EXPLOITING THE NOCICEPTIVE WITHDRAWAL REFLEXES IN REHABILITATION OF HEMIPLEGIC GAIT: A CASE STUDY

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Abstract

Background:

A closed loop system for improving gait in hemiplegic patients by supporting the production of the swing phase using electrical stimulations evoking the nociceptive withdrawal reflex was designed and evaluated in one chronic hemiplegic subject.

Methods:

Electrical stimulations were delivered to 4 locations on the sole of the foot at 3 different time points between heel-off and toe-off. The system exploits the modular organization of the nociceptive withdrawal reflex and its site and phase modulation during gait in order evoke optimal flexion of the hip, knee and ankle joints in early swing phase. A Model Reference Adaptive Controller (MRAC) was designed to select the optimal stimulation parameters. The hypothesis was that the MRAC-system result in better walking pattern compared with a pre-programmed fixed pattern controller. Based on the patient unperturbed gait and his withdrawal strategies an individual controller target for hip, knee and ankle flexion were set. The patient walked 10 min with the MRAC-system, 10 min with the fixed pre-programmed pattern and 10 min with no-stimulation.

Results and Conclusions:

The results indicate that both stimulation paradigms resulted in a more functional gait compared with no-stimulation and that the control strategy in the MRAC system is superior and will be able to adapt better to the varying needs during rehabilitation therapy.

Key words:

Nociceptive withdrawal reflex, Reflex modulation, Human locomotion, Automated Control, Model reference adaptive control

Izvleček

Izhodišča:

Razvili smo zaprtozančni sistem za ponovno učenje hoje pri osebah s hemiplegijo, ki podpira izvedbo zamaha z uporabo električne stimulacije, ki sproža umaknitveni refleks. Sistem smo testirali pri eni osebi s hemiplegijo v kronični fazi.

Metode:

Električno stimulacijo smo aplicirali na 4 različnih mestih na podplatu in ob 3 različnih diskretnih časih v ciklu hoje na intervalu, ki je definiran z dvigom pete in dvigom prstov. Sistem temelji na modularni organiziranosti umaknitvenega refleksa, katerega intenziteta krčenja kolka, kolena in gležnja je odvisna od lokacije in trenutka nociceptivne stimulacije. Izbira optimalnih parametrov stimulacije je izvedena z adaptivnim regulatorjem, ki sledi izbrani referenci modela željenega odziva. V tem delu smo preizkusili hipotezo, da z adaptivnim spreminjanjem stimulacije dosežemo boljši vzorec hoje kot s fiksno stimulacijsko shemo. Najprej smo izmerili kinematiko hoje pri osebi, ki je sodelovala pri testiranju, ter določili specifične deficite. Nato smo glede na individualne odzive pri različnih kombinacijah nociceptivne stimulacije določili željeno kinematiko kolka, kolena in gležnja. Testirana oseba je najprej hodila 10 minut z uporabo adaptivnega regulatorja, 10 minut brez stimulacije ter nazadnje še 10 minut z uporabo fiksne stimulacijske sheme.

Rezultati in zaključki:

Rezultati kažejo, da smo z obema načinoma stimulacije dosegli bolj funkcionalno hojo. Kažejo tudi, da adaptivni regulator omogoča večjo stopnjo prilagajanja spremenljivim potrebam po pomoči med terapijo.

Ključne besede:

nociceptivni umaknitveni refleks, modulacija refleksa, hoja, avtomatsko vodenje, adaptivno vodenje

INTRODUCTION

Patients who have suffered a stroke often have problems in the lower limb leading to a compromised gait pattern. The affected limb presents kinematic deviations from normal. In the swing-phase the typical deviations are decreased hip flexion, decreased knee flexion, decreased knee extension at heel strike and decreased ankle dorsiflexion throughout the swing-phase (1).

To support the stroke patients gait in the swing phase the withdrawal reflex can be stimulated resulting in a synergistic flexor response. Thus hip and knee flexors and ankle dorsiflexors withdraws the limb from the stimulus (Figure 1A).

This approach were used by Braun et al (2) to initiate the swing phase in paraplegics and is especially beneficial because of the deep location of the main hip flexor (iliopsoas) that makes it unsuitable for direct surface stimulation.

Since the pioneer discoveries of Sherrington (3), reflex responses have been conceived as stereotyped flexion responses; however, it has been suggested by Grimby (4), that there is a more refined organization of the spinal withdrawal reflexes. This has been studied in detail in rats (5) and cats (6,7).

Recent studies in humans indicate that the reflex response is dependent on the stimulation site (8), intensity (9), frequency (9) and where in the gait cycle the stimulation is presented

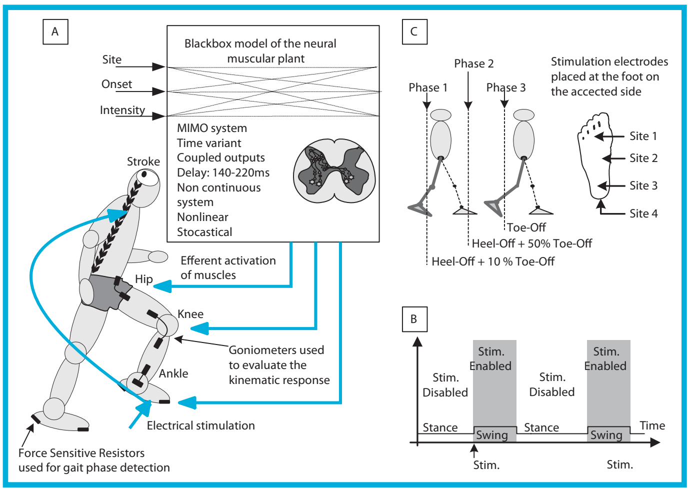

Figure 1A: The neuro-muscular plant from stimulation to kinematic response. Moderately painful electrical stimulations lead to afferent input to spinal circuits which respond with activation of the muscle groups controlling the stimulated limb (and interacting with the entire locomotion pattern). This removes the affected site from the stimulus by activation of muscles controlling the hip, knee and ankle joint depending on the stimulation parameters. ***B:*** *Stimulations can only be enabled in the swing phase.* ***C:*** *Stimulation is delivered to 4 locations of the sole of the foot at 3 different time points between heel-off and toe-off.*

(10-12). In these studies the nociceptive withdrawal reflex was elicited by painful electrical stimulation of the sole of the foot.

The feasibility of using the withdrawal reflex in a system for improving gait in hemiplegic patients by supporting the swing phase was examined in this study. The system exploited the differences in withdrawal strategies depending on stimulation site and stimulation onset during gait to tailor the desired movement for the individual patient.

Two control systems for swing phase support have to be designed and compared: An open loop system and a closed loop system. Gait is assessed, evaluated and controlled based on measurements of joint ankles acquired by mean of goniometers (Figure 1A).

METHODS AND MATERIALS

A. Modeling and control

Modeling and control of the neuro-muscular plant (Figure 1A) is a fairly complex problem. The knowledge of the neural pathways from the cutaneus stimulation to the kinematic response is limited to rough drafts of different mechanisms and is not described well enough to build a precise parametric model.

In the recovery after a stroke the reflex pathways may change substantially and to characterize this plastic system it is clear that some kind of adaptive model is required.

The neuro-muscular plant can be characterized as a Multiple Input Multiple Output (MIMO) system (Figure 1A). The input *Site* and *Phase* are categorical variables without any intrinsic ordering and *Intensity* is a continuous variable (Figure 1A). The output is coupled, highly time variant, stochastic and nonlinear and there are significant long control latencies in the system, since the mechanical response occurs 140-360ms from stimulation onset (12,13). Compared to a normal swing phase that lasts approximately 400ms it is obvious that only one stimulation can be delivered and evaluated in each swing phase.

Stimulation in the stance phase could lead to inappropriate perturbations, instability and trembling. Thus stimulation can only be enabled when the body is supported by the contralateral limb. The control system is therefore a non-continuous system only enabled in late stance and early in the swing phase (Figure 1B). Further, some kind of adaptation between every step is required in the controller design to handle reflex habituation and gradual improvement in walking performance during therapy.

Since a precise parametric model cannot be derived based on prior knowledge to the neuro-muscular plant the determination of the plant model needs to be recursively derived from input-output data and the model parameters have to be adjusted dynamically in order compensate for drift variations in the neuro-muscular plant due to neuro plastic changes. This is possible with MRAC (Figure 2A) (14). This study therefore tests the feasibility of MRAC in a system for swing phase support in a case study with one chronic hemiplegic subject.

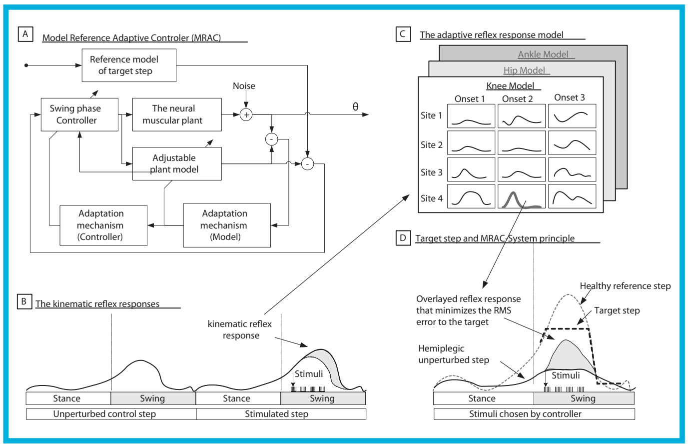

***Figure 2A:** The Model Reference Adaptive Control System. **B:** The reflex response curve. **C:** Modeling of the reflex responses curve for each stimuli configuration. **D:** MRAC controller principle.*

B. Experimental setup

The hemiplegic subject: One hemiplegic subject participated in the study (Male, age 46, right body side affected, time from onset of stroke 5¹/₂ year, Functional Ambulation Category (FAC) Level 5). A physiotherapists specialized in gait rehabilitation evaluated the patient gait and reported that the fundamental problem of the patients gait was lack of knee extension in late swing and start of stance. Informed consent was obtained from the subject and the Helsinki Declaration was respected.

Electrical stimulation: The nociceptive withdrawal reflex was elicited by transcutaneous electrical stimulation (Noxitest, Aalborg, Denmark) delivered to one of four sites on the sole of the foot on the affected side (Figure 1C): the 3rd metatarsophalangeal (MP) joint, the medial arch of the foot, the plantar side of the calcaneus, and the posterior side of calcaneus. The stimulation was delivered through self-adhesive electrodes (2.63 cm^2 surface area, Ag–AgCl, AMBU, Denmark), with a common reference electrode (7x10 cm electrode, Pals, Axelgaard Ltd., USA) placed on the dorsum of the foot. Each stimulus consisted of a constant current pulse burst of five individual 1ms pulses delivered at 200 Hz. This stimulus was repeated four times at a frequency of 15 Hz.

The stimulation intensity at the individual electrode sites was normalized to the pain threshold. Hence, the stimulus intensity was set at the pain threshold detected at each electrode site multiplied by a fixed factor common for all sites. This factor was adjusted according to the detected response and the unpleasantness of the stimulus.

The pain threshold for a single stimulus was determined with the subject in sitting position using a staircase method consisting of a series of increasing and decreasing stimuli. The stimulation could be delivered at three phases of the gait cycle between heel-off and toe-off on the affected side: phase 1: 10% of the heel-off/toe-off period, phase 2: 50% of the heel-off/toe-off period, and phase 3: toe-off on the ipsilateral leg (Figure 1C).

Data acquisition: Three goniometers (type SG150 and SG110/A, Biometrics Ltd, Gwent, U.K.) were mounted on the lateral side of the affected limb across the ankle, knee, and hip joints to monitor the kinematic response (Figure 1A). Timing of heel and toe contact with the ground were measured by Force Sensitive Resistors (FSR)s (LuSense, PS3, Standard 174, area 2.48 cm^2, thickness 0.2 mm, measurement range 2.5-500 N) firmly attached with adhesive tape distal to the big toe, and to the medial process of calcaneus (Figure 1A). All data were sampled at 4 kHz, displayed on a monitor and stored for later analysis.

Experimental protocol: Stimulation electrodes, FSRs and goniometers were mounted, and the pain threshold was determined. The experiment was split in two sub-sessions:

Part-I: The initial assessment of the baseline gait and measurements of reflex responses to stimulation. The data from this part was used to build an initial model of the patients gait to be used in Part-II. A sequence of 15 unperturbed control steps were acquired and used for calculating the stimulation onsets as a time delay after heel-off. Stimulation was delivered in a random sequence, repeating each combination of stimulation site and phase five times. The inter stimulus interval was randomized to be between 4-6 steps. All data (kinematics and forces) were acquired starting 4 seconds prior to the stimulation onset and ending 4 seconds after the stimulation onset.

Part-II: Test of swing phase controller systems with automated stimulations. To evaluate the performance of the MRAC-system an open loop controller using a predefined Fixed Pattern of Stimulation (FPS) was implemented. Since the automatic stimulations was delivered on almost every step data were acquired with a ringbuffer containing the last 8 seconds data and stored at each heel-on preceding the automated stimulations.

The adaptive neuro-muscular plant model consisted of two parts: A model for the kinematic reflex responses and a model for the baseline performance. In Part-I the baseline model was extracted as an average of all unperturbed control steps, however to reflect gait improvements as well as fatigue it was important to update the baseline model in Part-II. Therefore a non-controlled-rest-step was acquired with a 5 step interval with the stimulations disabled. The reflex response models were updated in the other 4 controller-corrected-steps where stimulations were enabled.

The kinematic reflex responses were defined as the subtraction of the post-stimulation goniogram from the corresponding goniogram recorded in the step cycle immediately preceding the stimulation (Figure 2B). Based on the data acquired in Part-I a moving average (MA) approach was used to model the reflex response. The MA model used 5 reflex responses with similar input configuration i.e. 36 MA models were implemented to represent the adaptive model describing movements in all three joints for the three stimulation phases and four stimulation sites (Figure 2C). This model was initially derived for the hemiplegic subject based on data from Part-I and during Part-II the adaptation mechanism (Figure 2A) updated it preceding each controller-corrected-step via the MA approach.

Reference model of target step: To define a realistic target for this specific hemiplegic subject it was necessary both to compare the unperturbed gait of the patient with a normal healthy reference and to evaluate the patients specific need. This resulted in an individual controller target for each joint (Figure 2D) and a *weight matrix* with a value for each joint that ensured that it was possible to prioritize the specific joint needing most support from the control system.

Lacking knee extension was the primary problem for the patient in this study and therefore a knee target trajectory with additional knee extension in late swing phase were

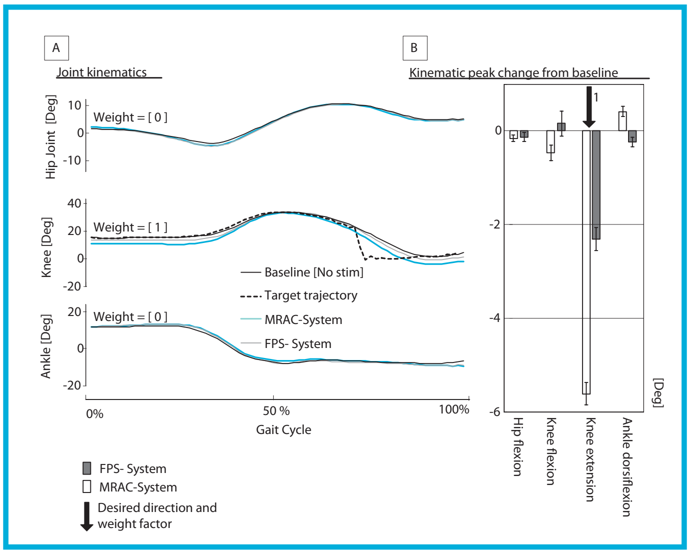

Figure 3A: The average joint kinematics for each of the three 10 min sessions; baseline, MRAC and FPS. A controller target with additional knee extension in late swing was selected for the knee joint. Notice that MRAC-system is obtaining most knee extension in late swing and early stance. *B:* Kinematic peak change from baseline.

selected (Figure 3A) and the *weight matrix* were set to: [Hip=0, Knee=1, Ankle=0]

MRAC Swing phase Controller: At the end of each swing phase (defined by heel-on) the controller was activated. The predicted step was calculated for all input options based on the adaptive plant model. The *weight matrix* were used to calculate a weighted sum of RMS error to the target step (Figure 2D) and the input that minimized the weighted RMS error was chosen for the subsequent stimulus and delivered within the next swing phase (defined by heel-off).

Fixed pattern of stimulation (FPS): The stimulation pattern of the FPS-System was selected according to a larger ongoing clinical study where stimulations were delivered to the arc of the foot at heel-off.

RESULTS

Both stimulation paradigms resulted in an improvement in the patients gait pattern with additional knee extension in late swing and early stance (Figure 3A). The FPS- system added 2.3±0.5° Standard error of the mean (SEM) while the MRAC system added 5.5±0.5° SEM in late swing.

DISCUSSION

The future prospect of the MRAC-system is a clinical application to be used in gait rehabilitation of the acute stroke patient. The idea behind the system is dual.

The first is to provide acute stroke patients an aid for walking in the recovery phase after a stroke by combined insensitive physical task-oriented training and electrical stimulation (FET). This will steer the leg trough the swing phase of gait by using the optimal stimulation parameters.

The second is that this approach will promote neuro plasticity and thereby the patient could improve even more like seen in the study by Quintern et al. (15) that used electrical stimulation of flexor reflex afferents during gait retraining, and concluded that it enhances the recovery of gait function in patients with hemiparesis after acute stroke.

The MRAC-system was using alternating stimulation parameters during the session. This also have a dual effect where the first effect is to optimize the gait pattern to meet the controller target and the second is to maintain a large reflex response by breaking down the effect of habituation. The second effect is demonstrated by Dimitrijević et al. (16) that stimulated multiple sites with repetitive stimulation and found that stimulation sites 3-4cm from the a habituated site still evoke a full response. Automatic adjustment of intensity levels could also be implemented. The adjustments could be tuned according to a measure of overall habituation, e.g. when the response drops by 20% the intensity should increase by 20%. This might also help to dishabituate the reflex as demonstrated by Granat et al (17) who stimulated the common peroneal nerve in spinal cord injured patients and proved that a burst of high intensity stimulation dishabituates the reflex response.

CONCLUSIONS

Two online, real-time, swing phase controllers were designed, implemented and tested on one chronic hemiplegic subject. One open-loop system using a Fixed Pattern of Stimulation (FPS) and a closed loop Model Reference Adaptive Control system. Both resulted in improved functional gait pattern compared with no-stimulation by providing additional knee extension in late swing phase and into the early stance phase.

However the MRAC-system was superior and based on this case study it is hypothesized that the MRAC system will be able to adapt better to the varying needs during rehabilitation therapy but further studies are needed to verify this on a larger patient group.

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References:

1. Moore S, Schurr K, Wales A, Moseley A, Herbert R. Observation and analysis of hemiplegic gait: swing phase. Aust J Physiother 1993; 39(4): 271-278.

2. Braun Z, Mizrahi J, Najenson T, Graupe D. Activation of paraplegic patients by functional electrical stimulation: training and biomechanical evaluation. Scand J Rehabil Med Suppl. 1985; (12): 93-101.

3. Sherrington CS. Flexion-reflex of the limb, crossed extension-reflex, and reflex stepping and standing. J Physiol 1910; 40(1-2): 28-121.

4. Grimby L. Normal plantar response: integration of flexor and extensor reflex components. J Neurol Neurosurg Psychiatry 1963 Feb.; 26: 39-50.

5. Schouenborg J, Kalliomaki J. Functional organization of the nociceptive withdrawal reflexes. I. Activation of hindlimb muscles in the rat. Exp Brain Res 1990; 83(1): 67-78.

6. Levinsson A, Garwicz M, Schouenborg J. Sensorimotor transformation in cat nociceptive withdrawal reflex system. Eur J Neurosci 1999; 11(12): 4327-4332.

7. Haghbarth KE. Excitatory and inhibitory skin areas for flexor and extensor motoneurons. Acta Physiol Scand Suppl. 1952; 26(94): 1-58.

8 Andersen OK, Sonnenborg FA, Arendt-Nielsen L. Modular organization of human leg withdrawal reflexes elicited by electrical stimulation of the foot sole. Muscle Nerve 1999; 22(11): 1520-1530.

9. Spaich EG, Collet T, Arendt-Nielsen L, Andersen OK. Repetitive painful stimulation evokes site, phase, and frequency modulated responses during the swing phase of the gait cycle : pre-liminary results. In: Gantchev N, ed. From basic motor control to functional recovery IV. Sofia: Marin Drinov Academic Publishing House, 2005: 136-140.

10. Andersen OK, Spaich EG, Madeleine P, Arendt-Nielsen L. Gradual enlargement of human withdrawal reflex receptive fields following repetitive painful stimulation. Brain Res 2005 May; 1042(2): 194-204.

11. Spaich EG, Arendt-Nielsen L, Andersen OK. Modulation of lower limb withdrawal reflexes during gait: a topographical study. J Neurophysiol 2004; 91(1): 258-266.

12. Spaich EG, Hinge HH, Arendt-Nielsen L, Andersen OK. Modulation of the withdrawal reflex during hemiplegic gait: effect of stimulation site and gait phase. Clin Neurophysiol 2006; 117(11): 2482-2495.

13. Crenna P, Frigo C. Evidence of phase-dependent nociceptive reflexes during locomotion in man. Exp Neurol 1984; 85(2): 336-345.

14. Landau ID. Survey of model reference adaptive techniques - theory and applications. Automatica 1974; 10(4): 353-379.

15. Quintern J, Krewer C, Bisle G, Husemann B, Heller S. Enhancement of gait retraining by electrical stimulation of flexor reflex afferents in acute stroke patients: a randomized, controlled clinical study. In: 9th Annual Conference of the International FES Society, September 2004 - Bournemouth, UK, Sept. 2004.

16. Dimitrijević MR, Nathan PW. Studies of spasticity in man. 5. Dishabituation of the flexion reflex in spinal man. Brain 1971; 94(1): 77-90.

17. Granat MH, Nicol DJ, Baxendale RH, Andrews BJ. Dishabituation of the flexion reflex in spinal cord-injured man and its application in the restoration of gait. Brain Res 1991; 559(2): 344-346.