SHORT COMMUNICATION

Intrathecal baclofen normalizes motor strategy for squatting in familial spastic paraplegia: a case study

B. Dan[1,2*], G. Cheron[1,3]

[1] Laboratory of Movement Biomechanics, ISEPK; [2] Department of Neurology, Queen Fabiola University Hospital, Université Libre de Bruxelles; [3] Laboratory of Neurophysiology, Université de Mons-Hainaut, Brussels, Belgium

Summary – We aimed to assess whether intrathecal baclofen could alter the motor strategy for squatting of a patient with pure familial spastic paraplegia. Before baclofen injection and two, four and six hours after it, the patient was evaluated as follows: self-report of walking stiffness and movement initiation; muscle tone with the Ashworth scale; and kinematic and electromyographic analysis of the squatting movement using the opto-electronic ELITE system. The patient's subjective improvement and decrease in muscle tone were dramatic after baclofen injection. Kinematic analysis of squatting showed gradual improvement. Before the injection, the movement was performed with loss of trunk verticality, backward shift of the hip, multiphasic ascending phase of the knee angular velocity and dynamic ankle stiffening. After baclofen injection, the movement was made with vertical translation of body segments and monophasic ascending phase of the knee angular velocity. The effect was maximal six hours after the injection. Electromyographic activities showed a non-specific co-contraction pattern before the injection, and a reciprocal pattern two hours after it. Moreover, a physiological anticipatory deactivation of the hamstring muscles appeared two hours after the injection. In this study of a single patient with familial spastic paraplegia, intrathecal baclofen has facilitated the emergence of normal, supraspinally determined movement patterns. © 2000 Éditions scientifiques et médicales Elsevier SAS

baclofen / electromyography / familial spastic paraplegia / kinematics / motor control / posture

Résumé – Normalisation de la stratégie motrice pour s'accroupir chez le patient paraplégique sous baclofène intrathécal. Étude d'un cas. Cette étude a pour but de déterminer si l'injection intrathécale de baclofène peut entraîner une modification de la stratégie motrice utilisée par un patient atteint de paraplégie spastique familiale pure pour s'accroupir. Le patient a été évalué de la manière suivante avant l'injection, ainsi que deux, quatre et six heures après celle-ci : évaluation personnelle de la raideur à la marche et de la difficulté à initier le mouvement, évaluation du tonus musculaire suivant l'échelle d'Ashworth et analyse cinématique et électromyographique du mouvement d'accroupissement à l'aide du système optoélectronique ELITE. L'amélioration subjective rapportée par le patient et la diminution du tonus musculaire étaient marquées après l'injection de baclofène. L'analyse cinématique de l'accroupissement a démontré une amélioration progressive. Avant l'injection, le mouvement était réalisé avec une perte de la verticalité du tronc, un déplacement postérieur de la hanche, une phase ascendante multiphasique de la vitesse angulaire du genou et une rigidification dynamique de la cheville. Après l'injection, le mouvement était réalisé avec une translation verticale

* *Correspondance and reprints:* B. Dan, HUDERF, 15, avenue J.J. Crocq, 1020 Brussels, Belgium.

des segments du corps et une phase ascendante monophasique de la vitesse angulaire du genou. Les effets étaient maximaux six heures après l'injection. Les activités électromyographiques montraient une cocontraction non spécifique avant l'injection et une inhibition réciproque deux heures après celle-ci. De plus, une désactivation anticipative des muscles ischiojambiers apparaissait deux heures après l'injection. Dans cette étude d'un patient unique atteint de paraplégie spastique familiale, le baclofène a donc favorisé l'émergence d'une organisation normale du mouvement.

INTRODUCTION

Pure familial spastic paraplegia (FSP) is a group of genetic conditions characterized by spastic paraparesis secondary to degeneration of the pyramidal tracts below the cervical level. In this condition, the effectiveness of oral antispasticity medication such as baclofen is generally considered to be limited. Baclofen is a structural analog of the inhibitory neurotransmitter γ-aminobutyric acid (GABA$_B$). It binds to presynaptic GABA$_B$ receptors in the spinal cord, impeding the release of afferent excitatory neurotransmitters involved in both mono- and polysynaptic reflexes at the spinal level [3, 17]. As it poorly crosses the blood-brain barrier and the aimed site of action is in superficial layers of the spinal cord, baclofen can be injected intrathecally. Early reports on the effect of intrathecal baclofen on spasticity in seven previous FSP patients have been encouraging [13, 15, 16, 19], although the effect on motor function has not been systematically addressed. Landau has stressed that treatment of spasticity does not necessarily imply functional improvement [11]. However, intrathecal baclofen has been shown to substantially improve daily living in a number of spastic patients [2, 12, 18]. Some authors have suggested that this improvement could be at least partially related to better motor control unmasked by intrathecal baclofen [8, 10].

In this single-case study, we aimed to assess whether intrathecal baclofen could alter the motor strategy for squatting of a patient with pure FSP, and if this could lead to the emergence of normal patterns.

METHODS AND MATERIALS

The studied patient is a 41-year-old man with pure FSP inherited in an autosomal dominant mode. He had complained of leg stiffness since early childhood, predominating in the morning and increased by stress, and has occasional painful spasms in the lower limbs. On a 0-to-10 numerical rating scale of intensity (NRS), he evaluates his usual stiffness during walking between 4 and 9, and his relative difficulty in initiating a movement from a static position between 5 and 9. He takes no medication. He has spasticity in the lower limbs, muscle power in the normal range, very brisk reflexes in the lower limbs, extensor plantar responses and spastic gait. Neurologic examination is otherwise normal.

The following evaluation of the patient was performed before intrathecal injection of 75 μg (0.77 μg/kg) of baclofen via lumbar puncture, and two, four and six hours after the injection:
– patient's NRS self-evaluation of walking stiffness and movement initiation;
– muscle tone assessment with the Ashworth scale [1] during passive flexion and extension of the hips, knees and ankles with the patient lying supine;
– kinematic and electromyographic (EMG) analysis of ten trials of squatting movement following the same paradigm and ELITE technology as used previously [4, 5] for placement of markers and EMG electrodes.

Analysis of variance between sets of data (ANOVA) was computed using the Statistica Software (Softcom). The protocol of this study was approved by the Ethics Committee of Queen Fabiola University Hospital. The patient signed an informed consent form.

RESULTS

The patient's NRS evaluations of stiffness and difficulty in movement initiation were 8, 4, 1, 1 and 8, 4, 3, 1, respectively, before baclofen injection and two, four and six hours after it. The corresponding mean Ashworth score went down from 4.0 to 1.3, 1.2 and 1.0 (*figure 2H*).

The stick diagrams in *figure 1* show the evolution of the squatting performance before and after baclofen injection. Quantification and statistical significance of the corresponding kinematic parameters are given for all the trials in *figure 2*. Before the injection (*figure 1A*),
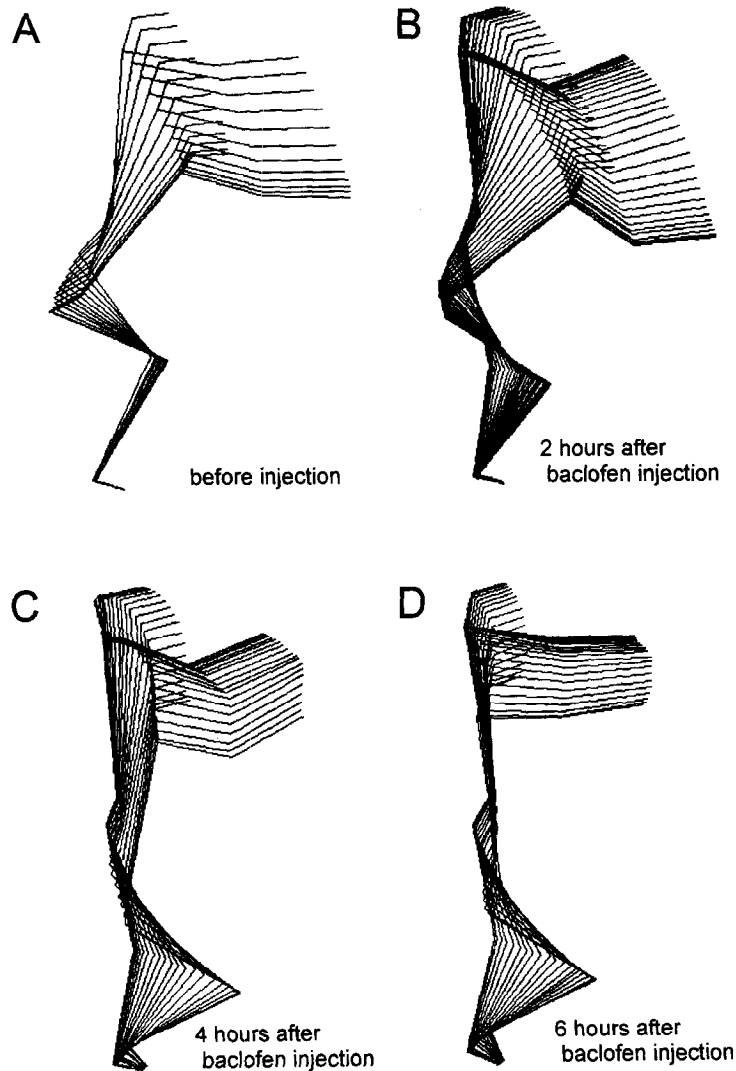
Figure 1. Sagittal stick diagrams of the squatting movement. (A) Before intrathecal baclofen injection, (B) two, (C) four and (D) six hours after the injection. The stick diagrams were constructed by defining body segments between self-reflective markers placed on the patient's skin on the lateral aspect of the nose at the height of the infra-orbital edge, the ear tragus, the upper limit of the acromion, the lateral epicondyle of the elbow, the styloid process of the wrist, the antero-superior iliac spine, the greater trochanter, the lateral condyle of the knee, the external malleolus, and the distal end of the fifth metatarsal.

the movement comprised an important flexion of the trunk over the thigh *(figure 2C)*, a minimal flexion of the ankle joint *(figure 2E)* and a backward shift of the hip. Two hours after the injection *(figure 1B)*, the movement of the trunk was unchanged *(figure 2C)* but the amplitude of ankle flexion was much higher *(figure 2E)*, associated with forward displacement of the knee and reduced backward shift of the hip. Four hours after the injection *(figure 1C)*, the amplitude of trunk

flexion was markedly decreased *(figure 2C)* and the trajectory of the hip was made vertical. Six hours after the injection *(figure 1D)*, trunk flexion had become minimal and the hip trajectory was vertical. These changes were accompanied by gradual angular stabilization of the head *(figure 2A)*, preservation of arm horizontality *(figure 2B)*, increased angular amplitude and velocity of knee joint flexion *(figure 2D, F)* and reduced duration of the movement *(figure 2G)*.
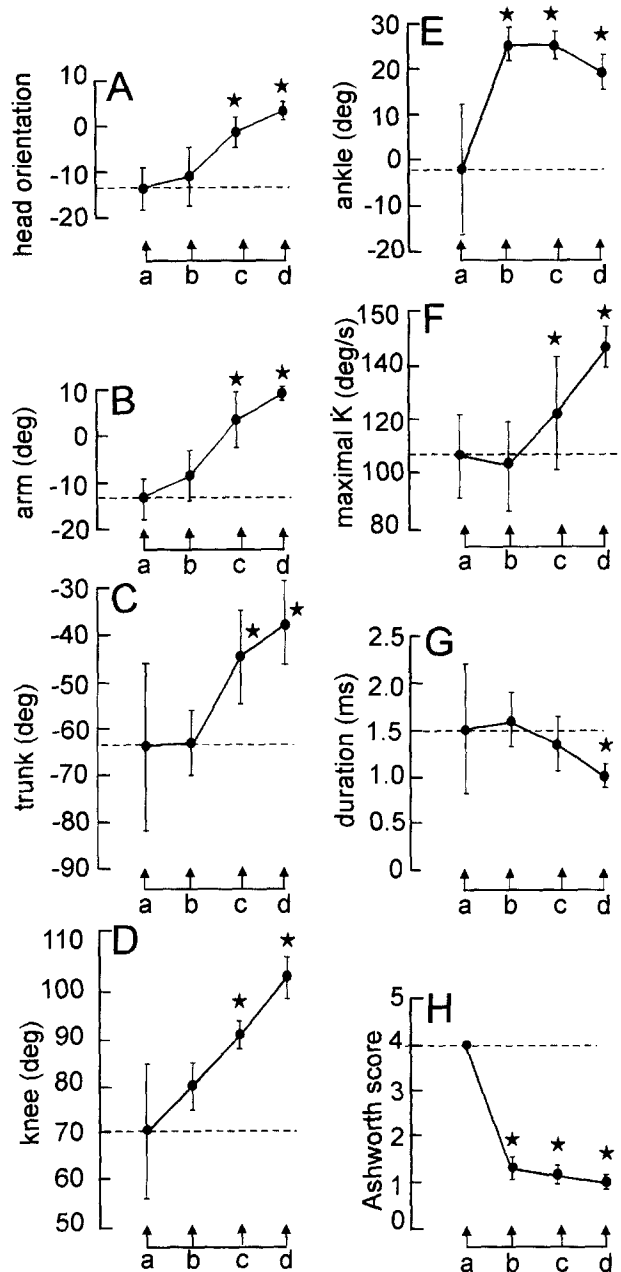
Figure 2. Effect of baclofen on kinematic parameters of the squatting movement. Mean and standard deviation of differential angles between the onset and the end of the movement for (A) head orientation (angle of ear-nose markers relative to the horizontal), (B) arm orientation (angle of shoulder-elbow markers relative to the horizontal), (C) trunk orientation (angle of shoulder-hip marker relative to the vertical), (D) knee angle, and (E) ankle angle, (F) Maximal knee angular velocity, (G) duration of the movement, (H) Ashworth spasticity score. (a) Before intrathecal baclofen injection, (b) two, (c) four and (d) six hours after the injection. The black stars indicate statistical difference (*P* < 0.005) with respect to pre-injection data.

Figure 3 shows the typical EMG patterns related to the squatting performance before (A) and two hours after baclofen injection (B). Before the injection, the ascending phase of the knee angular velocity was prolonged and irregular. A marked tonic activity was present in all recorded muscles except for the tibialis anterior. The activity of the latter muscle progressively increased just after the onset of movement. No clear change in EMG activities was noted in the other recorded muscles while the movement was performed except for the quadriceps in the final phase of squatting. Two hours after the injection, the ascending phase of the knee angular velocity was more rapid and regular. Tonic activity was minimal in most recorded muscles prior to the onset of the movement but remained notably high in the hamstring muscle. However, a clear deactivation (see open arrows in *figure 3B*) occurred in these muscles 211–284 ms before the onset of movement. A phasic EMG burst occurred at the onset of movement. A reciprocal pattern between the hamstring and the vastus lateralis muscles is clearly recognizable (see black star in *figure 3B*).

DISCUSSION

This study has focused on the effect of a single dose of intrathecal baclofen on the realization of the squatting movement in a patient with FSP. We found that intrathecal baclofen injection was followed by significant decrease in spasticity with a maximal effect achieved four hours after the injection, consistent with previous reports in patients with spasticity of spinal origin [13]. Subjective improvement concerned suppleness and to a lesser extent initiation of movement. The studied movement is a multi-joint, whole-body movement involving voluntary rupture of posture, an equilibrium challenge and dissociated movement schemes in the upper and lower parts of the body. The motor pattern used by the patient to perform it gradually changed during the few hours following the injection. The motor strategy used by normal adults for performing rapid flexion of the lower limbs from an initial standing posture has recently been characterized [4]. It combines movement dissociation (maintained extension of the trunk and upper limbs), nearly vertical translation of the body segments with an oblique trajectory of the knee; short, monophasic ascending phase of the knee angular velocity; and, in most subjects; anticipatory deactivation of hamstring muscles. A similar motor strategy has been demonstrated in normal children
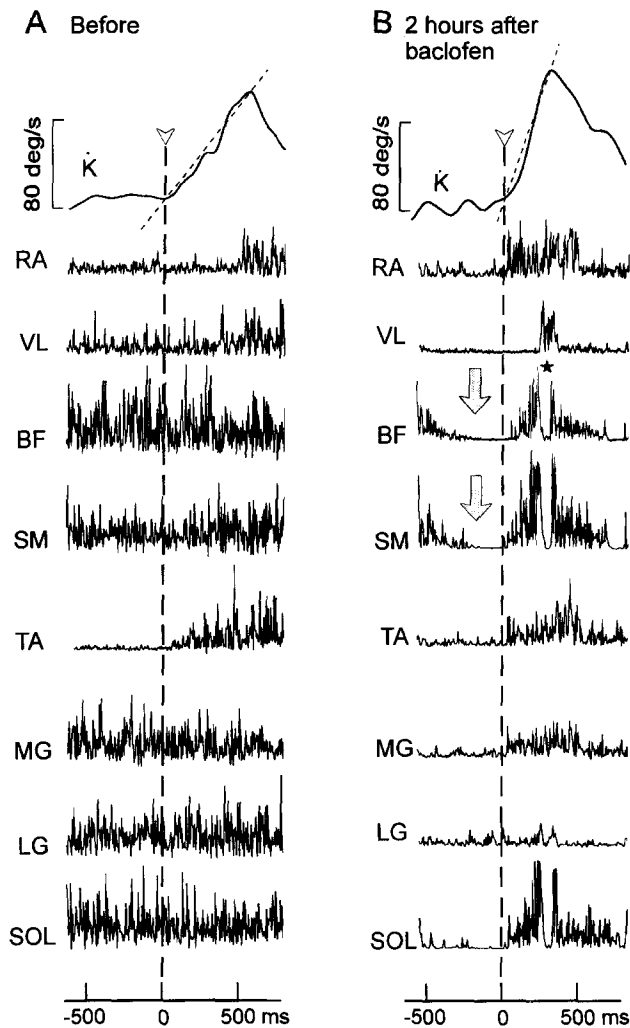
ciated execution of the movement (global flexion), complete loss of trunk verticality, backward shift of the hip, locking of the ankle; prolonged, multiphasic ascending phase of the knee angular velocity and, in most patients, anticipatory activation of the soleus muscle. This motor strategy can be regarded as adaptive, reflecting the elaboration of alternative optimal patterns according to priorities which differ from normal subjects because of the underlying cerebral problem [9]. Similarly, the strategy used by our patient before the baclofen injection may represent a functional adaptation to his neurologic impairment. It has some common features with that described in spastic diplegia, mainly the non-specific muscle co-contraction, the dynamical locking of the ankle joint and the global (non-selective) execution of the movement. These features reflect exaggerated monosynaptic stretch reflexes whose effects add to those of reduced facilitation of polysynaptic reflexes which are also dependent on supraspinal control [6]. Intrathecal baclofen has been shown to increase the threshold of these polysynaptic reflexes [17]. Indeed, two hours after baclofen injection, the co-contraction pattern disappeared, replaced by a reciprocal pattern. Moreover, an anticipatory deactivation of the hamstring muscles occurred before the onset of the movement. This reflects a feed-forward mode of motor control, as that demonstrated for normal subjects [4, 5]. This further supports the hypothesis that this early inhibition is elaborated supraspinally in the motor cortex, as recently demonstrated in animal studies [7]. In this view, the emergence of the normal strategy would be essentially facilitated by pharmacologic inhibition of spinal reflexes, as expected from the low cisternal-to-lumbar ratio of baclofen obtained with lumbar injection [14]. However, continuing refinement of kinetics and kinematics is relatively slower than that of muscle patterns, becoming very close to normal six hours after baclofen injection [4]. This delay probably represents a process of adaptation to the changed system. This single case study illustrates that intrathecal baclofen can restore some normal movement patterns in FSP by decreasing spasticity.

Figure 3. Knee angular velocity and muscle activities during the squatting movement. (A) Before intrathecal baclofen injection, and (B) two hours after the injection. Electromyographic signals are rectified. K: knee angular velocity; RA: rectus anterior muscle; VL: vastus lateralis muscle; BF: biceps femoris muscle; SM: semimembranous muscle; TA: tibialis anterior muscle; LG: lateral gastrocnemius muscle; MG: medial gastrocnemius muscle; SOL: soleus muscle. The onset of movement is indexed by a vertical striped line. The striped line superimposed on the knee velocity profile joins the onset of movement and the velocity peak. The arrows mark the onset of the anticipatory deactivation of the hamstring muscles. The black star indexes the reciprocal pattern.

aged three to 12 years [5]. A distinct but consistent motor strategy for the squatting movement has been described in spastic diplegia [5]. It combines undisso-

ACKNOWLEDGEMENTS

REFERENCES

1 Ashworth B. Preliminary trial of carisoprodol in multiple sclerosis. Practitioner 1964 ; 192 : 540-2.

2 Azouvi P, Mane M, Thiebaut JP, Denys P, Rémy-Néris O, Bussel B. Intrathecal baclofen administration for control of severe spinal spasticity: functional improvement and long-term follow-up. Arch Phys Med Rehabil 1996 ; 77 : 35-9.

3 Bowery NG, Hill DR, Hudson AL, Doble A, Middlemiss DN, Shaw J, et al. Baclofen decreases neurotransmitter release in the mammalian CNS by an action at a novel GABA receptor. Nature 1980 ; 283 : 92-4.

4 Cheron G, Bengoetxea A, Pozzo T, Bourgeois M, Draye JP. Evidence of a preprogrammed deactivation of the hamstring muscles for triggering rapid changes of posture in humans. Electroencephalogr Clin Neurophysiol 1997 ; 105 : 58-71.

5 Dan B, Bouillot E, Bengoetxea A, Noël P, Kahn A, Cheron G. Adaptive motor strategy for squatting in spastic diplegia. Eur J Paediatr Neurol 1999 ; 3 : 159-65.

6 Dietz V. Human neuronal control of automatic functional movements: interaction between central programs and afferent input. Physiol Rev 1992 ; 72 : 33-69.

7 Hoffman DS, Strick PL. Effects of a primary motor cortex lesion on step-tracking movements of the wrist. J Neurophysiol 1995 ; 73 : 891-5.

8 Latash ML, Penn RD, Corcos DM, Gottlieb GL. Effects of intrathecal baclofen on voluntary motor control in spastic paresis. J Neurosurg 1990 ; 72 : 388-92.

9 Latash ML, Anson JG. What are anormal movements in atypical populations? Behav Brain Sciences 1996 ; 19 : 55-68.

10 Latash ML, Penn RD. Changes in voluntary motor control induced by intrathecal baclofen in patients with spasticity of different etiology. Physiother Res Int 1996 ; 1 : 229-46.

11 Landau WM. Spasticity: the fable of a neurological demon and the emperor's new therapy [editorial]. Arch Neurol 1974 ; 31 : 217-9.

12 Loubser PG, Narayan RK, Sandin KJ, Donovan WH, Russell KD. Continuous infusion of intrathecal baclofen: long-term effects on spasticity in spinal cord injury. Paraplegia 1991 ; 29 : 48-64.

13 Meythaler JM, Steers WD, Tuel SM, Cross LL, Sesco DC, Haworth CS. Intrathecal baclofen in hereditary spastic paraparesis. Arch Phys Med Rehabil 1992 ; 73 : 794-7.

14 Müller H, Zierski J, Dralle D. Pharmacokinetics of intrathecal baclofen. In: Müller H, Zierski J, Penn RD, eds. Local-Spinal Therapy of Spasticity. New York: Springer-Verlag; 1988. p. 223-6.

15 Ochs G, Struppler A, Meyerson BA, Linderoth B, Gybels J, Gardner BP, et al. Intrathecal baclofen for long-term treatment of spasticity: a multi-centre study. Neurol Neurosurg Psychiatry 1989 ; 52 : 933-9.

16 Ordia JI, Fischer E, Adamski E, Spatz EL. Chronic intrathecal delivery of baclofen by a programmable pump for the treatment of severe spasticity. J Neurosurg 1996 ; 85 : 452-7.

17 Parise M, Garcia-Larrea L, Mertens P, Sindou M, Mauguière F. Clinical use of polysynaptic flexion reflexes in the management of spasticity with intrathecal baclofen. Electroencephalogr Clin Neurophysiol 1997 ; 27 : 141-8.

18 Parke B, Penn RD, Savoy SM, Corcos D. Functional outcome after delivery of intrathecal baclofen. Arch Phys Med Rehabil 1989 ; 70 : 30-2.

19 Saltuari L, Kronenberg M, Marosi MJ, Kofler M, Russegger L, Rifici C, et al. Indication, efficiency and complications of intrathecal pump supported baclofen treatment in spinal spasticity. Acta Neurol 1992 ; 14 : 187-94.