compensatory mechanisms of
492 the non-paretic limb (based on the principle of constraint-induced movement therapy [30]) by
493 making the cursor easier to control with the CoP excursions of the paretic side. Moreover,
494 visual field defects, both homonymous defects and those defects related to optic nerve lesion,
495 may be improved—at least to some extent—in patients [31] towards better visuomotor
496 integration [32] contributing to improved balance. The clinical stroke study under the hypothesis
497 that our low-cost HMI towards volitionally driven NMES assisted dynamic visuomotor balance
498 therapy can ameliorate post-stroke ankle-specific control problems in visually cued weight
499 shifting during bipedal standing is conducted at the Institute of Neurosciences Kolkata, India. It
500 is expected to reduce the fall incidence rates in chronic stroke survivors, which can be high as
501 2.2 to 4.9 falls each person-year [33]. Indeed, for showing the efficacy of this HMI for post-stroke
502 balance therapy towards restorative neurorehabilitation, the critical step is subject selection,
503 i.e., stroke survivors who have sufficient residual sensorimotor function necessary for
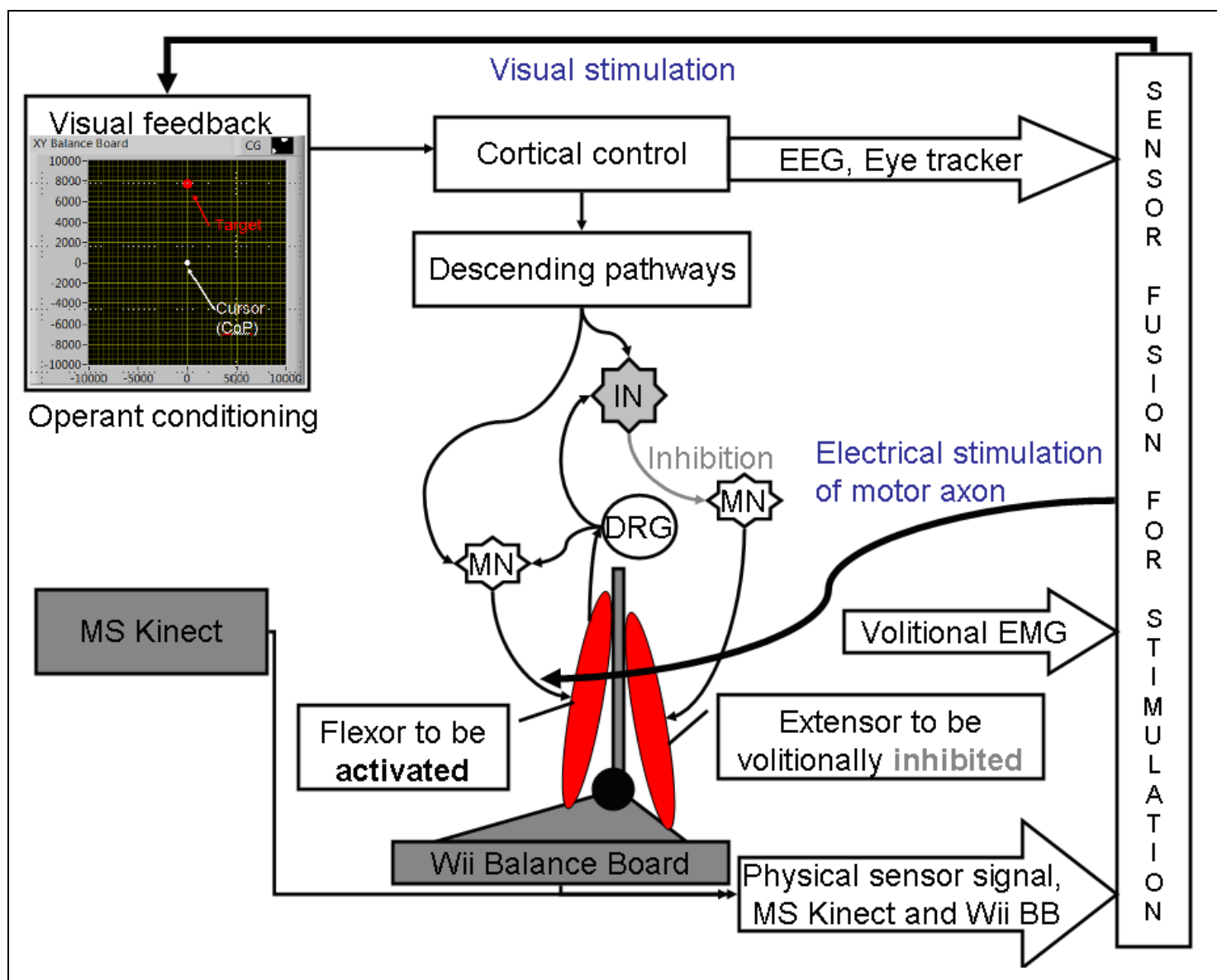504 recovery[34].
505

515
516 **REFERENCES**:

517 1. Sacco, R. L., *et al.* An updated definition of stroke for the 21st century: a statement for
518   healthcare professionals from the American Heart Association/American Stroke
519   Association. *Stroke; a journal of cerebral circulation* **44** (7), 2064–2089, doi:
520   10.1161/STR.0b013e318296aeca (2013).
521 2. Das, A., Botticello, A. L., Wylie, G. R. & Radhakrishnan, K. Neurologic Disability: A Hidden
522   Epidemic for India. *Neurology* **79** (21), 2146–2147, doi: 10.1212/WNL.0b013e3182752cdb
523   (2012).
524 3. Verheyden, G. S. A. F., *et al.* Interventions for preventing falls in people after stroke. *The*
525   *Cochrane database of systematic reviews* **5**, CD008728, doi:
526   10.1002/14651858.CD008728.pub2 (2013).
527 4. Campbell, G. B. & Matthews, J. T. An integrative review of factors associated with falls
528   during post-stroke rehabilitation. *Journal of Nursing Scholarship: An Official Publication of*
529   *Sigma Theta Tau International Honor Society of Nursing / Sigma Theta Tau* **42** (4), 395–404,
530   doi: 10.1111/j.1547-5069.2010.01369.x (2010).
531 5. Geurts, A. C. H., de Haart, M., van Nes, I. J. W. & Duysens, J. A review of standing balance
532   recovery from stroke. *Gait & posture* **22** (3), 267–281, doi: 10.1016/j.gaitpost.2004.10.002
533   (2005).
534 6. Marigold, D. S., *et al.* Exercise leads to faster postural reflexes, improved balance and
535   mobility, and fewer falls in older persons with chronic stroke. *Journal of the American*
536   *Geriatrics Society* **53** (3), 416–423, doi: 10.1111/j.1532-5415.2005.53158.x (2005).
537 7. Mansfield, A., Mochizuki, G., Inness, E. L. & McIlroy, W. E. Clinical correlates of between-
538   limb synchronization of standing balance control and falls during inpatient stroke
539   rehabilitation. *Neurorehabilitation and neural repair* **26** (6), 627–635, doi:
540   10.1177/1545968311429688 (2012).
541 8. Dutta, A., Lahiri, U., Das, A., Nitsche, M. A. & Guiraud, D. Post-stroke balance rehabilitation
542   under multi-level electrotherapy: a conceptual review. *Neuroprosthetics* **8**, 403, doi:
543   10.3389/fnins.2014.00403 (2014).
544 9. Agnes Roby-Brami, S. F. Reaching and Grasping Strategies in Hemiparetic Patients. *Human*
545   *Kinetics Journals* at <http://journals.humankinetics.com/mc-back-
546   issues/mcvolume1issue1january/reachingandgraspingstrategiesinhemipareticpatients>
547   (2010).
548 10. Sabut, S. K., Sikdar, C., Kumar, R. & Mahadevappa, M. Functional electrical stimulation of
549   dorsiflexor muscle: effects on dorsiflexor strength, plantarflexor spasticity, and motor
550   recovery in stroke patients. *NeuroRehabilitation* **29** (4), 393–400, doi: 10.3233/NRE-2011-
551   0717 (2011).
552 11. Hwang, S., Tae, K., Sohn, R., Kim, J., Son, J. & Kim, Y. The balance recovery mechanisms
553   against unexpected forward perturbation. *Annals of biomedical engineering* **37** (8), 1629–
554   1637, doi: 10.1007/s10439-009-9717-y (2009).
555 12. Gatev, P., Thomas, S., Kepple, T. & Hallett, M. Feedforward ankle strategy of balance during
556   quiet stance in adults. *The Journal of physiology* **514 (Pt 3)**, 915–928 (1999).
557 13. Knash, M. E., Kido, A., Gorassini, M., Chan, K. M. & Stein, R. B. Electrical stimulation of the
558   human common peroneal nerve elicits lasting facilitation of cortical motor-evoked
559   potentials. *Experimental brain research* **153** (3), 366–377, doi: 10.1007/s00221-003-1628-9
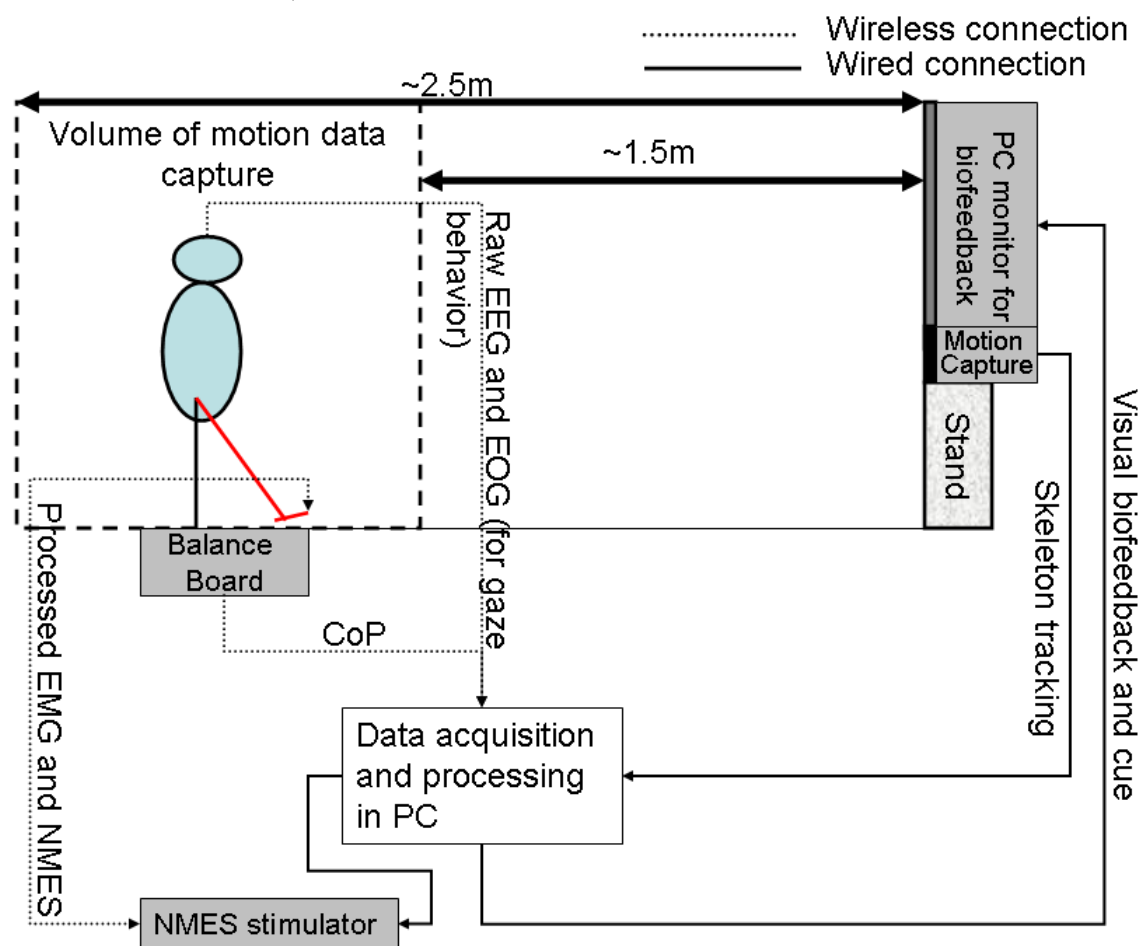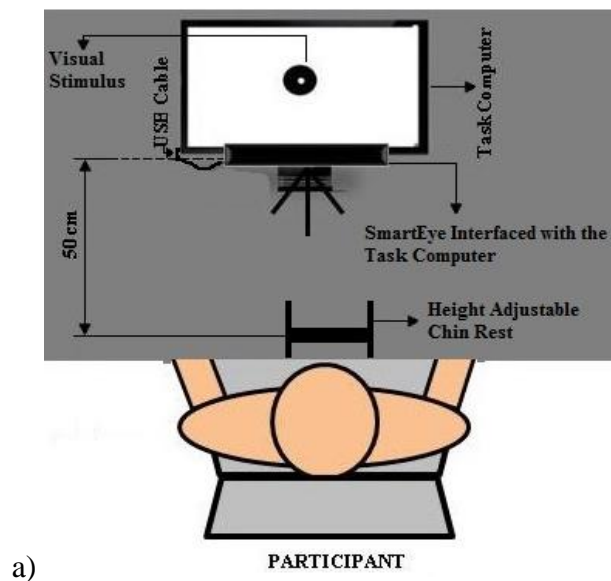560   (2003).

561 14. Khaslavskaia, S. & Sinkjaer, T. Motor cortex excitability following repetitive electrical
562   stimulation of the common peroneal nerve depends on the voluntary drive. *Experimental*
563   *brain research* **162** (4), 497–502, doi: 10.1007/s00221-004-2153-1 (2005).
564 15. Perez, M. A., Field-Fote, E. C. & Floeter, M. K. Patterned sensory stimulation induces
565   plasticity in reciprocal ia inhibition in humans. *The Journal of neuroscience: the official*
566   *journal of the Society for Neuroscience* **23** (6), 2014–2018 (2003).
567 16. Makeig, S. Mind Monitoring via Mobile Brain-Body Imaging. *Foundations of Augmented*
568   *Cognition. Neuroergonomics and Operational Neuroscience* , 749–758at
569   <http://link.springer.com/chapter/10.1007/978-3-642-02812-0_85> (2009).
570 17. Ojeda, A., Bigdely-Shamlo, N. & Makeig, S. MoBILAB: an open source toolbox for analysis
571   and visualization of mobile brain/body imaging data. *Frontiers in Human Neuroscience* **8**,
572   121, doi: 10.3389/fnhum.2014.00121 (2014).
573 18. Dutta, A., Chugh, S., Banerjee, A. & Dutta, A. Point-of-care-testing of standing posture with
574   Wii balance board and microsoft kinect during transcranial direct current stimulation: A
575   feasibility study. *NeuroRehabilitation* **34** (4), 789–798, doi: 10.3233/NRE-141077 (2014).
576 19. Brainard, D. H. The Psychophysics Toolbox. *Spatial Vision* **10** (4), 433–436 (1997).
577 20. Nataraj, R. Feedback control of standing balance using functional neuromuscular
578   stimulation following spinal cord injury. Ohio.gov, PhD Thesis,
579   https://etd.ohiolink.edu/ap/10?0::NO:10:P10_ETD_SUBID:52547 (2011).
580 21. Dutta, A., Paulus, W. & A. Nitsche, M. Translational Methods for Non-Invasive Electrical
581   Stimulation to Facilitate Gait Rehabilitation Following Stroke - The Future Directions.
582   *Neuroscience and Biomedical Engineering* **1** (1), 22–33, doi:
583   10.2174/2213385211301010005 (2013).
584 22. Banerjee, A., Khattar, B. & Dutta, A. A Low-Cost Biofeedback System for Electromyogram-
585   Triggered Functional Electrical Stimulation Therapy: An Indo-German Feasibility Study. *ISRN*
586   *Stroke* **2014**, e827453, doi: 10.1155/2014/827453 (2014).
587 23. Kerkhoff, G., Reinhart, S., Ziegler, W., Artinger, F., Marquardt, C. & Keller, I. Smooth pursuit
588   eye movement training promotes recovery from auditory and visual neglect: a randomized
589   controlled study. *Neurorehabilitation and Neural Repair* **27** (9), 789–798, doi:
590   10.1177/1545968313491012 (2013).
591 24. Carl, J. R. & Gellman, R. S. Human smooth pursuit: stimulus-dependent responses. *Journal*
592   *of Neurophysiology* **57** (5), 1446–1463 (1987).
593 25. Clark, R. A., Bryant, A. L., Pua, Y., McCrory, P., Bennell, K. & Hunt, M. Validity and reliability
594   of the Nintendo Wii Balance Board for assessment of standing balance. *Gait & posture* **31**
595   (3), 307–310, doi: 10.1016/j.gaitpost.2009.11.012 (2010).
596 26. Clark, R. A., Pua, Y.-H., *et al.* Validity of the Microsoft Kinect for assessment of postural
597   control. *Gait & posture* **36** (3), 372–377, doi: 10.1016/j.gaitpost.2012.03.033 (2012).
598 27. Khattar, B., Banerjee, A., Reddi, R. & Dutta, A. Feasibility of Functional Electrical
599   Stimulation-Assisted Neurorehabilitation following Stroke in India: A Case Series. *Case*
600   *Reports in Neurological Medicine* **2012**, e830873, doi: 10.1155/2012/830873 (2012).
601 28. Sailer, U., Flanagan, J. R. & Johansson, R. S. Eye-hand coordination during learning of a
602   novel visuomotor task. *The Journal of neuroscience: the official journal of the Society for*
603   *Neuroscience* **25** (39), 8833–8842, doi: 10.1523/JNEUROSCI.2658-05.2005 (2005).

604 29. Herr, H. & Popovic, M. Angular momentum in human walking. *The Journal of Experimental*
605   *Biology* **211** (Pt 4), 467–481, doi: 10.1242/jeb.008573 (2008).
606 30. Taub, E. & Morris, D. M. Constraint-induced movement therapy to enhance recovery after
607   stroke. *Current atherosclerosis reports* **3** (4), 279–286 (2001).
608 31. Kasten, E., Wuest, S. & Sabel, B. A. Residual vision in transition zones in patients with
609   cerebral blindness. *Journal of Clinical and Experimental Neuropsychology* **20** (5), 581–598,
610   doi: 10.1076/jcen.20.5.581.1129 (1998).
611 32. Marshall, S. P. Identifying Cognitive State from Eye Metrics. *Aviation, Space, and*
612   *Environmental Medicine* **78** (5), B165–B175 (2007).
613 33. Weerdesteyn, V., de Niet, M., van Duijnhoven, H. J. R. & Geurts, A. C. H. Falls in individuals
614   with stroke. *Journal of Rehabilitation Research and Development* **45** (8), 1195–1213 (2008).
615 34. Stinear, C. M., Barber, P. A., Petoe, M., Anwar, S. & Byblow, W. D. The PREP algorithm
616   predicts potential for upper limb recovery after stroke. *Brain: A Journal of Neurology* **135**
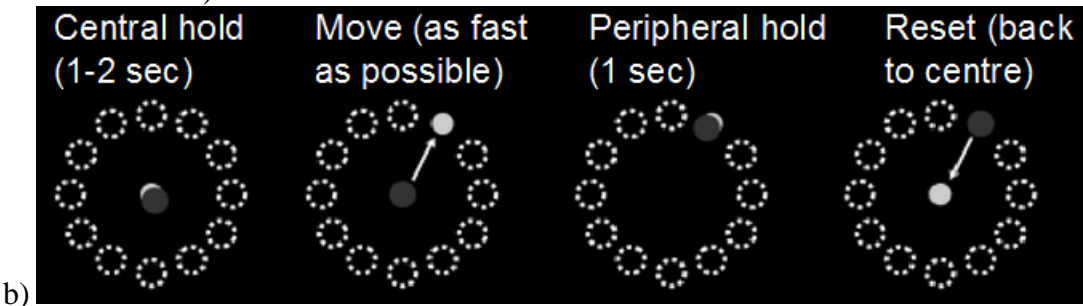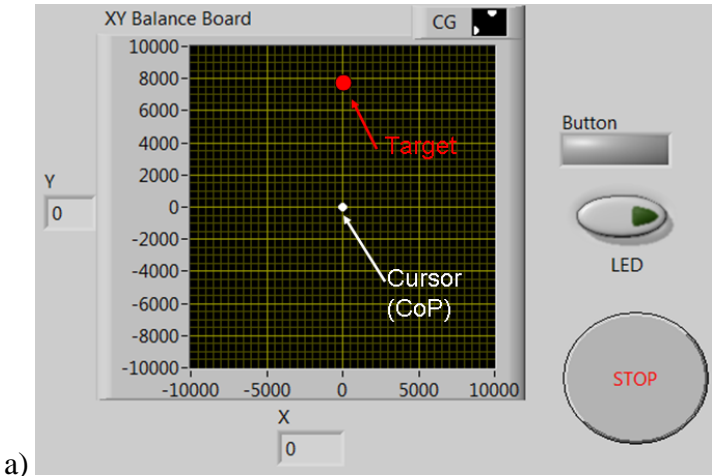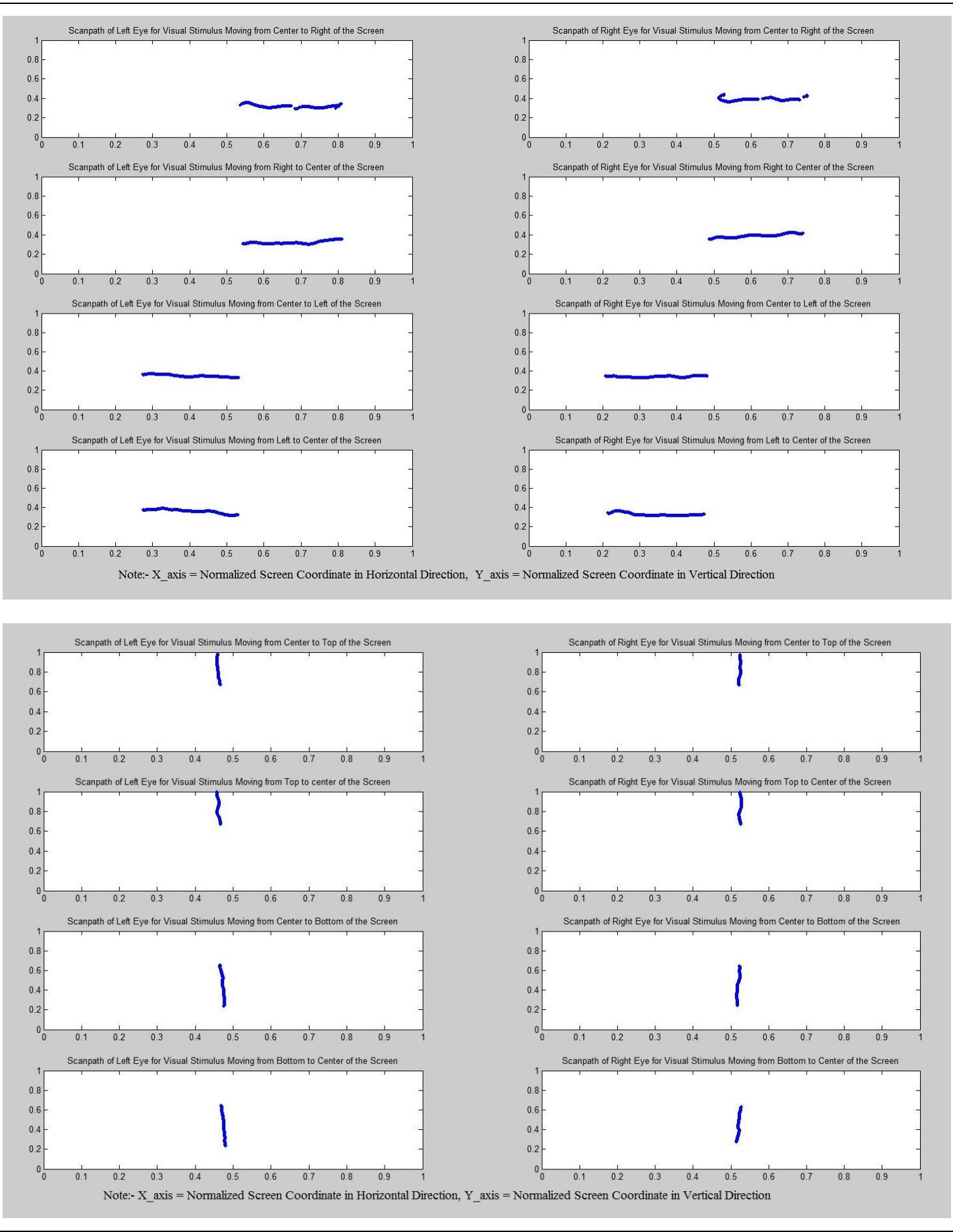617   (Pt 8), 2527–2535, doi: 10.1093/brain/aws146 (2012).
618

Figure 1
Click here to download Figure: Figure 1n.doc

Figure 1

Figure 2
Click here to download Figure: Figure 2n.doc

a)

b)

Figure 3

a)

b)

c)

Figure 4

Note:- X_axis = Normalized Screen Coordinate in Horizontal Direction, Y_axis = Normalized Screen Coordinate in Vertical Direction

Note:- X_axis = Normalized Screen Coordinate in Horizontal Direction, Y_axis = Normalized Screen Coordinate in Vertical Direction
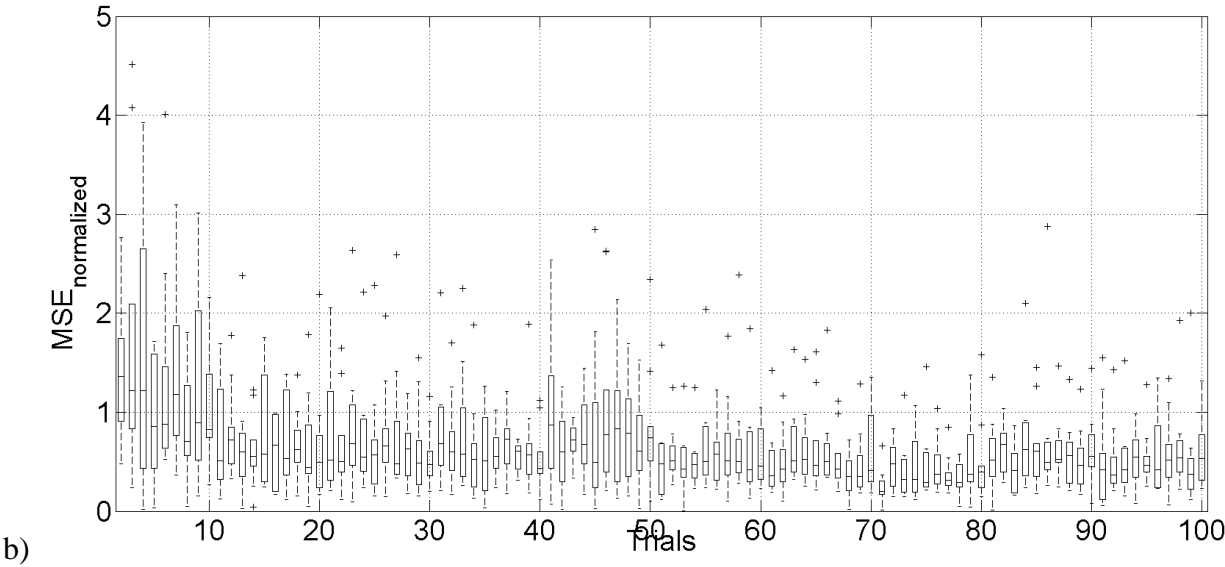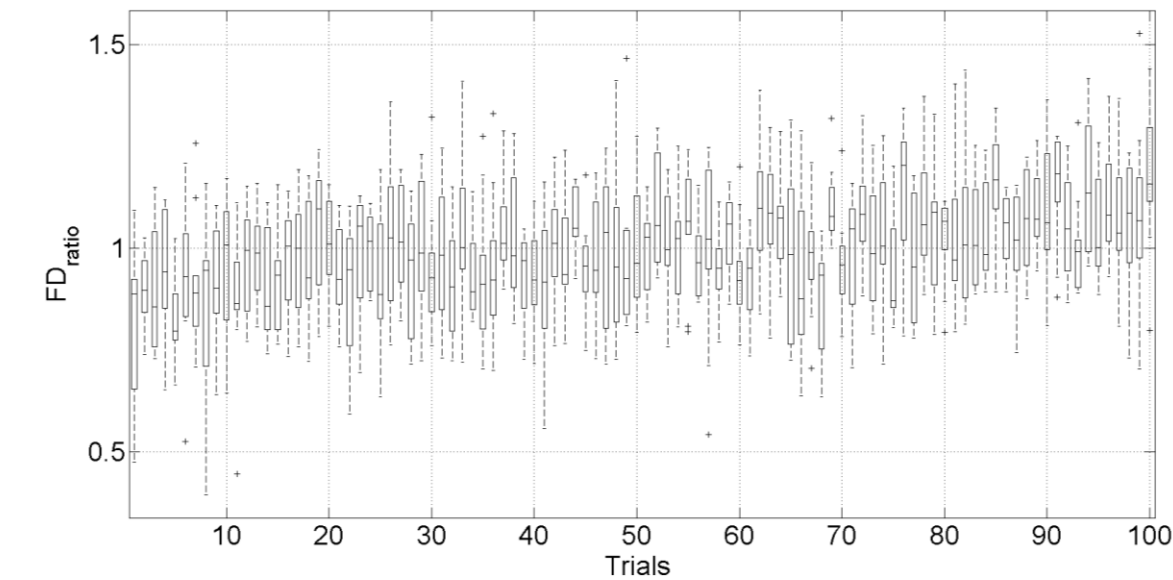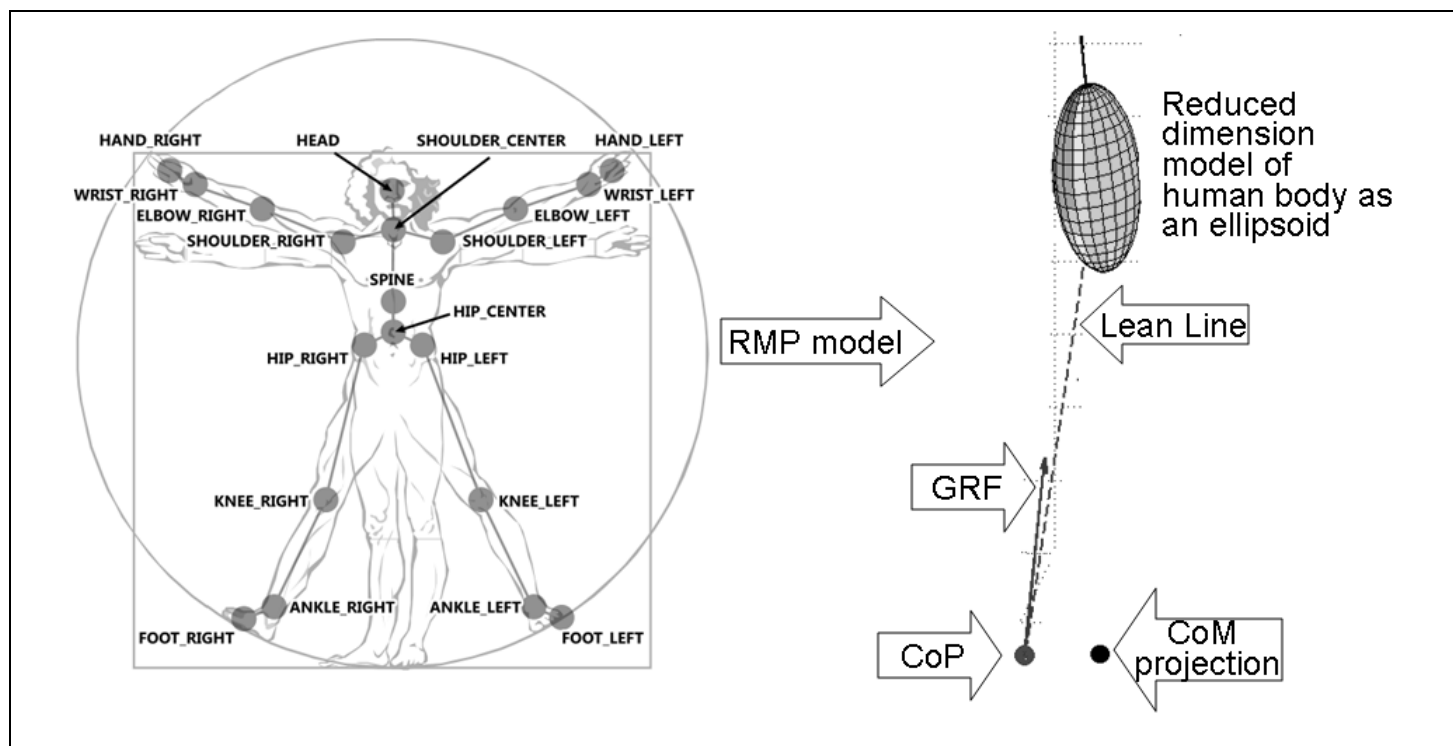
a)

b)

Figure 6
Click here to download Figure: Figure 6n.doc

Table

	Feature 1 (%)	Feature 2 (%)	Feature 3 (per minute)	Feature 4 (%)	Feature 5 (%)
Left Eye	1	3.66	6.829326829	95.51495017	4.485049835
Right Eye	0.66677	6	6.341463415	94.39962031	5.600379687

	Feature 1 (%)	Feature 2 (%)	Feature 3 (per minute)	Feature 4 (%)	Feature 5 (%)
Left Eye					
Right Eye					

Feature 6 (%)

46.78446

24.985499

Excel Spreadsheet- Table of Materials/Equipment

Name of Reagent/ Equipment	Company	Catalog Number
NMES stimulator	Vivaltis, France	PhenixUSBNeo
Balance Board	Nintendo, USA	Wii Balance Board
Motion Capture	Microsoft, USA	XBOX-360 Kinect
Eye Tracker	Eye Tribe	The Eye Tribe
EEG Data Acquisition System	Emotiv, Australia	Emotiv Neuroheadset
EEG passive electrode	Olimex	EEG-PE
EEG active electrode	Olimex	EEG-AE
Computer with PC monitor	Dell	
Softwares, EMG electrodes, NMES electrodes, and cables		

Comments/Description	Cost estimates (Euros)
NMES stimulator cum EMG sensor (Figure 2b)	5217.4
Balance Board (Figure 2b)	100
Motion Capture (Figure 2b)	150
SmartEye Tracker (Figure 2a)	100
Wireless EEG headset (Figure 2b)	400
EEG passive electrode for EOG and references (6 in number)(Figure 2b)	10x5
EEG active electrode (10 in number)(Figure 2b)	10x9
Data processing and visual feedback (Figure 2)	500
Total	6467.4

jove
JOURNAL OF VISUALIZED EXPERIMENTS

1 Alewife Center #200
Cambridge, MA 02140
tel. 617.945.9051
www.jove.com

ARTICLE AND VIDEO LICENSE AGREEMENT

Title of Article: *A human-machine-interface integrating biosignal sensors, eye tracker, and motion capture with a neuromuscular electrical system for post-stroke balance rehabilitation*

Author(s): Dutta, A; Das, A; Lahiri, U.

Item 1 (check one box): The Author elects to have the Materials be made available (as described at http://www.jove.com/publish) via: ☑ Standard Access ☐ Open Access

Item 2 (check one box):

☑ The Author is NOT a United States government employee.

☐ The Author is a United States government employee and the Materials were prepared in the course of his or her duties as a United States government employee.

☐ The Author is a United States government employee but the Materials were NOT prepared in the course of his or her duties as a United States government employee.

ARTICLE AND VIDEO LICENSE AGREEMENT

1. <u>Defined Terms</u>. As used in this Article and Video License Agreement, the following terms shall have the following meanings: "**Agreement**" means this Article and Video License Agreement; "**Article**" means the article specified on the last page of this Agreement, including any associated materials such as texts, figures, tables, artwork, abstracts, or summaries contained therein; "**Author**" means the author who is a signatory to this Agreement; "**Collective Work**" means a work, such as a periodical issue, anthology or encyclopedia, in which the Materials in their entirety in unmodified form, along with a number of other contributions, constituting separate and independent works in themselves, are assembled into a collective whole; "**CRC License**" means the Creative Commons Attribution-Non Commercial-No Derivs 3.0 Unported Agreement, the terms and conditions of which can be found at: http://creativecommons.org/licenses/by-nc-nd/3.0/legalcode; "**Derivative Work**" means a work based upon the Materials or upon the Materials and other pre-existing works, such as a translation, musical arrangement, dramatization, fictionalization, motion picture version, sound recording, art reproduction, abridgment, condensation, or any other form in which the Materials may be recast, transformed, or adapted; "**Institution**" means the institution, listed on the last page of this Agreement, by which the Author was employed at the time of the creation of the Materials; "**JoVE**" means MyJove Corporation, a Massachusetts corporation and the publisher of *The Journal of Visualized Experiments*; "**Materials**" means the Article and / or the Video; "**Parties**" means the Author and JoVE; "**Video**" means any video(s) made by the Author, alone or in conjunction with any other parties, or by JoVE or its affiliates or agents, individually or in collaboration with the Author or any other parties, incorporating all or any portion of the Article, and in which the Author may or may not appear.

2. <u>Background</u>. The Author, who is the author of the Article, in order to ensure the dissemination and protection of the Article, desires to have the JoVE publish the Article and create and transmit videos based on the Article. In furtherance of such goals, the Parties desire to memorialize in this Agreement the respective rights of each Party in and to the Article and the Video.

3. <u>Grant of Rights in Article</u>. In consideration of JoVE agreeing to publish the Article, the Author hereby grants to JoVE, subject to **Sections 4** and **7** below, the exclusive, royalty-free, perpetual (for the full term of copyright in the Article, including any extensions thereto) license (a) to publish, reproduce, distribute, display and store the Article in all forms, formats and media whether now known or hereafter developed (including without limitation in print, digital and electronic form) throughout the world, (b) to translate the Article into other languages, create adaptations, summaries or extracts of the Article or other Derivative Works (including, without limitation, the Video) or Collective Works based on all or any portion of the Article and exercise all of the rights set forth in (a) above in such translations, adaptations, summaries, extracts, Derivative Works or Collective Works and (c) to license others to do any or all of the above. The foregoing rights may be exercised in all media and formats, whether now known or hereafter devised, and include the right to make such modifications as are technically necessary to exercise the rights in other media and formats. If the "Open Access" box has been checked in **Item 1** above, JoVE and the Author hereby grant to the public all such rights in the Article as provided in, but subject to all limitations and requirements set forth in, the CRC License.

1

612542.6

jove
JOURNAL OF
VISUALIZED EXPERIMENTS

1 Alewife Center #200
Cambridge, MA 02140
tel. 617.945.9051
www.jove.com

ARTICLE AND VIDEO LICENSE AGREEMENT

4. <u>Retention of Rights in Article</u>. Notwithstanding the exclusive license granted to JoVE in **Section 3** above, the Author shall, with respect to the Article, retain the non-exclusive right to use all or part of the Article for the non-commercial purpose of giving lectures, presentations or teaching classes, and to post a copy of the Article on the Institution's website or the Author's personal website, in each case provided that a link to the Article on the JoVE website is provided and notice of JoVE's copyright in the Article is included. All non-copyright intellectual property rights in and to the Article, such as patent rights, shall remain with the Author.

5. <u>Grant of Rights in Video – Standard Access</u>. This **Section 5** applies if the "Standard Access" box has been checked in **Item 1** above or if no box has been checked in **Item 1** above. In consideration of JoVE agreeing to produce, display or otherwise assist with the Video, the Author hereby acknowledges and agrees that, Subject to **Section 7** below, JoVE is and shall be the sole and exclusive owner of all rights of any nature, including, without limitation, all copyrights, in and to the Video. To the extent that, by law, the Author is deemed, now or at any time in the future, to have any rights of any nature in or to the Video, the Author hereby disclaims all such rights and transfers all such rights to JoVE.

6. <u>Grant of Rights in Video – Open Access</u>. This **Section 6** applies only if the "Open Access" box has been checked in **Item 1** above. In consideration of JoVE agreeing to produce, display or otherwise assist with the Video, the Author hereby grants to JoVE, subject to **Section 7** below, the exclusive, royalty-free, perpetual (for the full term of copyright in the Article, including any extensions thereto) license (a) to publish, reproduce, distribute, display and store the Video in all forms, formats and media whether now known or hereafter developed (including without limitation in print, digital and electronic form) throughout the world, (b) to translate the Video into other languages, create adaptations, summaries or extracts of the Video or other Derivative Works or Collective Works based on all or any portion of the Video and exercise all of the rights set forth in (a) above in such translations, adaptations, summaries, extracts, Derivative Works or Collective Works and (c) to license others to do any or all of the above. The foregoing rights may be exercised in all media and formats, whether now known or hereafter devised, and include the right to make such modifications as are technically necessary to exercise the rights in other media and formats. For any Video to which this Section 6 is applicable, JoVE and the Author hereby grant to the public all such rights in the Video as provided in, but subject to all limitations and requirements set forth in, the CRC License.

7. <u>Government Employees</u>. If the Author is a United States government employee and the Article was prepared in the course of his or her duties as a United States government employee, as indicated in **Item 2** above, and any of the licenses or grants granted by the Author hereunder exceed the scope of the 17 U.S.C. 403, then the rights granted hereunder shall be limited to the maximum rights permitted under such statute. In such case, all provisions contained herein that are not in conflict with such statute shall remain in full force and effect, and all provisions contained herein that do so conflict shall be deemed to be amended so as to provide to JoVE the maximum rights permissible within such statute.

8. <u>Likeness, Privacy, Personality</u>. The Author hereby grants JoVE the right to use the Author's name, voice, likeness, picture, photograph, image, biography and performance in any way, commercial or otherwise, in connection with the Materials and the sale, promotion and distribution thereof. The Author hereby waives any and all rights he or she may have, relating to his or her appearance in the Video or otherwise relating to the Materials, under all applicable privacy, likeness, personality or similar laws.

9. <u>Author Warranties</u>. The Author represents and warrants that the Article is original, that it has not been published, that the copyright interest is owned by the Author (or, if more than one author is listed at the beginning of this Agreement, by such authors collectively) and has not been assigned, licensed, or otherwise transferred to any other party. The Author represents and warrants that the author(s) listed at the top of this Agreement are the only authors of the Materials. If more than one author is listed at the top of this Agreement and if any such author has not entered into a separate Article and Video License Agreement with JoVE relating to the Materials, the Author represents and warrants that the Author has been authorized by each of the other such authors to execute this Agreement on his or her behalf and to bind him or her with respect to the terms of this Agreement as if each of them had been a party hereto as an Author. The Author warrants that the use, reproduction, distribution, public or private performance or display, and/or modification of all or any portion of the Materials does not and will not violate, infringe and/or misappropriate the patent, trademark, intellectual property or other rights of any third party. The Author represents and warrants that it has and will continue to comply with all government, institutional and other regulations, including, without limitation all institutional, laboratory, hospital, ethical, human and animal treatment, privacy, and all other rules, regulations, laws, procedures or guidelines, applicable to the Materials, and that all research involving human and animal subjects has been approved by the Author's relevant institutional review board.

10. <u>JoVE Discretion</u>. If the Author requests the assistance of JoVE in producing the Video in the Author's facility, the Author shall ensure that the presence of JoVE employees, agents or independent contractors is in accordance with the relevant regulations of the Author's institution. If more than one author is listed at the beginning of this Agreement, JoVE may, in its sole discretion, elect not take any action with respect to the Article until such time as it has received complete, executed Article and Video License Agreements from each such author. JoVE reserves the right, in its absolute and sole discretion and without giving any reason therefore, to accept or decline any work submitted to JoVE. JoVE and its employees, agents and independent contractors shall have

2

ARTICLE AND VIDEO LICENSE AGREEMENT

j⊙ve
JOURNAL OF
VISUALIZED EXPERIMENTS

1 Alewife Center #200
Cambridge, MA 02140
tel. 617.945.9051
www.jove.com

full, unfettered access to the facilities of the Author or of the Author's institution as necessary to make the Video, whether actually published or not. JoVE has sole discretion as to the method of making and publishing the Materials, including, without limitation, to all decisions regarding editing, lighting, filming, timing of publication, if any, length, quality, content and the like.

11. Indemnification. The Author agrees to indemnify JoVE and/or its successors and assigns from and against any and all claims, costs, and expenses, including attorney's fees, arising out of any breach of any warranty or other representations contained herein. The Author further agrees to indemnify and hold harmless JoVE from and against any and all claims, costs, and expenses, including attorney's fees, resulting from the breach by the Author of any representation or warranty contained herein or from allegations or instances of violation of intellectual property rights, damage to the Author's or the Author's institution's facilities, fraud, libel, defamation, research, equipment, experiments, property damage, personal injury, violations of institutional, laboratory, hospital, ethical, human and animal treatment, privacy or other rules, regulations, laws, procedures or guidelines, liabilities and other losses or damages related in any way to the submission of work to JoVE, making of videos by JoVE, or publication in JoVE or elsewhere by JoVE. The Author shall be responsible for, and shall hold JoVE harmless from, damages caused by lack of sterilization, lack of cleanliness or by contamination due to the making of a video by JoVE its employees, agents or independent contractors. All sterilization, cleanliness or decontamination procedures shall be solely the responsibility of the Author and shall be undertaken at the Author's

expense. All indemnifications provided herein shall include JoVE's attorney's fees and costs related to said losses or damages. Such indemnification and holding harmless shall include such losses or damages incurred by, or in connection with, acts or omissions of JoVE, its employees, agents or independent contractors.

12. Fees. To cover the cost incurred for publication, JoVE must receive payment before production and publication the Materials. Payment is due in 21 days of invoice. Should the Materials not be published due to an editorial or production decision, these funds will be returned to the Author. Withdrawal by the Author of any submitted Materials after final peer review approval will result in a US$1,200 fee to cover pre-production expenses incurred by JoVE. If payment is not received by the completion of filming, production and publication of the Materials will be suspended until payment is received.

13. Transfer, Governing Law. This Agreement may be assigned by JoVE and shall inure to the benefits of any of JoVE's successors and assignees. This Agreement shall be governed and construed by the internal laws of the Commonwealth of Massachusetts without giving effect to any conflict of law provision thereunder. This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together shall be deemed to me one and the same agreement. A signed copy of this Agreement delivered by facsimile, e-mail or other means of electronic transmission shall be deemed to have the same legal effect as delivery of an original signed copy of this Agreement.

A signed copy of this document must be sent with all new submissions. Only one Agreement required per submission.

CORRESPONDING AUTHOR:

Name: _Dr. Anirban Dutta_

Department: _DEMAR_

Institution: _INRIA, France_

Article Title: _A human-machine-interface integrating biosignal sensors, eye tracker, and motion capture with a neuromuscular electrical stimulation system for post-stroke rehabilitation_

Signature: _[signature]_   Date: _06/12/2014_

Please submit a signed and dated copy of this license by one of the following three methods:
1) Upload a scanned copy of the document as a pfd on the JoVE submission site;
2) Fax the document to +1.866.381.2236;
3) Mail the document to JoVE / Attn: JoVE Editorial / 1 Alewife Center #200 / Cambridge, MA 02139

For questions, please email submissions@jove.com or call +1.617.945.9051

612542.6

COVER LETTER FOR SUBMISSION OF REVISED MANUSCRIPTS

Editorial Board
Journal of Visualized Experiments

Subject: **REBUTTAL COMMENTS**

I am enclosing herewith the revised manuscript titled, **A human-machine-interface integrating low-cost sensors with a neuromuscular electrical stimulation system for post-stroke balance rehabilitation**, submitted to your esteemed journal for review.

Editorial comments:

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues. The JoVE editor will not copy-edit your manuscript and any errors in the submitted revision may be present in the published version. There remains many copy-editing errors throughout that significantly reduces the clarity of the manuscript.
1. Thanks. We have tried to thoroughly proof-read the draft.

2. There continues to be textual overlap in the manuscript. This textual overlap should be revised to include original and novel language and failure to do so will prevent publication of the manuscript.
2. Sorry, we have revised the statements.

3. 3.3.2: How is the minimum baseline NMES level determined? What is clinically being observed and how do these observations determine the minimum baseline NMES level? Please provide a reference on how to do so.
3. Thanks. We have revised accordingly. "3.3.2. Set a minimum baseline NMES level (pulse-width and current level) necessary for upright standing according to clinical observation (i.e., zero body weight support)[20]. For setting the minimum baseline NMES level, one can set the stimulation frequency at 20Hz and then increase the pulse-width and/or current level until upright standing is achieved. Here, NMES of knee extensors is required to generate enough torque to prevent knee buckling."

4. 3.3.4: How is the calibration done? What steps are done with respect to the software? What is the "routine"?
4. The "routine" is the Matlab program that needs to be run. We have revised accordingly. "3.3.4. Run 'CalibSensors.m' program in Matlab to collect calibration data from Motion Capture Sensor, Balance Board, and EEG data acquisition systems while the subject performs various visually cued reach movements that affects center of mass (CoM) and center of pressure (CoP) location. The calibration program will identify subject-specific maximum EMG level (MEL) of the muscles and maximum excursions of CoM/CoP (CoM_{max}/CoP_{max}) during the reach movements."

5. 3.3.5: What is the calibration software routine? Please provide more explicit details, i.e, command lines?
5. The "routine" is the Matlab program that needs to be run.
6. 4.1: WHat is the CollectBaseline software routine? Please provide more explicit details, i.e, command lines?
6. The "routine" is the Matlab program that needs to be run. "5.1. Run 'CollectBaseline.m' program in

Matlab to collect baseline resting-state eyes-open multi-sensor data by asking the subject to stand still for 2 minutes while looking straight at the CoP target on the PC monitor (see Figure 3a)."

7. Please include Representative Results that show the efficacy of the protocol. Previous revisions had these Representative Results but this most recent revision has removed it. Furthermore, please include how to analyze the data (either a reference on how to do so or explicit details in the protocol on how to do so) in the Protocol following step 4).
7. We apologize. We have now added the Representative Results in Figures 4 and 5.
Figure 4. Top panel shows an illustrative figure of the smooth pursuit during horizontal movement. Bottom panel shows an illustrative figure of the smooth pursuit during vertical movement.

Figure 5. a) Changes in the ratio of fixation duration on the target and the fixation duration on the cursor - FDratio - extracted from electrooculogram during visuomotor balance task (VBT) trials. b) Changes in the baseline normalized mean squared error (MSEnorm) during VBT trials.

8. Please highlight 2.75 pages or less of the Protocol (including headings and spacing) that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol. The highlighted steps should form a cohesive narrative with a logical flow from one highlighted step to the next. Remember that non-highlighted Protocol steps will remain in the manuscript, and therefore will still be available to the reader.
8. Thanks. We have now highlighted 2.75 pages or less of the Protocol in grey for the video.

9. Please ensure that the highlighted steps form a cohesive narrative with a logical flow from one highlighted step to the next. Please highlight complete sentences (not parts of sentences). Please ensure that the highlighted part of the step includes at least one action that is written in imperative tense.
9. Yes, we have written the protocol in imperative tense.

With the submission of this manuscript I would like to undertake that the above mentioned manuscript has not been published elsewhere, accepted for publication elsewhere and that my co-authors are fully aware of this submission.

Kind regards,
Anirban Dutta, Ph.D.
Principal Investigator of NeuroPhys4NeuroRehab project
DEMAR team of INRIA, Université de Montpellier, CNRS
34095 Montpellier Cedex 5 France
Web: http://team.inria.fr/nphys4nrehab