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Cerebral contributions to motor adaptation

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Contributions: PI and GTO designed research, DK and PI performed research, DK and PI analyzed data, DK, PI and GTO wrote paper.

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Abstract

Human movements are flexible as they continuously adapt to changes in the environment. The recalibration of corrective responses to sustained perturbations (e.g., constant force) altering one's movement contributes to this flexibility. We asked whether the recalibration of corrective actions involve cerebral structures using stroke as a disease model. We characterized changes in muscle activity in stroke survivors and controls before, during, and after walking on a split-belt treadmill moving the legs at different speeds. The recalibration of corrective muscle activity was comparable between stroke survivors and controls, which was unexpected given the known deficits in feedback responses post-stroke. Also, the intact recalibration in stroke survivors contrasted their limited ability to adjust their muscle activity during steady state split-belt walking. Our results suggest that the recalibration and execution of motor commands are partially dissociable: cerebral lesions interfere with the execution, but not the recalibration, of motor commands upon novel movement demands.

Significance statement. Corrective responses mediated by feedback have been shown to adapt according to task demands. They also reflect updates in the recalibration of the motor system to sustained and predictable changes in the environment. The extent of cortical involvement in this process is unknown. Here we demonstrate that cortical lesions from stroke alter the execution of motor patterns, but not their recalibration. This is important since it suggests that stroke survivors retain the potential to correct movements through error-based protocols, which is an ability that could be exploited for rehabilitation purposes.

Introduction

Humans continuously adapt their movements to changes in the body or environment through corrective responses and adjustment of planned actions. Corrective responses are rapidly triggered upon unexpected movement disturbances (Bhushan and Shadmehr, 1999; Jordan and Rumelhart, 1992). Conversely, planned actions are predictive in nature and are updated through sustained perturbations (e.g., constant force) altering one's movement (Wolpert et al., 1998). Recent work has shown that corrective motor commands also adapt to persistent changes in the environment, such that the subjects perceive the novel situation as the new "normal" (e.g. Iturralde and Torres-Oviedo, 2019). However, little is known about the neural processes contributing to the recalibration of corrective responses.

It has been suggested that planned and corrective actions share an internal representation of the environmental dynamics (Maeda et al., 2018; Wagner and Smith, 2008), thus their recalibration could rely on updates to these internal models (Wolpert et al., 1998). If so, the recalibration of corrective responses after sustained exposure to a novel environment is likely dependent on cerebellar structures (Morton and Bastian, 2006; Smith and Shadmehr, 2005), but not cerebral structures (Choi et al., 2009; Reisman et al., 2007). On the other hand, corrective responses are cerebral-dependent as evidenced by the deficient nature of corrective responses in stroke survivors (i.e., poor muscle coordination, amplitude, or latency) (De Kam et al., 2018, 2017; Marigold and Eng, 2006) and impaired task-dependent modulation of this corrective activity (De Kam et al., 2018; Trumbower et al., 2013). Thus, it is plausible that the recalibration of corrective responses is also affected after cerebral lesions, which would imply cerebral-dependent adaptation of corrective actions. Here, we evaluate the involvement of cerebral structures in the recalibration of reactive control through the analysis of corrective muscle activity in individuals with cerebral lesions after stroke.

We characterized stroke-related deficits in muscle activity before, during, and after split-belt walking, which induces robust locomotor adaptation (Reisman et al., 2007). We hypothesized that the execution of motor patterns in a novel walking situation and the subsequent recalibration

of corrective responses would be impaired post-stroke. This was based on literature indicating cerebral-related deficits in the modulation of corrective responses (De Kam et al., 2018) and poor muscle coordination post-stroke in general (Bowden et al., 2010; Cheung et al., 2012; Clark et al., 2010). Should our hypothesis be supported, our results would suggest that cerebral structures are involved in both the execution and recalibration of corrective actions that result from extended exposure to novel environmental demands.

Methods

Subjects

We tested 16 stroke survivors in the chronic phase (> 6 months) with unilateral supratentorial lesions (i.e. without brainstem or cerebellar lesions; Age 62±9.9 years, 6 Females, Table 1) and 16 age and gender matched controls (Age 61±9.7 years, 6 Females). We applied the following inclusion criteria: 1) be able to walk with or without a hand-held device at a self-paced speed for at least 5 minutes, 2) have no orthopedic or pain conditions interfering with the assessment, 3) have no neurological conditions except stroke, 4) have no severe cognitive impairments (defined as mini-mental state exam < 24), 5) have no contraindications for performing moderate intensity exercise and 6) use no medication that interferes with cognitive function. We excluded from data analysis 4 out of the 32 participants invited for testing. One stroke participant (P7) was excluded because of severe muscle atrophy and weakness on the sound limb (i.e., non-paretic side), which was present prior to the brain lesion. Another stroke participant (P3) was excluded because of poor muscle recordings due to technical difficulties during testing. One control participant (C1) was excluded because this person failed to follow the testing instructions. Lastly, we had to remove C7 (i.e. age-matched control of P7) because our regression analyses required equal sample sizes across groups. Namely, including fewer participants in the regression of one group reduces the regressor estimates due to more noise in the averaged data. The study protocol was approved by the Institutional Review Board at the University of Pittsburgh. All study participants gave written informed consent prior to participation.

Experimental setup and protocol

We investigated how participants adapted their kinematic and muscle activation patterns on an instrumented split-belt treadmill (Bertec, Columbus, Ohio, USA) with two belts that moved at

either the same speed (tied condition) or at different speeds (split condition). We first measured subjects' overground walking speed using the 6 minutes walking test (Kervio et al., 2003; Rikli and Jones, 1998) and we then performed the Fugl-Myer assessment (Fugl-Meyer et al., 1975). Subsequently, subjects walked on the split-belt treadmill. We kept the mean speed across the belts constant in the tied and split conditions. Each subjects' mean belt speed was set to 0.35 m/s below their overground walking speed during the 6 minutes walking test, yielding a comfortable speed for treadmill walking. The mean belt speed, denoted as medium speed, is reported for each subject in Table 1. In the split condition, the speed of one belt was decreased (slow belt) and the speed on the other belt was increased (fast belt) by 33% of the medium speed to obtain a belt speed ratio of 2:1. Stroke survivors walked with their paretic leg on the slow belt, whereas healthy subjects walked with their non-dominant leg on the slow belt. The treadmill protocol consisted of 5 periods: 1) 50 strides (i.e. time between two subsequent heel strikes of the same leg) walking at medium speed to familiarize subjects with treadmill walking, 2) a Short Exposure (10 strides) to the split condition to allow subjects to briefly experience the split condition prior motor adaptation, 3) 150 strides of Baseline walking at medium speed to characterize subjects' baseline gait, 4) 900 strides of Adaptation to the split condition, which is a long enough period for locomotor adaptation (e.g. Iturralde and Torres-Oviedo, 2019) and 5) 600 strides of Post-Adaptation at medium speed to measure adaptation effects (i.e., after-effects) and their decay (Figure 1A). Subjects had several resting breaks during the experiment and some stroke individuals completed fewer strides during Adaptation and Post-Adaptation to prevent fatigue (Table 1 shows number of strides completed per subject). Participants wore a safety harness, not supporting body-weight, attached to a sliding rail in the ceiling to prevent falls. Moreover, subjects could hold on to a handrail in front of the treadmill, but were instructed to do so only if needed.

Data collection

We collected kinetic, kinematic, and electromyography (EMG) data to characterize individuals' walking pattern. The ground reaction force aligned with gravity (Fz, sampled at 1000Hz) was used to identify the instants at which the feet landed (i.e., heel-strike: Fz>10N) or were lifted from the ground (i.e. toe-off: Fz<10N) (Iturralde and Torres-Oviedo, 2019). The positions of the ankles (lateral malleolus) and hips (greater trochanter) were recorded at 100Hz using a 3D

motion analysis system (Vicon Motion Systems, Oxford, UK). Activity of 15 muscles was recorded bilaterally at 2000Hz using a Delsys Trigno System (Delsys Inc., Natick, Massachusetts): Gluteus medius (GLU), Tensor fasciae latae (TFL), Adductor magnus (ADM), Hip flexors (HIP), Rectus femoris (RF), Vastus lateralis (VL), Vastus medialis (VM), Semitendinosus (SMT), Semimembranosus (SMB), Biceps femoris (BF), Gastrocnemius medialis (MG), Gastrocnemius lateralis (LG), Soleus (SOL), Peroneus (PER), and Tibialis anterior (TA). . EMG signals were high-pass filtered with a 30Hz 4nd order Butterworth dual-pass filter and subsequently rectified (Merletti and Parker, 2005).

Data analysis

Kinematic parameters: We characterized the adaptation of step length asymmetry (StepAsym, Eq1, Figure 1B), which is conventionally used to quantify gait changes during split-belt walking (Reisman et al., 2007; Torres-Oviedo et al., 2011). We defined StepAsym as the difference between consecutive steps of the legs in terms of step length, where step length is the distance between the feet (i.e., ankle markers) at heel strike. In our definition, StepAsym is positive when the step length of the fast leg (i.e. dominant or non-paretic) is larger than the one of the slow leg (non-dominant or paretic). We also quantified spatial (StepPosition) and temporal (StepTime) gait features that contribute to StepAsym, since those are differentially affected across stroke survivors and they exhibit distinct adaptation patterns in unimpaired adults during split-belt walking (Finley et al., 2015). Finally, StepVelocity was defined as the difference between the legs in terms of velocity of the foot with respect to the body when in contact with the ground. All parameters were expressed in units of distance and they were normalized to the sum of left and right step lengths in order to account for differences in step sizes across subjects (Sombric et al., 2017).

EMG parameters: We characterized the modulation of muscle activity across the different walking conditions using the average activity of each muscle for fixed phases of the gait cycle (Figure 1C). Specifically, we divided the gait cycle into 4 phases: first double support (DS; between ipsilateral heel strike and contralateral toe off), single stance (SINGLE; from

contralateral toe-off to contralateral heel-strike), second double support (DS; between contralateral heel strike and ipsilateral toe off) and swing (SWING; between ipsilateral toe-off and ipsilateral heel-strike). We further divided each of these phases to achieve better temporal resolution. Specifically, both DS phases were divided in two equal sub-phases and the SINGLE and SWING phases were sub-divided in four equal sub-phases. Muscle activity amplitude was averaged in time for each of these subintervals for every stride and muscle resulting in 180 muscle activity variables per leg per stride cycle: 12 subinterval x 15 muscles.

EMG activity for each muscle was linearly scaled to baseline walking (last 40 strides), such that a value of 0 corresponded to the average of the interval with the lowest average activity and 1 corresponded to the average of the interval with the highest average activity (Iturralde and Torres-Oviedo, 2019). This normalization enabled us to aggregate the EMG activity across subjects to perform group analyses. Of note, we excluded from analysis the activity of soleus from one stroke survivor because technical difficulties during data collection.

Epochs of interest: Kinematic and EMG parameters were used to characterize subjects' behavior at the beginning ('early') and at the end ('late') of each experimental condition. Specifically, the epochs of interest included: late Baseline walking, early and late Adaptation and early Post-adaptation. The 'early' epochs were characterized by the median of the initial 5 strides and 'late' epochs by the median of the last 40 strides of the condition of interest. We chose medians across strides, rather than means to minimize the impact of outlier values. In all cases, we excluded the very first and very last stride of each condition to avoid artifacts from starting and stopping the treadmill. Subsequently, we subtracted the late Baseline behavior from all epochs of interest. This allowed us to identify group differences in subjects' modulation of kinematic and EMG parameters beyond those due to distinct baseline biases. Moreover, we computed the differences between EMG activity early Post-Adaptation vs. late Adaptation to quantify changes in EMG activity upon sudden removal of the perturbation.

Sensorimotor recalibration of corrective muscle responses: We studied the structure (i.e., activity across multiple muscles) of corrective motor responses upon sudden changes in the walking

environment (Figure 2), since this reflects the extent of sensorimotor recalibration (Iturralde and Torres-Oviedo, 2019). We defined corrective responses as the rapid changes in motor output (ΔEMG) immediately after a transition in the walking environment. Corrective responses were quantified as the difference in muscle activity immediately after an environmental transition (EMG_{after}) compared to the muscle activity before the transition (EMG_{before}, Figure 2A). Thus, corrective response (ΔEMG)=EMG_{after}–EMG_{before}. Since we had multiple strides before and after a transition, we used the median EMG activity across either 40 or 5 strides to quantify EMG_{before} and EMG_{after} a given transition, respectively.

Corrective responses, ΔEMG, were labelled according to the environmental transition and split-belt environment that was inducing them. More specifically, ΔEMG_{on} referred to corrective responses when the split environment was introduced ('on' transition) and ΔEMG_{off} referred to those when the split environment was removed ('off' transition). Also, corrective responses were labelled '(+)' or '(-)' to indicate the specific split environment that was generating them. Specifically, in the '(+)' environment the dominant leg, or non-paretic leg in patients, walked faster than the other leg, whereas in the '(-)' environment the non-dominant leg, or paretic leg in patients, walked faster than the other leg (Figure 2A). Thus, $\Delta EMG_{on(+)}$ was computed as the difference between EMG activity before and after the '+' environment was introduced.

We were specifically interested in the structure of corrective responses post-adaptation because this structure indicates the extent to which subjects recalibrate their motor system (Iturralde and Torres-Oviedo, 2019). Namely, the structure of these corrective responses is determined by both changes in the environment and changes in the motor systems' adaptive state. We discerned the environment-based and adaptive-based contributions to corrective responses post-adaptation ($\Delta EMG_{off(+)}$) with a regression model ($\Delta EMG_{off(+)}$ = adaptive-based + environment-based + ε). In the case of an environment-based response, the corrective pattern $\Delta EMG_{on(+)}$ upon introducing the '+' split environment is simply disengaged once this environment is removed (i.e., both belts moving at the same speed (Iturralde and Torres-Oviedo, 2019)). Thus, in this case the structure of corrective responses post-adaptation $\Delta EMG_{off(+)}$ (i.e., when the split '+' environment is turned off) resembles the numerical opposite of $\Delta EMG_{on(+)}$ ($\Delta EMG_{off(+)}$=-$\Delta EMG_{on(+)}$ Figure 2B). Conversely, adaptive-based responses are observed if subjects perceive the split-belt

environment '(+)' as the 'new normal'. Consequently, removing the '(+)' environment is processed as a perturbation in the opposite direction as the one originally experienced (i.e. it would be equivalent to introduction of the '(-)' environment, Figure 2A). Thus, in the case of adaptive corrective responses, the structure of $\Delta EMG_{off(+)}$ resembles corrective responses to transitioning into the opposite '(-)' split-belt environment ($\Delta EMG_{off(+)}=\Delta EMG_{on(-)}$; Figure 2C). Note that the corrective responses post-adaptation ($\Delta EMG_{off(+)}$) exhibit features of both environment-based and adaptive-based responses. Thus, we used a regression analysis to determine the extent to which the structure of corrective responses post-adaptation was environment-based or adaptive-based (Figure 2D):

$$\widehat{\Delta EMG}_{off(+)} = -\beta_{no-adapt}\widehat{\Delta EMG}_{on(+)} + \beta_{adapt}\widehat{\Delta EMG}_{on(-)} + \varepsilon$$

In the regression equation, the parameters $\beta_{no\text{-}adapt}$ and β_{adapt} are respectively interpreted as the extent to which the structure of corrective responses indicates transitions in the environment (i.e., environment-based) or the adaptation of subjects' motor system (i.e., adaptive-based). Note that every vector is divided by its norm (i.e., $\widehat{\Delta EMG}_{off(+)} = \Delta EMG_{off(+)} / \left\|\Delta EMG_{off(+)}\right\|$). This was done because we were interested in identifying stroke-related deficits in the structure, rather than the magnitude of corrective responses, which is known to be different (e.g. De Kam *et al.*, 2017). For example, we find that the amplitude of corrective responses $\Delta EMG_{on(+)}$ for each leg was smaller for the stroke ($\left\|\Delta EMG_{on(+)}\right\|$ =2.6 and 2.2) than the control group (3.3 and 3.7).

Note that $\Delta EMG_{on(-)}$ was not directly measured to avoid exposing subjects to multiple environmental transitions prior to the Adaptation period. Instead, we inferred these responses by exploiting the symmetry of the transition between the two legs. The only difference between the '+' and '-' environments is which leg increases speed and which leg decreases it. We used this similarity to infer the (not recorded) corrective responses ($\Delta EMG_{on(-)}$) of each leg to transitioning into the '-' environment from the (measured) corrective responses ($\Delta EMG_{on(+)}$) to transitioning to the '+' environment. In other words, we assumed that the (not recorded) non-dominant leg's responses to the "on (-)" transition would be similar to the (recorded) dominant leg's responses to the "on (+)" transition, and vice versa. We are aware that this assumption might not be valid for some post-stroke individuals, given their inherent motor asymmetry. Thus, group differences in β_{adapt} values, which are estimated using the not recorded $\Delta EMG_{on(-)}$ in our regression analysis, might be due to the experimental limitation of our study. To address this possibility, we

performed a *post-hoc* analysis to compare the regression coefficients between a subset of patients and controls (n=7 on each subgroup) that had similar asymmetry in their EMG activity during baseline walking (p=0.1). The baseline asymmetry in EMG activity across the legs was quantified in each subject by first computing a 180-dimension vector (15 muscles x 12 gait cycle phases) of the baseline muscle activity for each leg and then calculating the cosine between those baseline vectors for the legs of each individual.

Structure of muscle activity patterns in a novel walking environment: We characterized changes in the structure of steady state muscle activity from baseline walking to late Adaptation ($\Delta EMG_{SS} = EMG_{late\ Adaptation} - EMG_{late\ Baseline}$). This was defined as the pattern of activity across all muscles and all gait cycle intervals (15 muscles x 12 intervals = 180 data points for a given epoch). The ΔEMG_{SS} 180-dimensional vector for each subject was used to assess structural differences between stroke survivors and controls. We specifically computed a cosine between the ΔEMG_{SS} for each individual and a 'reference pattern' ΔEMG_{SS}, which was defined as the median ΔEMG_{SS} of the control group. This reference pattern for ΔEMG_{SS} was calculated as the group median of all control subjects when computing the similarity metric for each leg of the stroke survivors, whereas for individual control subjects we excluded the subjects' own data to compute the reference vector. A cosine closer to 1 indicates that the subject-specific and 'reference' vectors are more aligned and therefore, the structures of the muscle patterns that they represent are similar.

Statistical analyses

Modulation of muscle activity within groups: Modulation of muscle activity was first evaluated for each group individually. Specifically, we compared muscle activity between the epochs of interest using a Wilcoxon signed-rank test (non-parametric equivalent of paired t-test) for each individual muscle and for each gait cycle phase, resulting in 360 comparisons per epoch (12 intervals x 15 muscles x 2 legs. We subsequently corrected the significance threshold for each epoch using a Benjamini-Hochberg procedure (Benjamini and Hochberg, 1995) to indicate significant changes in our figures, but all data in both groups was used in the structural analyses.

Structure of muscle activity patterns during steady state walking: We used a Wilcoxon ranksum test to compare the groups on their ΔEMG_{SS} for each leg during late adaptation in the split-belt condition. We specifically compared the group's similarity in ΔEMG_{SS} to the reference pattern obtained with the cosine analysis.

Sensorimotor recalibration of corrective muscle responses: We compared the regressor coefficients $\beta_{no\text{-}adapt}$ and β_{adapt} for each group to determine if stroke survivors and controls differed in the adaptation of corrective responses. Since the regressor estimates of $\beta_{no\text{-}adapt}$ and β_{adapt} in a regression model are not independent, between-group comparisons were performed in the 2D space covered by $\beta_{no\text{-}adapt}$ and β_{adapt}. The differences between the groups were compared using a chi-squared distribution, which could be considered as a high-dimensional t-test (Härdle and Simar, 2007).

Correlation analyses: We asked whether individual subjects' adaptation of muscle activity was related to the severity of motor impairment (i.e. Fugl-Meyer score). To this end, we performed Spearman correlations between 1) the Fugl-Meyer score and 2) outcome measures that reflected sensorimotor recalibration (i.e. β_{adapt} and $\beta_{no\text{-}adapt}$) and the similarity metric comparing the structure of muscle activity during late adaptation in the split-belt condition for each individual vs. a reference ΔEMG_{SS}.

Modulation of kinematic parameters: We compared stroke survivors and controls in how they modulated kinematic parameters. To this end, we performed a repeated measures ANOVA for each kinematic outcome (StepAsym, StepPosition, StepTime and StepVelocity) with GROUP (stroke vs. Controls), EPOCH (early Adaptation, late Adaptation and early Post-Adaptation) and the interaction between both variables as predictors. Note that we did this analysis with unbiased data (i.e., baseline subtracted) because we were interested in differences in modulation across groups, beyond their baseline biases. In case of a significant GROUP or GROUPxEPOCH interaction effect, we performed between group comparisons for each epoch using Bonferroni corrected independent t-tests (adjusted α=0.017).

Speed-matched post-hoc analysis We found that stroke survivors walked slower than controls during the experiment (averaged medium speed= 0.78±0.24 vs. 1.07±0.12 m/s, ranksum test $p<0.01$), which could confound between-group differences in muscle activity. Thus, we repeated our analyses with only the 10 fastest participants in the stroke group and the 10 slowest controls to determine if structural differences between our groups were due to walking speed, rather than brain lesion. Walking speed was not significantly different for these speed-matched subgroups (0.88±0.18 vs .1.0±0.15 m/s, ranksum test $p=0.10$). Importantly, selection of the fastest stroke survivors did not result in a selection of patients with less severe motor impairments (Fugl Meyer score = 29.5±3.4 vs 28.5±5.1, $p=0.67$, for subgroup included vs. subgroup excluded in the speed-matched comparison respectively).

Results

Cerebral lesions interfered with the structure of muscle activity in a novel walking environment.

We computed a similarity metric ΔEMG_{SS}, which indicated the similarity between the structure of individual's muscle activity modulation in steady state walking relative the average pattern in controls ('reference pattern'). We found that the non-paretic' leg activity at steady state was similar to the one of controls, whereas the paretic leg was not (Figure 3A). Differences in the structure of muscle activity modulation between the groups can be appreciated in Figure 3B. Specifically, similarity metric ΔEMG_{SS} was lower in the paretic leg compared to controls (Figure 3A; $p=0.001$) and between-group differences were trending ($p=0.057$) when comparing the non-paretic leg activity to that of controls. These between-group differences were not observed when patients and controls walked at similar speeds (median ± interquartile range in controls vs. stroke survivors for the non-paretic leg: 0.58±0.26 vs. 0.51±0.22, $p=0.47$; paretic leg: 0.39+0.13 vs. 0.28±0.18, $p=0.1$). Interestingly, a more atypical structure in muscle activity modulation in the paretic leg was associated with poorer voluntary leg motor control as measured by the Fugl-Meyer scale (rho = 0.59, $p=0.028$, Figure 3C), but not in the non-paretic leg (rho = -0.29, $p=0.32$ data not shown). In conclusion, the structure of muscle activity at steady state was different

between patients and controls and individuals with more atypical paretic activity were those with lower voluntary function.

Sensorimotor recalibration of corrective responses was intact after cerebral lesion

The structure of corrective responses for each group indicated that on average both groups recalibrated their gait similarly. This is qualitatively indicated by the "checker boards" illustrated in Figure 4. Notice that in both groups the observed corrective responses post-adaptation (Figure 4C) look more similar to those predicted by the adaptive (Figure 4B) than the environment-based modulation (Figure 4A). The environment-based and adaptive-based contributions to corrective responses post-adaptation were quantified with a regression model, which reproduced the data well (Figure 5 left panels). We observed that the regression coefficient β_{adapt} was greater than $\beta_{no\text{-}adapt}$ in both groups for the leg that walked slow (i.e., non-dominant leg in controls: CI for β_{adapt}=[0.68-0.85] vs. CI for $\beta_{no\text{-}adapt}$=[0.18-0.35]; paretic leg in stroke: CI for β_{adapt}=[0.55-0.77] vs. CI for $\beta_{no\text{-}adapt}$=[0.10-0.32]) and the leg that walked fast (i.e., dominant leg in controls: CI for β_{adapt}=[0.73-0.89] vs. CI for $\beta_{no\text{-}adapt}$=[0.09-0.25], non-paretic leg in stroke: CI for β_{adapt}=[0.54-0.71] vs. CI for $\beta_{no\text{-}adapt}$=[0.46-0.62]). These coefficients were not different between groups when estimated from the averaged paretic leg activity across stroke survivors vs. that of the non-dominant leg across controls (Chi^2=3.2, p=0.20), indicating that averaged responses in the slow leg were adapted to the same extent in stroke survivors and controls. Conversely, we found between-group differences when comparing the coefficients of the averaged non-paretic activity in the stroke group vs. that of the dominant leg in the control group (Chi^2=48.9, p=2.4*10^{-11}, Figure 5A, bottom panel). Thus, we observed between-group differences in the regression coefficients for the non-paretic, but not the paretic, compared to control legs.

As a post-hoc analysis, we considered the possibility that these group differences in the non-paretic side could arise from our estimation of the adaptive-based modulation ($\Delta EMG_{on(-)}$). Notably, this muscle activity was not recorded but it was inferred from the muscle activity of the other leg, assuming symmetry of corrective responses across legs. Given that stroke survivors exhibit asymmetric motor patterns, the paretic leg's $\Delta EMG_{on(+)}$ may not be a good estimate for the non-paretic leg's $\Delta EMG_{on(-)}$, thereby leading to underestimation of β_{adapt} in this leg. Thus, we

performed a subgroup analysis in which stroke survivors and controls were matched for symmetry in their muscle activity during baseline walking. We did not find between-group differences for either leg of the stroke group compared to the controls when asymmetry in baseline muscle activity was matched between the groups (Figure 5B; paretic vs. non-dominant control leg Chi^2=4.1, p=0.13 and non-paretic vs. dominant control legs Chi^2=2.5, p=0.29). In conclusion, the observed structure of corrective responses post-adaptation were more similar to the one predicted by adaptive, rather than environment-based, modulation in patients with cerebral lesions and controls.

While recalibration of corrective responses post-stroke did not differ from controls at the group level when asymmetries were accounted for, we considered the possibility that some individuals would exhibit less recalibration compared to others. Consistently, Figure 6A shows a wide range of β_{adapt} and $\beta_{non\text{-}adapt}$ regression values at the individual level. Also, note that the regression model had smaller R^2 when applied to each subject's corrective responses post-adaptation (controls' non-dominant leg: R^2=0.38±0.18; controls' dominant leg: 34±0.17; paretic leg: 0.18±18; non-paretic leg: 0.18±18) than to the group's corrective response (reported in previous section). However, the regression model was significant in all individuals, except for one stroke survivor (p=0.19). In sum, we find large ranges of regression coefficients in control and post-stroke individuals.

We further asked if stroke survivors would exhibit less recalibration if they had more severe leg motor impairments (i.e. Fugl-Meyer Scale). Thus, we computed the Spearman correlation between individual subjects' regressors and their leg motor score (Figure 6B). We found that β_{adapt} of neither the paretic or non-paretic legs was correlated to the Fugl-Meyer score (paretic: rho=0.34, p=0.23; non-paretic: rho=0.23, p=0.43). On the other hand, motor function measured with the Fugl-Meyer score was associated with the paretic's $\beta_{no\text{-}adapt}$ and not the non-paretic's $\beta_{no\text{-}adapt}$ (Paretic: rho=0.60, p=0.024; non-paretic: rho=0.02, p=0.94). However, this correlation was driven by the individual with the largest negative $\beta_{no\text{-}adapt}$ since the correlation was no longer significant when this subject was excluded (rho=0.37, p=0.22). As such, we are cautious about interpreting this result as a positive association between environment-based corrective response

and leg motor scores. Together our correlation analyses indicate that recalibration of corrective responses is not associated with the quality of voluntary motor control.

Stroke-related deficits in muscle coordination are not reflected in asymmetry parameters

While stroke survivors exhibited deficits in the execution of updated motor commands during steady state split-belt walking (i.e. ΔEMG_{SS}), we observed no differences between the groups in the modulation of asymmetry parameters (i.e. stepAsym, stepPosition, stepTime and stepVelocity, Figure 7). Specifically, we observed no main effects of GROUP or GROUPxEPOCH interaction effects for the interlimb kinematic parameters ($p>0.05$). Comparable results were obtained in our speed-matched analysis. Thus, interlimb kinematic parameters are less sensitive to stroke-related deficits in locomotor adaptation than our outcome measures for muscle coordination.

Discussion

We studied the involvement of cerebral structures in the sensorimotor recalibration of gait using stroke as a clinical model. We found that on average stroke survivors exhibit similar recalibration of corrective responses in the paretic leg relative to controls, which was surprising given the known deficits in paretic responses post-stroke. On the other hand, we found cerebral lesions affected the paretic legs' muscle activity in the steady-state of split-belt walking. Thus, we find an interesting dissociation between execution and recalibration of corrective actions: the execution of motor patterns upon novel demands is cerebral-dependent, but the recalibration is not. These results do not support our original hypothesis that execution and recalibration of corrective responses would be a cerebral-mediated process. Our findings suggest as though this latter process might only depend on other structures such as the cerebellum.

Sensorimotor recalibration of corrective responses after cerebral lesions

Our results suggest that while corrective responses are affected by lesions to cerebral structures (De Kam et al., 2018, 2017; Marigold and Eng, 2006) and corticospinal tract (Christensen et al., 2001, 1999), the recalibration of this corrective activity is not strongly mediated by these neural

structures. More specifically, we found that the changes in corrective responses post-adaptation are similar between individuals with cerebral lesions and controls. This is clearly evident in the paretic leg, but not in the non-paretic leg, which exhibited lower adaptive-based changes (i.e. lower β_{adapt}). We speculate that β_{adapt} was lower in patients than controls because it was underestimated due to asymmetry in corrective responses post-stroke (De Kam et al., 2018; Marigold and Eng, 2006), rather than because poor recalibration in the non-paretic leg. Recall that $\Delta EMG_{on(-)}$ was not directly measured. Instead, $\Delta EMG_{on(-)}$ was estimated from $\Delta EMG_{on(+)}$ in the contralateral leg. Consequently, any asymmetry in muscle activity would lead to a bad predictor of the corrective responses that would result from recalibration (i.e., $EMG_{on(-)}$) and thereby reduce the possible β_{adapt}. In other words, asymmetries in corrective responses post-stroke would result in a poor representation of $\Delta EMG_{on(-)}$ (i.e., adaptive-based regressor), and thereby underestimation of β_{adapt} for the most asymmetric individuals. We performed an asymmetry-matched regression analysis to test the potential confounding effect of asymmetry on our results. While we could only include a limited number of subjects in this analysis (n=7 per group), the asymmetry-matched groups showed that the regression factors quantifying the recalibration of corrective responses were indeed influenced by the asymmetry of stroke survivors. Thus, future studies are needed to determine the potential impact of motor asymmetry on sensorimotor recalibration. Interestingly, these asymmetries affected more the estimation of β_{adapt} in the non-paretic than in the paretic leg, indicating that paretic corrective responses $\Delta EMG_{on(+)}$ are a poorer estimate of $\Delta EMG_{on(-)}$ in the non-paretic leg than vice versa. This is possibly because the missing paretic responses (De Kam et al., 2018) cannot be scaled up to reproduced non-paretic responses, while non-paretic activity can be scaled down to reproduce paretic missing activity. In sum, group differences of the full groups' non-paretic vs. control legs are likely due to underestimation of β_{adapt}, rather than poor sensorimotor recalibration in the non-paretic leg. However, future studies recording $\Delta EMG_{on(-)}$ are needed to determine if motor asymmetry is a factor reducing the recalibration of non-paretic corrective responses.

Discrepancies between the paretic and non-paretic extent of adaptive-based changes may reflect leg-specific recalibration. This is supported by the independent recalibration of the legs in hybrid walking (i.e. one leg moving forward faster than the other leg moving backward (Choi and Bastian, 2007)). However, leg-specific adaptation in hybrid walking may result from the peculiar

444 nature of this task and may, therefore, not apply to other locomotor adaptation paradigms. In
445 fact, more recent studies have demonstrated interlimb transfer of adapted motor patterns during
446 conventional split-belt walking (Krishnan et al., 2018, 2017), which argues against leg-specific
447 recalibration. Thus, we believe that recalibration of corrective responses is not affected after
448 cerebral lesions, which is also supported by a lack of association between individual stroke
449 survivors' motor impairments (i.e., Fugl-Meyer scores) and the amount of adaptive-based
450 modulation of corrective responses. Of note, we found an association between $\beta_{no\text{-}adapt}$ and Fugl-
451 Meyer scores driven by stroke survivors with negative $\beta_{no\text{-}adapt}$. These negative $\beta_{no\text{-}adapt}$ values,
452 also observed in controls (Iturralde and Torres-Oviedo, 2019), may reflect a startle-like (Oude
453 Nijhuis et al., 2010) generic response to an environmental transition, regardless of its direction.
454 Taken together, our results suggest that, while corrective responses are affected by cerebral
455 lesions (De Kam et al., 2018), their recalibration is not.
456
457
458 **Cerebral lesions affect the execution of updated motor commands in a new walking**
459 **environment**
460
461 We found that stroke survivors exhibited impaired modulation of steady state muscle activity,
462 particularly in their paretic leg. Interestingly, aberrant patterns of muscle activity did not impact
463 the modulation of kinematic asymmetry parameters (Reisman et al., 2007), which may indicate
464 that muscle activity is more sensitive to stroke-related deficits in motor output than parameters
465 quantifying kinematic asymmetries. Previous studies reported that long-term adaptation (i.e.
466 changes in spatiotemporal parameters from baseline walking to late adaptation) is impaired after
467 hemispherectomy (Choi et al., 2009), but not after focal hemisphere lesions due to stroke
468 (Reisman et al., 2007). These observations further suggest that changes in interlimb
469 spatiotemporal parameters become noticeable with more pronounced deficits, whereas more
470 subtle deficits can be detected by analysis of muscle activity. The impaired modulation of muscle
471 activity at steady state in the split-belt walking condition may reflect poor selectivity in
472 activation of muscles post-stroke. Notably, intact individuals upregulated proximal muscles (i.e.
473 quadriceps during early stance and hamstrings during late swing) without increasing distal
474 muscle activity during steady state split-belt walking. This pattern of modulation was diminished

in stroke survivors (Figure 3), particularly those with poorer leg motor selectivity. This observation is consistent with previous reports of missing selectivity in the activation of proximal and distal muscles in the gait of stroke survivors (Clark et al., 2010). Thus, impaired motor selectivity probably contributes to the aberrant patterns of muscle activity during steady state split-belt walking. In addition, stroke survivors' atypical steady state behavior may also be influenced by their perceptual deficits. Notably, individuals post-stroke have difficulty assessing their step length asymmetry (Wutzke et al., 2015), which could contribute to the adaptation of movements (Hoogkamer et al., 2015a). Alternatively, the atypical muscle activity patterns in stroke survivors may have resulted from a lower walking speed. Indeed, steady-state muscle activity became more similar across groups in our speed-matched analysis. Notably, between-group differences in our similarity metric were still substantial after controlling for speed (0.39+0.13 vs. 0.28±0.18), but this difference was no longer statistically significant. Therefore, we cannot completely rule out walking speed as a confounding factor influencing the distinct motor patterns at steady state between patients and controls. Lastly, the lack of modulation of steady state muscle activity did presumably not result of muscle atrophy, given that muscle groups that lacked modulation in the steady state (e.g., knee extensors) were highly modulated during corrective responses (See Figure 1D). We speculate steady state muscle activity depends on neural circuits involved in voluntary motor control, whereas this is not the case for corrective responses (De Kam et al., 2018). Taken together, our results suggest that stroke survivors exhibit impaired execution of updated motor commands in the steady state of split-belt walking, most likely due to their impaired motor function.

Partial dissociation between recalibration and execution of updated motor commands

We found that stroke survivors exhibited intact recalibration of corrective responses, but impaired muscle patterns at steady state split-belt walking, suggesting partial dissociation between motor performance in the altered environment and post-adaptation behavior. This finding is consistent with previous work demonstrating that the extent to which subjects adapt

503 their movements during split-belt walking does not predict their after-effects (Sombric et al.,
504 2019). Partial dissociation between steady-state and post-adaptation behavior is further
505 supported by the findings that after-effects are not sensitive to manipulation of steady-state
506 behavior through visual feedback (Long et al., 2016; Wu et al., 2014). Taken together, our
507 findings suggest that steady-state and post-adaptation behaviors are partially independent, and
508 possibly mediated through distinct neural processes.
509
510 We found that post-adaptation muscle activity was indicative of sensorimotor recalibration of
511 corrective responses also observed in previous studies (Iturralde and Torres-Oviedo, 2019;
512 Maeda et al., 2018). Since recalibration has also been observed in feedforward motor commands
513 upon perturbation removal (Taylor and Ivry, 2014; Tseng et al., 2007), our results provide further
514 evidence for shared internal models for generating corrective responses and feedforward motor
515 commands (Cluff and Scott, 2013; Maeda et al., 2018; Wagner and Smith, 2008; Yousif and
516 Diedrichsen, 2012). It has been shown that the cerebellum is involved in feedforward adaptation
517 and learning of internal models. (Martin et al., 1996; Morton and Bastian, 2006; Smith and
518 Shadmehr, 2005). In particular, sensorimotor recalibration in locomotion depends on the
519 intermediate cerebellum (Darmohray et al., 2019) and small focal lesions may not affect it
520 (Hoogkamer et al., 2015b). In addition, the cerebellum may also be involved in the adaptation of
521 corrective responses. This is supported by the cerebellar dependency on timely recruitment
522 (Herzfeld et al., 2014) and appropriate magnitude of feedback responses to predictable
523 perturbations (Jacobs and Horak, 2007). Taken together, our results are consistent with the idea
524 that, corrective responses depend on spinal cord and brainstem circuits for their execution
525 (Bolton, 2015; Weiler et al., 2019) and on the cerebellum for their adaptation, which would
526 explain why our participants with cerebral lesions showed intact recalibration of corrective
527 responses.
528
529 Our observation of stroke-related impairments in steady-state movement execution suggest that
530 these processes are cerebral-dependent, perhaps through connections between cerebral and
531 cerebellar structures (Hoshi et al., 2005; Kelly and Strick, 2003). Moreover, intact motor
532 pathways for voluntary motor control (e.g. corticospinal tract) are most likely involved in the
533 execution of steady-state motor commands (Schweighofer et al., 2018), given our finding that

individuals with poorer voluntary motor control also exhibited a more atypical structure of their steady state muscle activity. Such associations were not found for the execution of corrective responses (De Kam et al., 2018), suggesting that the execution of corrective responses uses different circuitry, most likely at the level of the brainstem (Bolton, 2015; Jacobs and Horak, 2007). Taken together our results are consistent with the idea that corrective and planned actions share an internal model, which relies on cerebellar structures for their adaptation and on cerebral structures for their execution.

Clinical implications

Our detailed characterization of muscle activity modulation during and after split-belt walking allows for the identification of muscle activity that could potentially be targeted by split-belt treadmill training. Our results support previous findings reporting movement after-effects in stroke survivors comparable to those of controls (Lauzière et al., 2016; Lewek et al., 2018; Reisman et al., 2013, 2007). We further show that the extent of sensorimotor recalibration underlying these after-effects vary greatly across post-stroke individuals. We speculate that individual differences in sensorimotor recalibration may explain why some stroke survivors improve their gait symmetry in response to repeated split-belt treadmill training while others do not (Betschart et al., 2018; Lewek et al., 2018; Reisman et al., 2013). If so, it may be possible to identify patients that will benefit from split-belt training within just a single session. Future studies are needed to determine if individuals' recalibration of corrective responses can predict their response to repeated training.

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Tables

Table 1. Clinical characteristics of stroke survivors

Subject	Age	Gender	Affected side	Lesion location	Fugl-Meyer score	Medium walking speed	Adapt strides	Post strides
P1	43	Female	R	Left MCA and basal ganglia	33	1.13	907	605
P2	64	Female	R	Left MCA and ACA, temporal lobe, basal ganglia	26	0.81	867	642
P3	64	Female	R	Left MCA, frontal, parietal lobe and basal ganglia	29	0.60	616	308
P4	58	Female	R	Left medial, frontal and parietal area's	21	0.45	901	624
P5	56	Female	L	Right parietal posterior and temporal lobes	31	0.94	941	615
P6	64	Male	L	Right MCA	31	0.34	452	300
P7	78	Male	L	Right MCA			486	217
P8	55	Female	L	Right MCA	23	0.87	903	602
P9	66	Male	R	Left MCA, frontal, temporal and parietal lobes	30	0.77	605	599
P10	60	Female	R	Left frontal	26	0.9	908	600
P11	77	Male	R	Thalamus	30	0.35	590	601
P12	59	Male	R	Left MCA	32	0.7	905	600
P13	52	Male	R	Left MCA	32	0.96	903	603
P14	66	Male	L	Right frontal superior, parietal and posterior area's	29	0.76	909	602
P15	75	Male	R	Left periventricular, temporal and basal ganglia	32	0.94	913	552
P16	49	Male	R	Frontotemporal parietal	33	0.71	931	303

Clinical characteristics of stroke survivors. Shaded subjects indicate those that are included in the speed-matched analysis. Dashed subjects indicate those that are included in the asymmetry matched analysis.

Figures

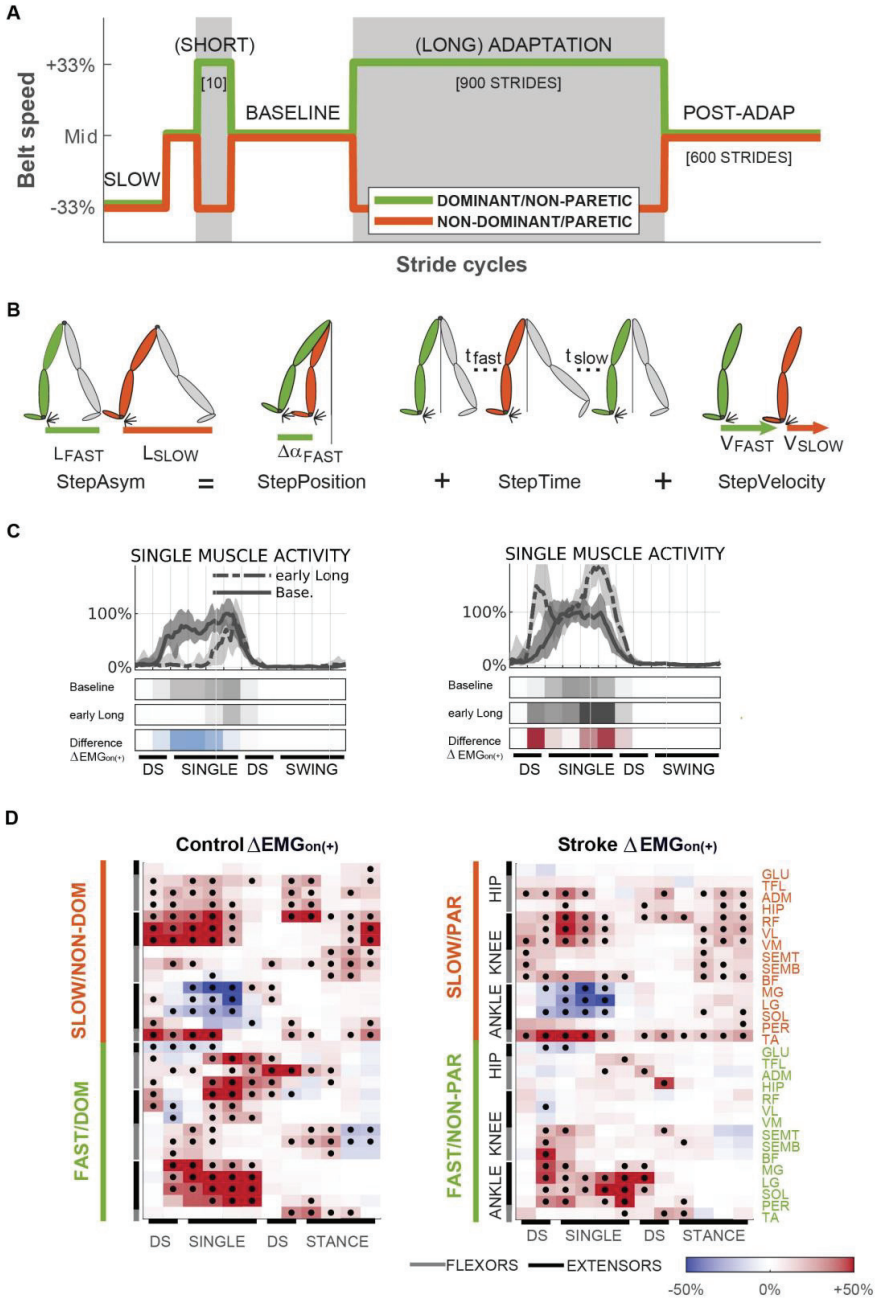

Figure 1. Overview of experimental methods. A) Schedule of belt speeds experienced by subjects. **B)** Schematic representation of definitions of kinematic parameters StepAsym, StepPosition, StepTime and StepVelocity, adapted from (Sombric et al., 2017) **C)** Sample EMG traces of one muscle (LG) during Baseline and late Adaptation for a representative control subject. Median activity across strides (lines), and the 16-84 percentile range (shaded). Data was lowpass filtered for visualization purposes. Colorbars below the traces represent averaged normalized values during 12 kinematically-aligned phases of the gait cycle (see Methods) for Baseline, early Adaptation, and the difference (red indicates increase, blue decrease). **D)** Corrective responses upon introduction of the '(+)' environment. Left panel represents controls, right panel represents stroke survivors. Colors represent group median increase (red) or decrease (blue) in activity. Black dots indicate statistical significance.

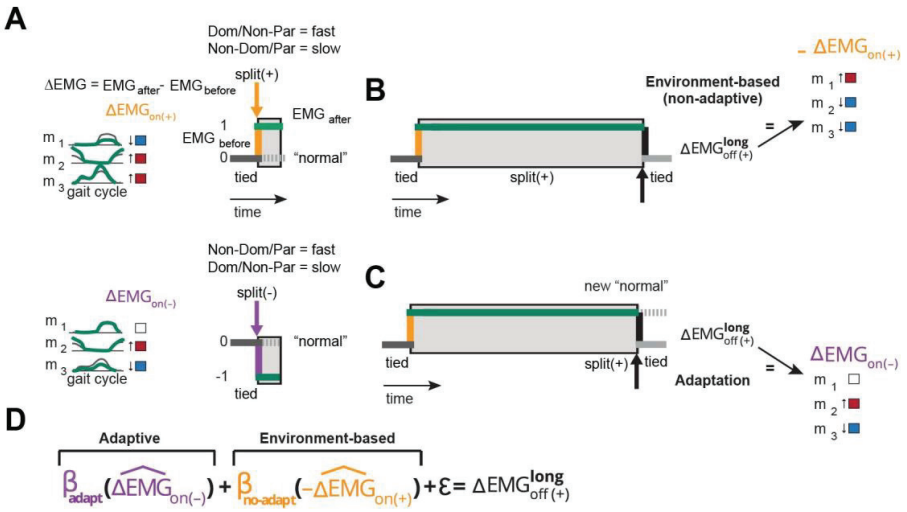

Figure 2. Environment-based and adaptive contributions to corrective responses. A) Schematic representation of corrective responses upon the introduction split-belt perturbation. The split environment is arbitrarily defined as "+" if the paretic leg is on the slow belt and the non-paretic one is on the fast belt (upper cartoon), whereas it is defined as "-" if the paretic leg is on the fast belt and the non-paretic one is on the slow belt. Changes in muscle activity (i.e. corrective response) upon the introduction of the "+" or "-" environment are color-coded as blue (decreased activity), red (increased activity) and white (no change in activity). **B)** In the case of an environment-based corrective response changes in muscle activity perturbation removal ($\Delta EMG_{off(+)}$) are opposite to those upon perturbation introduction. **C)** In the case of an adaptive corrective response, the split-environment is perceived as the new normal. Consequently, removal of the split-environment will be experienced as a perturbation in the opposite direction. Thus, the structure of the corrective response will resemble the one observed upon introduction of the "-" environment. **D)** Regression equation used to quantify the structure of corrective response $\Delta EMG_{off(+)}$. In this equation, β_{adapt} quantifies the similarity of $\Delta EMG_{off(+)}$ to the adaptation-based response and $\beta_{no\text{-}adapt}$ quantifies the similarity of $\Delta EMG_{off(+)}$ to the environment-based response.

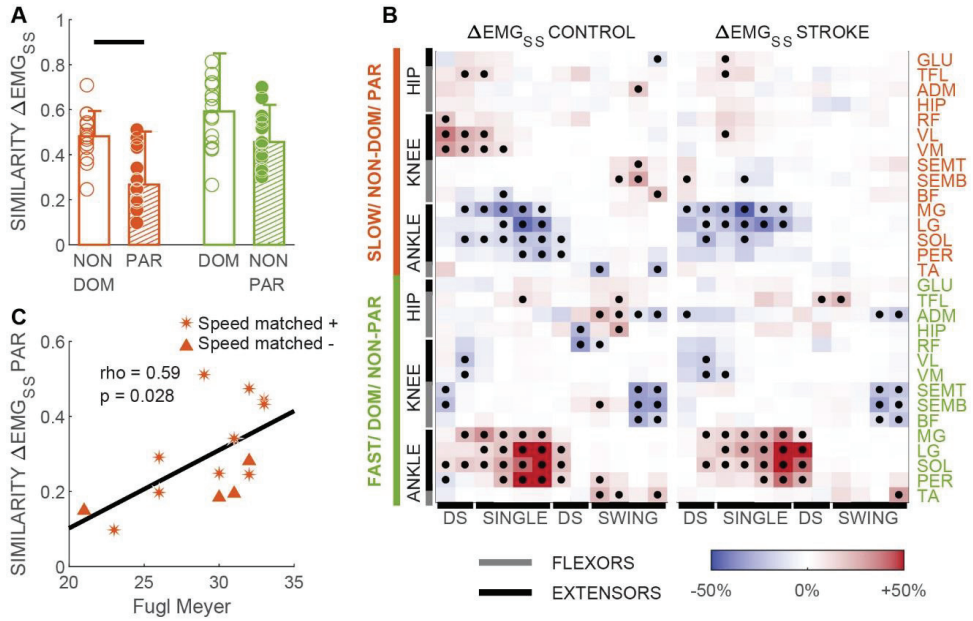

Figure 3. Structure of muscle activity modulation. A) Similarity of individual subjects' steady state muscle activity modulation to the reference pattern (i.e. expressed as the cosine between individual subject vector and group median of controls). Values closer to 1 indicate more similarity between vectors. Bars indicate group medians, error bars represent the interquartile range. Horizontal lines indicate significant differences in group medians as determined with a Wilcoxon Ranksum test ($p<0.05$). **B)** Visual representation of the structure of muscle activity modulation in the steady state of split-belt walking (ΔEMG_{SS}) relative to baseline walking. Red colors indicate increased activity and blue colors indicate decreased activity. Dots indicate statistical significance for non-parametric within group comparisons. We corrected the significance threshold for each epoch using a Benjamini-Hochberg procedure (Benjamini and Hochberg, 1995), setting the acceptable false discovery rate to 10%. In addition, we focused on significant differences between epochs that exceeded 10% of the maximum baseline activity for a given muscle since we considered these to be meaningful changes. Corrected p-thresholds for ΔEMG_{SS} were 0.058 for controls and 0.02 for stroke. **C)** Association between severity of motor symptoms (Fugl Meyer test) and structure of EMG modulation in steady state walking (ΔEMG_{SS}). Asterisks represent subjects included in the speed-matched analysis whereas triangles indicated subjects that were excluded. We found a significant correlation (i.e. Spearman's rho). This correlation indicated that stroke survivors who were less severely affected (i.e., higher Fugl-Meyer score) exhibited a steady state muscle pattern that was more similar to that of the reference muscle pattern (which was computed using EMG recordings from intact subjects).

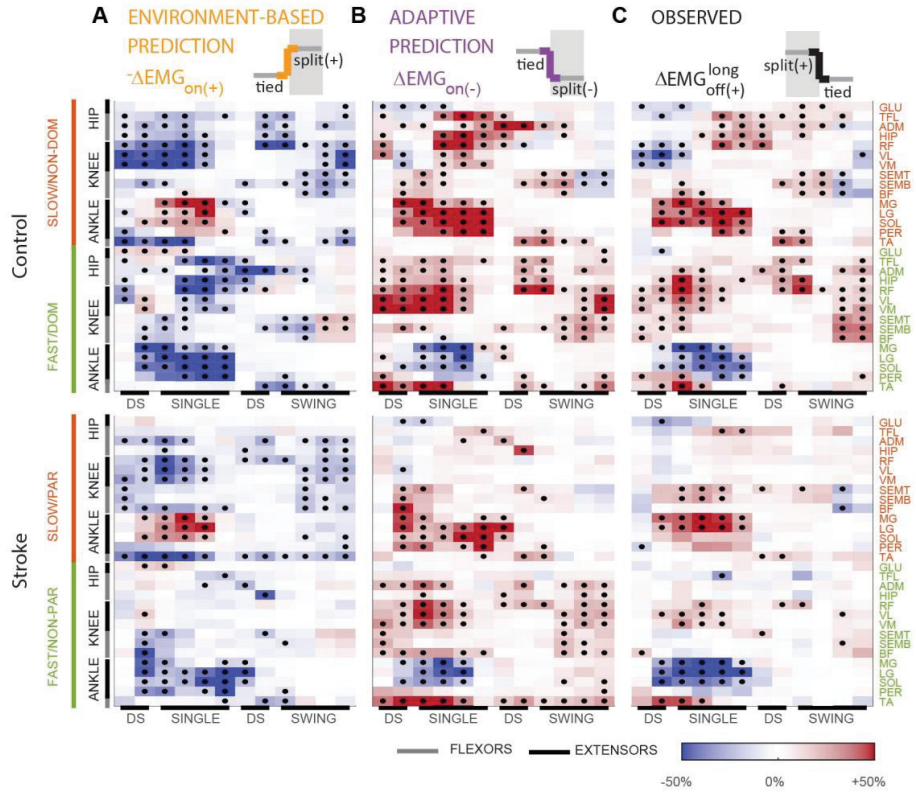

Figure 4. Predicted and measured structure of corrective responses after a long adaptation period. Data of controls are shown in the upper panels and those of the stroke participants in the lower panels. **A,B)** Expected corrective responses elicited by the 'off' transition under the environment-based (panel A) and adaptive (panel B) cases. Data (in color) and significance (black dots) were derived from the observed corrective responses upon the introduction of the '(+)' walking environment, by either taking the numerical opposite (environment-based) or by transposing leg activity (adaptation-based). **C)** Measured corrective responses upon removal of the '(+)' environment.

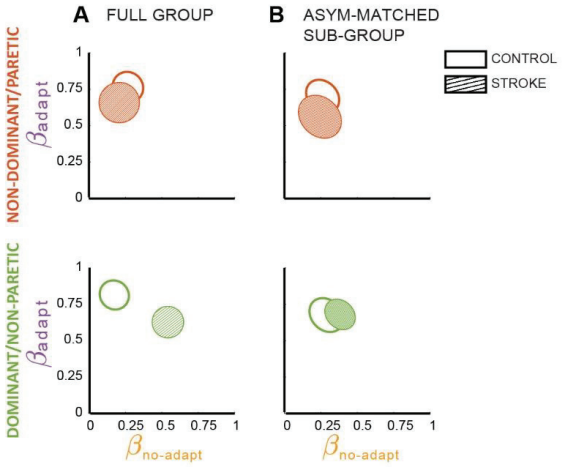

Figure 5. Adaptive and environment-based contributions to corrective responses. The ellipses represent the regression estimations of β_{adapt} and $\beta_{no\text{-}adapt}$ and their 95% confidence intervals for the control group (open) and the stroke group (hatched). **A)** Data obtained with 14 subjects per group. Paretic leg: R^2= 0.47, model p-value = $8.8*10^{-26}$. Non-paretic leg: R^2= 0.67, model p-value = $1.3*10^{-45}$. Dominant leg in controls R^2= 0.71, model p-value = $1.1*10^{-48}$. Non-dominant leg in controls R2= 0.68, model p-value = $3.1*10^{-45}$. **B)** Data obtained for asymmetry matched groups (i.e. n=7 per group). Non-dominant/paretic leg: controls: CI for β_{adapt} = [0.61 0.79] and CI for $\beta_{no\text{-}dapt}$ = [0.17-0.25], R^2= 0.64, model p-value = $1.2*10^{-40}$; stroke: CI for β_{adapt} = [0.45-0.68] and CI for $\beta_{no\text{-}adapt}$ = [0.13-0.36], R^2= 0.44, model p-value = $6.2*10^{-23}$); between-group comparison: Chi^2=4.1, p=0.13. Dominant/ non-paretic leg: controls: CI for β_{adapt} = [0.58 0.77] and CI for $\beta_{no\text{-}dapt}$ = [0.20-0.38], R^2= 0.63, model p-value = $8.4*10^{-39}$; stroke: CI for β_{adapt} = [0.60-0.76] and CI for $\beta_{no\text{-}adapt}$ = [0.30-0.46], R^2= 0.73, model p-value = $8.8*10^{-51}$); between-group comparison: Chi^2=2.5, p=0.29.

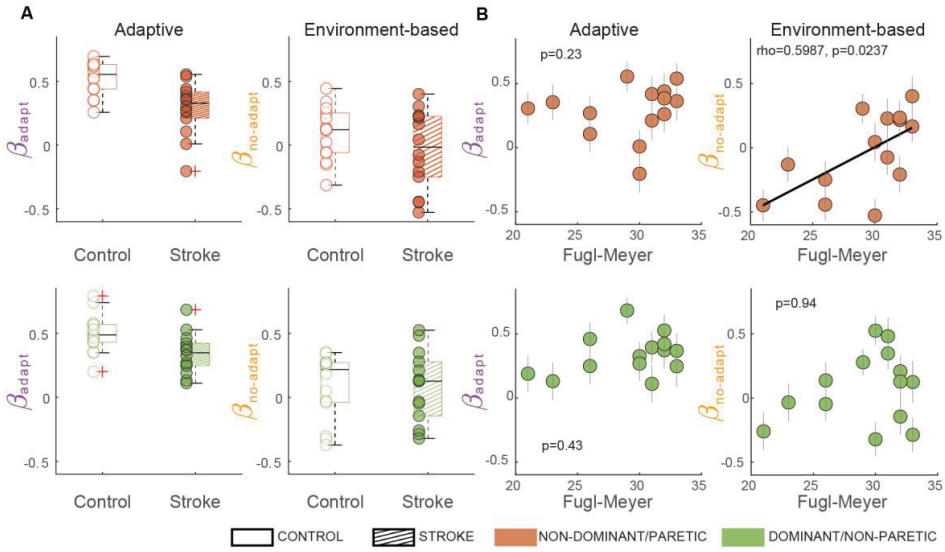

Figure 6. Individual regression results. A) Intersubject variability for the adaptive (β_{adapt}) and environment-based ($\beta_{no\text{-}adapt}$) contributions to corrective responses in the slow/paretic leg (upper panels) and the fast/nonparetic leg (lower panels). Median ± interquartile range for regressors are as follows: Non-dominant leg: β_{adapt}=0.55±0.19; $\beta_{non\text{-}adapt}$=0.12±0.30; p=$9.2*10^{-19}$±$7.7*10^{-13}$. Dominant leg: β_{adapt}=0.49±0.14; $\beta_{non\text{-}adapt}$=0.22±0.31; p=$1.2*10^{-15}$±$4.7*10^{-12}$. Paretic leg: β_{adapt}=0.33±0.21; $\beta_{non\text{-}adapt}$= -0.02±0.4;p=$2.1*10^{-8}$±$3.2*10^{-5}$. Non-paretic leg: β_{adapt}=0.35±0.17; $\beta_{non\text{-}adapt}$=0.13±0.42; p=$1.6*10^{-9}$±$6.2*10^{-6}$. **B)** Spearman correlations between leg motor function (Fugl-Meyer scale) and β_{adapt} and $\beta_{no\text{-}adapt}$ for each leg.

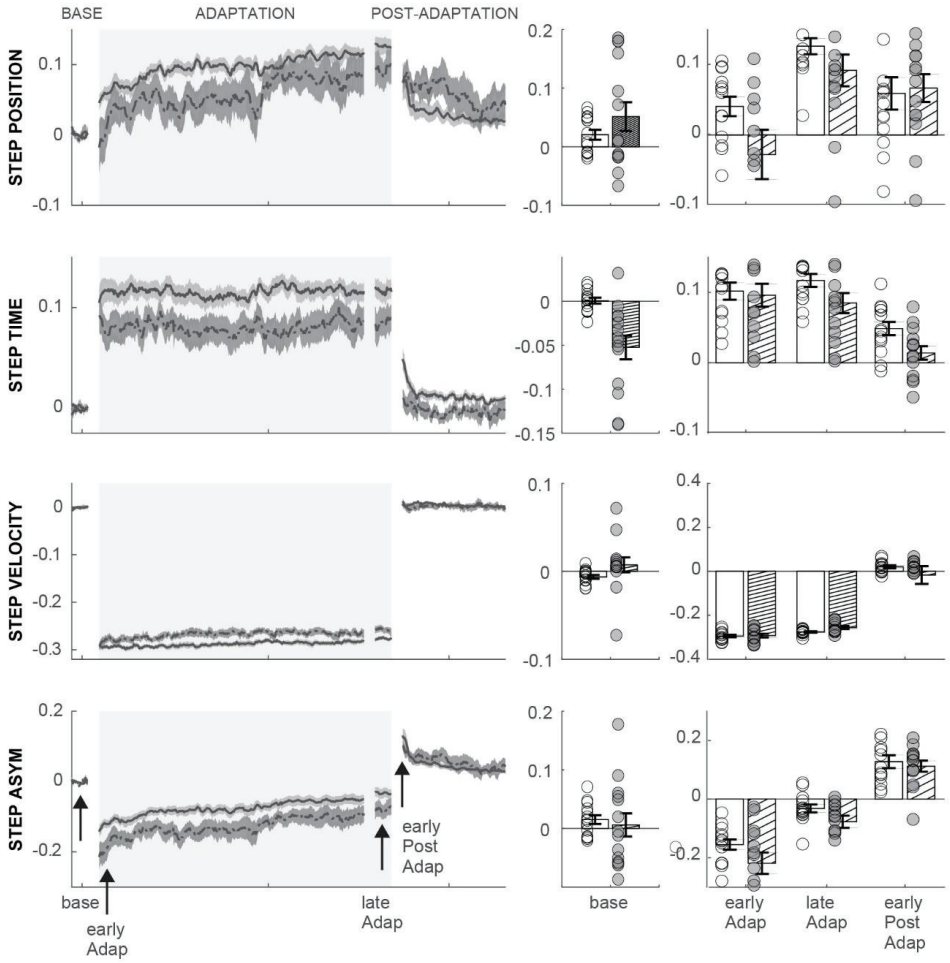

Figure 7. Modulation of kinematic parameters. A) Group averaged time courses for StepPosition, StepTime, StepVelocity and StepAsym. Note that individual subjects' baseline biases were subtracted to allow for comparison of modulation of parameters regardless of differences in baseline asymmetry. Shaded areas represent standard errors for each group. For visual purposes, data were smoothed using a running average (median) of 10 strides. Rectangles represent the epochs of interest. **B)** Interlimb kinematic parameters for each group during baseline. **C)** Between-group comparisons for kinematic parameters over the epochs of interest. We found no significant differences between the groups in any of the parameters. StepAsym (GROUP: $F_{(1,28)}$=3.48, p=0.07; GROUPxEPOCH: $F_{(2,56.)}$=1.16, p=0.31), stepPosition (GROUP: $F_{(1,28)}$=2.14, p=0.16; GROUPxEPOCH: $F_{(2,56.)}$=2.33, p=0.13), stepTime (GROUP: $F_{(1,28)}$=3.17 ,

p=0.09; GROUPxEPOCH: $F_{(2,56)}$=0.63, p=0.50) and stepVelocity (GROUP: $F_{(1,28)}$=1.41, p=0.25; GROUPxEPOCH: $F_{(2,56)}$=1.11, p=0.34).