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Short Topics

1．歩行の中枢とCPG

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KEY WORD

歩行中枢
脊髄
CPG
可塑性
リハビリテーション

POINT

- ヒトの脊髄にも歩行のための基本的運動出力を生成する神経機構が存在する．この脊髄神経機構は四足動物などで同定されているパターン発生器(CPG)と共通する性質を有する．
- ヒトのCPGもおそらく脊髄に広範に分布する神経回路からなり，その出力は求心性入力，CPGには可塑性な性質があり，時空間的にパターン化した入力を継続的に受けとることにより，入出力特性が変化する．

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はじめに

人間にとって立位歩行は最も基本的な身体運動の1つである．しかし，これを成立させる神経機序はまだまだ多くのなぞに満ちている．1900年代初頭からめざましい発展を遂げた神経生理学研究によって，ネコなど四足動物の歩行を発現させる神経機序はかなりの部分が明らかになった．

しかしながら，人間の立位歩行がどこまで四足歩行と共通で，どこからどの程度異なるのか，これに関わる問題はほとんど未解決といっても過言ではない．このことは，ヒトを対象とした実験で得られた結果を動物モデルを用いて確認するという生理学研究の正当な手法が，人間固有の機能の研究には適用困難であるという限界に起因する．この限界は依然として付きまとうものの，近年の経頭蓋磁気刺激や神経活動の画像化技術を用いた研究は非侵襲的に人間の神経活動を評価する新たな道を開いたし，脊髄損傷者を対象とした脊髄のパターン発生機構の研究は，臨床的成果を契機として基礎的側面の研究も加速させるに至った．

本稿では，特に近年飛躍的に進展した人間の脊髄歩行パターン発生機構に関わる研究成果についてまとめてみたい．

ロコモーションパターンを生成する神経機構

歩行に関与する神経機構をRossignol[1]，Orlovskyら[2]のモデルを基に図1にまとめた．高位中枢で決定された歩行開始の司令は中脳歩行誘発野など脳幹の歩行中枢を賦括し，最終的に脊髄へと伝達される．そこから時空間的にパ

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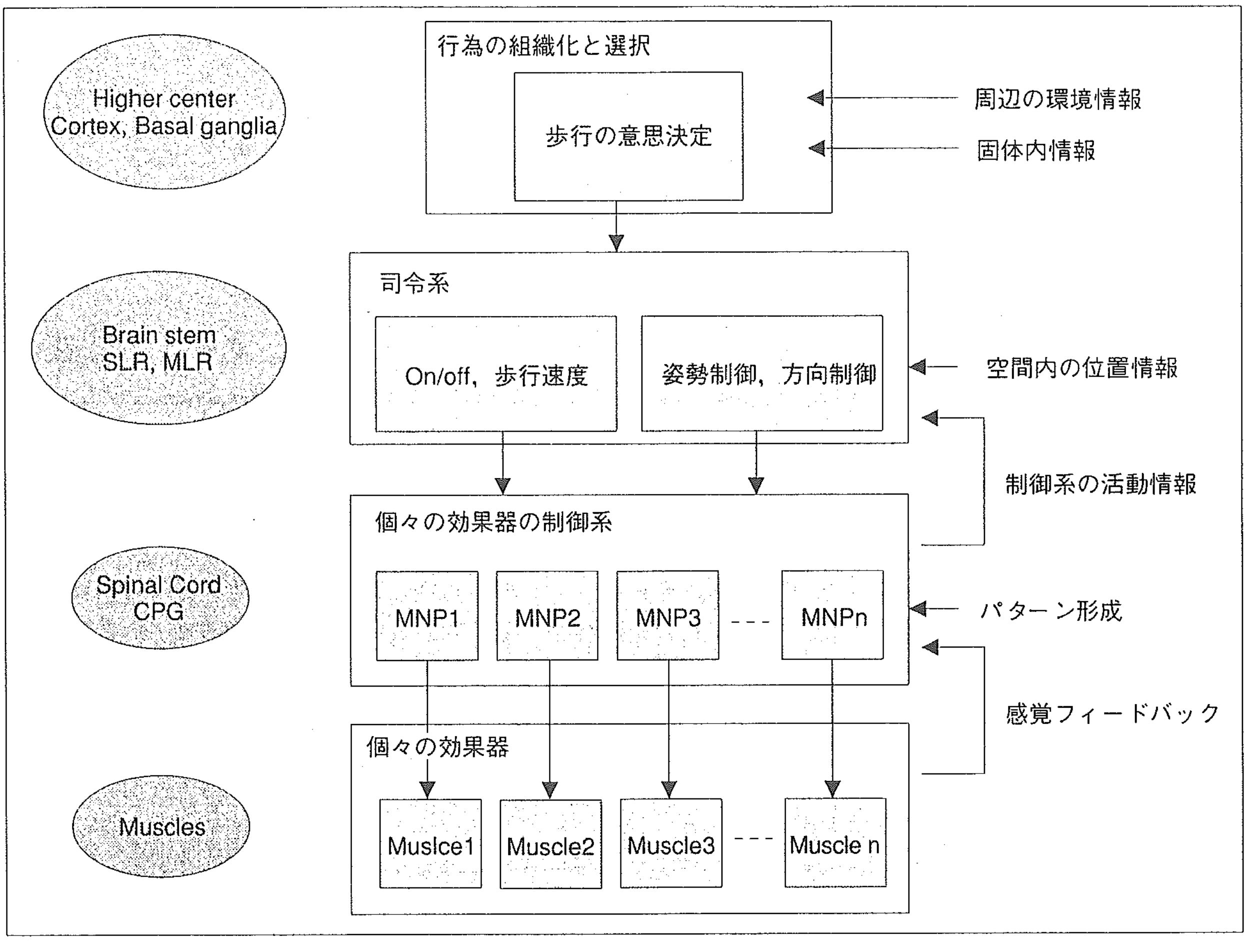

図1　歩行開始に関与する神経機構

Rossignol[1]，Orlovskyら[2]のモデルを基に作成．図中SLR：subthalamic locomotor region，MLR：mesencephalic locomotor region，CPG：central pattern generator，MNP：motoneuron pool.

ターン化した運動出力が筋へと送られる．この時空間的にパターン化した運動出力を生成する神経機構が，いわゆる脊髄セントラルパターンジェネレーター(central pattern generator；CPG)である．CPGの構造と機能は系統発生学上下等生物である軟体類から高等な哺乳類まで広範にわたって研究されており，本質的な性質はヒトに至るまで共通すると考えられている[2]．しかしながら，脊髄からの歩行出力の自律性は霊長類では四足動物などに比べてかなり低く，それは霊長類において皮質脊髄路の重要性が増大することと関係があると考えられている[3]．

ヒトの脊髄CPG

四足動物やその他の下等生物の移動運動がCPG的な神経回路に大きく依存していることは疑いない．しかしヒトでの研究はまだまだその数も少なく，脊髄CPGの存在自体を示唆する間接的証拠が最近になって多く報告されるようになったにすぎない．とはいえ，いわゆる乳幼児の足ふみ反射(newborn stepping)などの現象は昔から知られており，CPGの原型が生得的に備わっていることを示唆する現象と考えられている．最近，Yangらのグループは乳幼児の原始歩行について系統的に研究しており，ネコなど四足動物で確認されている荷重や股関節からの求心性入力とCPGの相互作用が乳幼児にもあてはまることなどを報告している[4]．

冒頭でも述べたように，ヒトの脊髄CPGに関する研究の近年の進展は脊髄損傷者の歩行リハビリテーションの臨床的研究の発展と関連し

ている．1990年代初頭のRossignolのグループ，Edgertonのグループによる脊髄ネコの実験成績から，トレッドミルを用いたステッピングトレーニングによって歩行機能が従来考えられていた以上に回復することが示された[5,6]．それらをきっかけに脊髄損傷者をトレッドミル上で他動的にステッピングさせる“免荷式ステッピングトレーニング”が人間でも行われるようになったのである．他動的ステッピングによって，たとえ麻痺領域の随意筋収縮が全くみられない完全対麻痺者であっても，ステッピング周期にあった歩行様の筋活動が誘発されることが明らかとなった[7,8,11,12]．さらに，誘発される歩行様筋活動はステッピング時に下肢に加わる荷重や股関節からの求心性入力に強く依存することが示され[13,14]，その点でネコなど四足動物のCPGの性質と合致した．

このように，対麻痺者のステッピングトレーニングはヒトの脊髄CPGの存在と性質に関わる研究の発展と切っても切れない関係にあるが，CPGの存在を示唆する現象の報告自体はもう少し遡ることができる．Busselらは既に1980年代の後半に対麻痺者のミオクローヌスとFRA(flexor reflex afferents)刺激の関係などを記録し，CPGの存在を示唆していたし(Busselら[15,16]，Calancieら[17]も対麻痺者の不随意性ステッピング運動を詳細に記録し，それが脊髄CPGからの出力である可能性がきわめて高いことを主張した．近年ではDimitrijevicのグループが対麻痺者の痙性治療に用いる脊髄硬膜外電気刺激を応用し，CPGの存在をより直接的方法に近いかたちで示している[10]．彼らは近年の報告[18]で，対麻痺者の脊髄に対し，硬膜外で一定強度の電気刺激を種々の周波数で与え，脊髄からの運動出力との関係を示している(図2)．それによると，臨床的完全対麻痺者5名の脊髄腰膨大部近辺を5～15Hzで刺激すると下肢の伸筋群に放電が誘発され，下肢全体を突っ張るような運動が出現したのに対し，それより高い周波数(25～50Hz)で刺激するとステッピングに似た動きが誘発されたという．これらの結果は，脊髄内の神経回路に末梢入力との相互作用によって異なる運動を生成する機能ユニットが存在することを示唆すると解釈されている．さらにGurfinkelら[19]は健常者において，下肢の筋あるいは腱への振動刺激でステッピングが誘発可能であることを示し，やはり求心性入力のみで脊髄からパターン化した出力が誘発可能なことを示した．

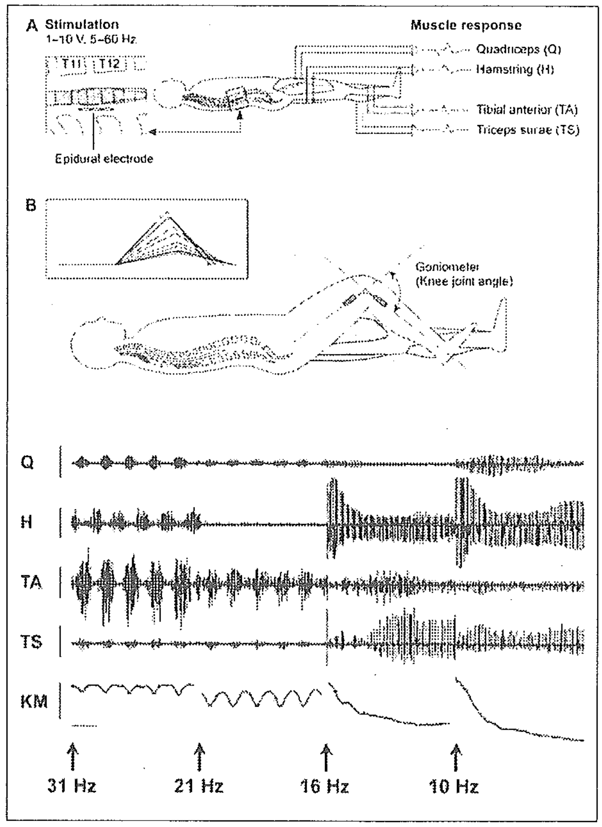

図2　Jilgeら[18]の脊髄硬膜外刺激の様子と，記録された脊髄からの運動出力と刺激周波数との関係(文献18を筆者改変)

ヒトCPGの性質

1．損傷高位と歩行様筋活動

Dietzら[9]は上行性入力によって歩行様の筋出力を発生する脊髄内の神経機構が脊髄内のいずれかの髄節に限局しているのか，それとも脊髄内に広く分布しているのかを明らかにするために，下降性入力が遮断されている完全対麻痺者のみを対象に，脊髄の損傷高位と他動的ステッピングで誘発される歩行様筋活動の強度および波形の関係を分析した．両筋の立脚相，遊脚

相それぞれの放電量と損傷高位との関係は，総じて損傷高位が高い損傷者の方が筋放電量が大きい傾向が，ヒラメ筋では立脚相，前脛骨筋では遊脚相でそれぞれ観察された．両筋は健常者においてこれらの歩行位相で活動することから，損傷高位が高い損傷者の歩行時筋活動の方が健常者に近いことが判明した．さらに筋放電波形の類似度を示す指標でも，全体的に損傷高位の高い損傷者の方が健常者のパターンに近いことが示された．Dietz らは，これらの結果は末梢入力によって歩行様筋活動を発生する神経機構が脊髄のある髄節に限局して存在するのではなく，脊髄内広範にわたって分布していることを示唆するものであり，ムッドパピー[注1]で示された結果[20]に一致するとした．

2．感覚入力との相互作用

Dietz のグループは近年，歩行トレーニングロボット(Lokomat, Hokoma 社，スイス)を開発し[21]，それを使った実験で，脊髄からの歩行様出力にとって股関節と荷重関連受容器(load receptor)からの入力が必須であることを明らかにした．筆者らのグループは，さらに立位で股関節の屈曲・伸展動作が可能な特殊な装置(Easystander, Ultimate 社，USA)を用い，対側からの求心性入力は左右脚が交互に動くときのみ脊髄からの歩行様出力に促通性の効果をもつことを明らかにした[22](図3)．すなわち，歩行様出力を生成する脊髄神経回路には対側からの交叉性経路も含まれており，しかもその経路を介する求心性入力はある位相でのみ促通性となる位相依存性があるらしい．

3．上肢と下肢の協調

近年この分野において注目を集めているのは，上肢と下肢の CPG の連関である．

Zehr のグループは上肢の周期的運動時には H-反射や皮膚反射が位相依存性および課題依存性に修飾されることを観察し，そのような性質は CPG の参画に起因するとした[23, 25]．

上肢 CPG と下肢 CPG の結合に関してもいくつか興味深い報告がなされている．手関節屈筋の H-反射を誘発する際に下肢の周期的な底背屈運動を付加すると，それに応じて H-反射の振幅が変調され[26]，それは脊髄頸膨大部と腰膨大部間を結合する固有ニューロンを介すると考えられる[27]．また，片側下肢への電気あるいは機械的刺激を歩行中に加えると両側上肢筋に応答が誘発されるが，立位時や他の運動課題中には誘発されないことから，上肢と下肢運動ニューロン間の結合は課題依存性に変調し，それぞれの CPG の活動が関係すると考えられている[28]．

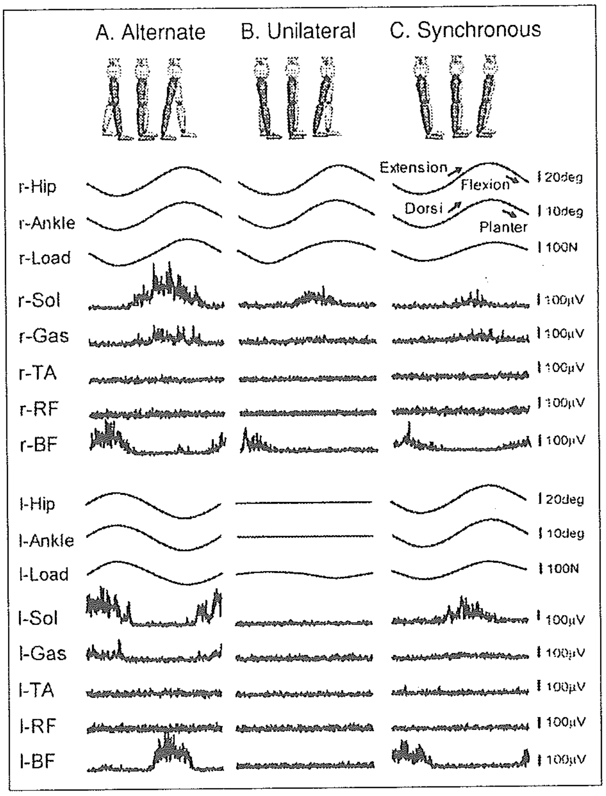

図3　左側脚の動作を変えたときの右側脚他動運動で誘発される歩行様筋活動の変化

左側下肢が交互性(alternate)，同側のみ(unilateral)，左右同位相(synchronous)で他動的に動かされた時の左右下腿筋電図と股関節，足関節の各関節角度，足部荷重の加算平均波形を表示．図中，Hip，股関節角度；Ankle，足関節角度；Load，足部荷重；Sol，ヒラメ筋；Gas，腓腹筋；TA，前脛骨筋；RF，大腿直筋；BF，大腿二頭筋．r-は右側，l-は左側を表す．

注1　Mudpuppy あるいは Waterdog．イモリの仲間．両生類

4．CPGの可塑性

従来，脊髄神経機構に可塑的な性質はないと考えられてきたが，近年脊髄の可塑性を示す実験結果が次々に報告されるようになり，そのような考え方は覆されつつある[29,30]．特に，脊髄および他の中枢神経系の use-dependent または activity-dependent な可塑性は，これからのニューロリハビリテーションの理論的枠組みにおいて重要な位置を占めるであろう．これまで，動物の実験成績に比べて，ヒトを対象とした研究報告はまだまだ少ない．主に脊髄損傷によって脳との結合が遮断された条件下で他動的トレーニングを介入し，その結果生じる脊髄神経回路の入出力関係の変化が，use-dependent な可塑性を表す現象ととらえられている．筆者らのグループも，歩行用の装具を用いたトレーニング後に完全対麻痺者の歩行用筋活動が増強する現象を観察しており[31]，CPG を含む脊髄神経回路の入出力関係が可塑的に変化したことを反映すると考えている．

まとめ

本稿では，主に人間の脊髄歩行パターン発生機構に関わる近年の研究成果を概観した．ヒトの二足歩行あるいは直立姿勢の制御機構自体まだまだ不明な点が多く，学術的に興味深い問題を数多く含んでいる．それらの問題は同時にリハビリテーションなどの臨床にも直結する課題であり，今後両面での研究が加速することが望まれる．

文　献

1) Rossignol S：Neural control of stereotypic limb movements. In：Handbook of Physiology, Sec12, Exercise：Regulation and integration of multiple systems(eds by Rowell LB and Shepherd JT), Oxford University Press, New York, 1996.
2) Orlovsky GN, Deliagina TG and Grillner S：Neural control of locomotion —from Mollusc to Man—. Oxford University Press, New York, 1999.
3) Vilensky JA and O'Connor BL：Stepping in non-human primates with a complete spinal cord transection：old and new data, and implications for humans(review). Ann NY Acad Sci 860：528-530, 1998.
4) Pang MY and Yang JF：The initiation of the swing phase in human infant stepping：importance of hip position and leg loading. J Physiol(Lond) 528：389-404, 2000.
5) Barbeau H and Rossignol S：Enhancement of locomotor recovery following spinal cord injury. Curr Opin Neurol 7：517-524, 1994.
6) Lovery RG, Gregor R, Roy RR et al：Weight-bearing hindlimb stepping in treadmill-exercised adult spinal cats. Brain Res 514：206-218, 1990.
7) Dietz V, Colombo G and Jensen L：Locomotor activity in spinal man. Lancet 344：1260-1263, 1994.
8) Dietz V, Colombo G, Jensen L et al：Locomotor capacity of spinal cord in paraplegic patients. Ann Neurol 37：574-582, 1995.
9) Dietz V, Nakazawa K, Wirz M et al：Level of spinal cord lesion determines locomotor activity in spinal man. Exp Brain Res 128：405-409, 1999.
10) Dimitrijevic MR, Gerasimenko Y and Pinter MM：Evidence for a spinal central pattern generator in humans. Ann NY Acad Sci 860：360-376, 1998.
11) Dobkin BH, Harkema SJ, Requejo PS et al：Modulation of locomotor-like EMG activity in subjects with complete and incomplete spinal cord injury. J Neurol Rehabil 9：183-190, 1995.
12) Kojima N, Nakazawa K, Yamamoto S-I et al：Phase-dependent electromyographic activity of the lower-limb muscles of a patient with clinically complete spinal cord injury during orthotic gait. Exp Brain Res 120：139-142, 1998.
13) Kojima N, Nakazawa K and Yano H：Effects of limb loading on the lower-limb EMG activity during orthotic locomotion in a paraplegic patient. Neurosci Lett 274(3)：211-213, 1999.
14) Harkema SJ, Hurley SL, Patel UK et al：Human lumbosacral spinal cord interprets loading during stepping. J Neurophysiol 77：797-811, 1997.
15) Bussel B, Roby-Brami A, Azouvi P et al：Myoclonus in a patient with spinal cord transection. Possible involvement of the spinal stepping generator. Brain 11：1235-1245, 1988.
16) Bussel B, Roby-Brami A, Yakovleff A et al：Late flexion reflex in paraplegic patients.

Evidence for a spinal stepping generator. Brain Res Bull 22 : 53-56, 1989.
17) Calancie B, Needham-Shropshire B, Jacobs P et al : Involuntary stepping after chronic spinal cord injury. Evidence for a central rhythm generator for locomotion in man. Brain 117 : 1143-1159, 1994.
18) Jilge B, Minassian K, Rattay F et al : Initiating extension of the lower limbs in subjects with complete spinal cord injury by epidural lumbar cord stimulation. Exp Brain Res 154 : 308-326, 2004.
19) Gurfinkel VS, Levik Yu S, Kazennikov OV et al : Locomotor-like movements evoked by leg muscle vibration in humans. Eur J Neurosci 10 : 1608-1612, 1998.
20) Cheng J, Stein R, Jovankovic K et al : Identification, localization and modulation of neural networks for walking in the mudpuppy (Necturus maculatus) spinal cord. J Neurosci 18 : 4295-4304, 1998.
21) Colombo G, Wirz M and Dietz V : Driven gait orthosis for improvement of locomotor training in paraplegic patients. Spinal Cord 39 : 252-255, 2001.
22) Kawashima N, Nozaki D, Abe MO et al : Alternate leg movement amplifies locomotor-like muscle activity in spinal cord injured persons. J Neurophysiol [Epub ahead of print] 2004 Sep 22.
23) Zehr EP, Collins DF, Frigon A et al : Neural control of rhythmic human arm movement : phase dependence and task modulation of hoffmann reflexes in forearm muscles. J Neurophysiol 89(1) : 12-21, 2003.
24) Zehr EP and Haridas C : Modulation of cutaneous reflexes in arm muscles during walking : further evidence of similar control mechanisms for rhythmic human arm and leg movements. Exp Brain Res 149(2) : 260-266, 2003.
25) Zehr EP and Kido A : Neural control of rhythmic, cyclical human arm movement : task dependency, nerve specificity and phase modulation of cutaneous reflexes. J Physiol 537 (Pt 3) : 1033-1045, 2001.
26) Cerri G, Borroni P and Baldissera F : Cyclic h-reflex modulation in resting forearm related to contractions of foot movers, not to foot movement. J Neurophysiol 90(1) : 81-88, 2003.
27) Dietz V : Spinal cord pattern generators for locomotion. Clin Neurophysiol 114(8) : 1379-1389, 2003.
28) Dietz V et al : Neuronal co-ordination of arm and leg movements during human locomotion. Eur J Neurosci 14 : 1906-1914, 2001.
29) Raineteau O and Schwab ME : Plasticity of motor systems after incomplete spinal cord injury. Nature Rev 2 : 263-273, 2001.
30) Muir GD and Steeves JD : Sensorimotor stimulation to improve locomotor recovery after spinal cord injury. TINS 20 : 72-77, 1997.
31) Nakazawa K, Kawashima N, Kakihana W et al : Induction of locomotor-like EMG activity in paraplegic persons by orthotic gait training. Exp Brain Res, 157(1) : 117-123, 2004.

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ORIGINAL ARTICLE

Enhanced Stretch Reflex Excitability of the Soleus Muscle in Persons With Incomplete Rather Than Complete Chronic Spinal Cord Injury

Kimitaka Nakazawa, PhD, Noritaka Kawashima, MSc, Masami Akai, MD

ABSTRACT. Nakazawa K, Kawashima N, Akai M. Enhanced stretch reflex excitability of the soleus muscle in persons with incomplete rather than complete chronic spinal cord injury. Arch Phys Med Rehabil 2006;87:71-5.

Objective: To compare excitabilities of spinal stretch reflex among clinically complete spinal cord injury (SCI), incomplete SCI, elderly healthy, and young healthy subjects.

Design: Case comparison.

Setting: Research laboratory.

Participants: Volunteer sample of 12 complete SCI, 10 incomplete SCI, 10 elderly, and 11 young subjects.

Intervention: Mechanically induced stretch reflex, H-reflex, and M response in electromyographic activity of the soleus muscle were recorded in all subjects.

Main Outcome Measures: Absolute peak-to-peak stretch reflex amplitude and maximum H-reflex (Hmax), and those values relative to the maximum M response (Mmax) amplitude (relative peak-to-peak stretch reflex amplitude) and H/M ratio.

Results: Both the absolute and relative peak-to-peak stretch reflex amplitudes showed the greatest values in incomplete SCI among the 4 groups. Although absolute and relative peak-to-peak stretch reflex amplitudes of the incomplete SCI group were greater than those of the complete SCI group, the H/M ratios of both groups were comparable, and were greater than those of the younger and elderly groups.

Conclusions: The results suggest that the greater absolute and relative peak-to-peak stretch reflex amplitudes of incomplete SCI were mostly due to the greater maximum motor potential (Mmax), while the elevated spinal motoneuronal excitability shown by the increased H/M ratio was maintained in the chronic stage after both complete and incomplete SCIs.

Key Words: Reflex, stretch; Rehabilitation; Spinal cord injuries.

AFTER SPINAL CORD INJURY (SCI), reorganization occurs both below and above the lesion sites in the central nervous system (CNS). This reorganization can be facilitated and directed toward functional recovery by imposed activity of paralyzed limbs, especially in cases of incomplete spinal cord lesions.[1] Therefore, learning more about the neuronal reorganization after SCI prepares the way for a better understanding of rehabilitation strategies and for the development of new approaches to restore functional movements in people with SCI.

The spinal stretch reflex is the simplest behavior of the vertebrate CNS. Many studies have attempted to elucidate the effects of SCI on stretch reflex responses in humans, because the stretch reflex excitability of lower-limb muscles is believed to strongly relate to typical physiologic symptoms such as spinal shock or spastic paralysis after injury.[2-12] It is generally accepted that SCI in humans and animals is followed by a spinal shock period with the loss of tendon tap reflexes and flaccid muscle tone. Several weeks to months after SCI, a "spastic syndrome" develops with exaggerated tendon reflexes, increased muscle tone, and muscle spasm.[9] Recently, however, Calancie et al[13] reported that the loss of tendon reflex was not observed even at the acute stage after incomplete SCI, whereas it was commonly observed in people with motor-complete injuries. In addition, while taps to the right patellar tendon elicited electromyographic responses in both the ipsilateral quadriceps muscle and in the contralateral thigh muscles (crossed-adductor response), specifically in most motor-incomplete SCIs, the response was never seen in the motor-complete SCIs. Thus, reorganization of stretch reflex responses after SCI seems to differ between motor-complete and incomplete injuries. The extent to which the reorganization process depends on the severity of SCI in humans is unknown.

In this study, we compared the spinal stretch reflex excitabilities among 4 groups: clinically complete SCI, incomplete SCI, elderly healthy, and young healthy subjects.

METHODS

Participants

Twelve clinically motor-complete and 10 motor-incomplete subjects with SCI participated in the experiment, along with 10 elderly and 11 younger healthy controls. Table 1 summarizes their physical characteristics. All SCI subjects were at least 12 months postinjury and none had taken any antispasticity medication for at least 6 months before the testing. The subjects gave written informed consent to the experimental procedures, which were approved by the ethics committee of Japan's National Rehabilitation Center for Persons with Disabilities, Japan.

Experiments

We recorded mechanically induced stretch reflex electromyographic responses, H-reflexes, and M responses from the right soleus muscles of all subjects.

Stretch Reflex Test

We used a specially designed machine[a] (fig 1) to elicit stretch reflex responses in the soleus muscle with subjects in a

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Table 1: Physical Characteristics of All Subjects

Subject*†	Age	Sex	Level Lesion	ASIA Grade	Time Since Injury (mo)
a	53	F	C8	D	475
b	66	M	C3	C	38
c	63	M	C6	D	223
d	52	M	C7	D	90
e	52	M	C5	D	438
f	45	M	C4	C	17
g	44	M	C4	D	15
h	32	M	C4	D	14
i	42	M	T12	C	12
j	30	M	T12	D	19
k	22	M	T8	A	19
l	28	M	T8	A	15
m	30	M	C7	B	54
n	32	F	C8	B	135
o	41	F	C7	B	297
p	35	M	C7	A	160
q	20	M	T4	B	28
r	48	M	T12	A	27
s	30	M	C6	A	45
t	20	M	C6	A	23
u	30	M	T11	A	12
v	27	M	T12	A	16

Abbreviations: ASIA, American Spinal Injury Association; F, female; M, male.
*Elderly (8 men, 2 women; mean age ± standard deviation [SD], 62.5±3.2y).
†Younger (8 men, 3 women; mean age ± SD, 25.7±5.2y).

sitting position. This machine can apply quick rotations at ankle joints in various postures, from standing upright to sitting. In this study, we induced stretch reflexes in the plantarflexor muscles as subjects sat with the hip and knee angles fixed at 70° and 60° (anatomic position is 0°), respectively. Subjects were seated comfortably in the machine with the right leg fixed to a footplate connected to a servo-controlled torque motor, which could generate quick rotations of the plates at various velocities and amplitudes with commands from a computer. We adjusted the axis of rotation of the footplate to the center of the ankle joint. To elicit stretch reflexes in the soleus muscle, the machine provided quick stretch stimuli to the ankle joint in the dorsiflexion direction at an angular velocity of approximately 400°/s; this stretch was repeated 5 times, with an interstimulus interval of 10 seconds.

For the electromyographic recording, we used bipolar Ag-AgCl surface electrodes (diameter, 7mm) placed 2cm distal to the endpoint of the medial head of the gastrocnemius muscle, with an interelectrode distance (center to center) of 15mm. A conventional bioamplifier[b] amplified and band-pass filtered (low-high cut, 20–1kHz) the electromyographic signals. The electromyographic, torque, and angle signals were all digitized at a sampling rate of 1kHz and stored for later analysis.

H-Reflex and M-Response Test

We elicited the H-reflexes and M responses in the soleus muscle by applying rectangular pulses of 1-ms duration to the posterior tibial nerve in the popliteal fossa with a constant voltage stimulator.[c] The postural condition was identical to that in the stretch reflex test, with the subjects sitting in the same machine. On the basis of the threshold intensity of the H-reflex, we increased the stimulus intensity from a level sufficiently below the threshold intensity until the M response reached a plateau; the same intensity was repeated 5 times. The sampling frequency for electromyographic signals and pulses were 5kHz.

Data Analysis

For the stretch reflex electromyographic response, we defined the background electromyographic level over 100ms before the onset of the ankle joint stretch, and the onset of the stretch reflex response as the moment when the electromyographic activity levels reached levels higher than the mean background electromyographic level plus 3 times its standard deviation. The stretch reflex electromyographic response was defined as the peak-to-peak electromyographic amplitude for 30ms after the onset of the stretch reflex electromyographic response.

For the H and M waves, we evaluated peak-to-peak values within time windows from 30 to 50ms and from 5 to 25ms after the electric stimulation, respectively. From the H-M recruitment curve, we determined the maximum H-reflex, M response, and H/M ratio for each subject.

Statistical Test

We used analysis of variance (ANOVA) with a post hoc test (Scheffé) to test for statistically significant differences in stretch reflex electromyographic responses, H-reflexes, and M responses among the 4 subject groups. Data are presented as the mean and standard error of the mean (SEM). Significance was accepted at P less than .05.

RESULTS

Stretch Reflex

Figure 1 illustrates a typical example of the stretch reflex electromyographic response. Typically, single twitch-like bursts appeared in electromyographic activity after mechanical stretches to the soleus muscle. We evaluated the peak-to-peak amplitudes of reflex electromyographic responses both as absolute values and as values relative to the maximum motor potential (Mmax) obtained in the H-reflex and M response tests. The mean latency of the reflex electromyographic response ± SEM was 47.22±0.73ms from the stretch onset, indicating that the responses were short-latency spinally mediated reflexes. Figure 2A compares the stretch reflex amplitudes among the different subject groups. The ANOVA comparison

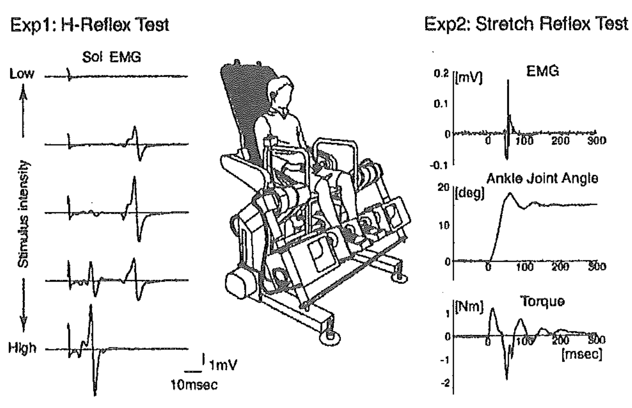

Fig 1. The machine used in both the stretch reflex and H-reflex experiments, and representative raw electromyograms (EMGs), joint angles, and torque signal waveforms in both tests. Abbreviations: Exp1, experiment 1; Exp2, experiment 2; Sol, soleus.

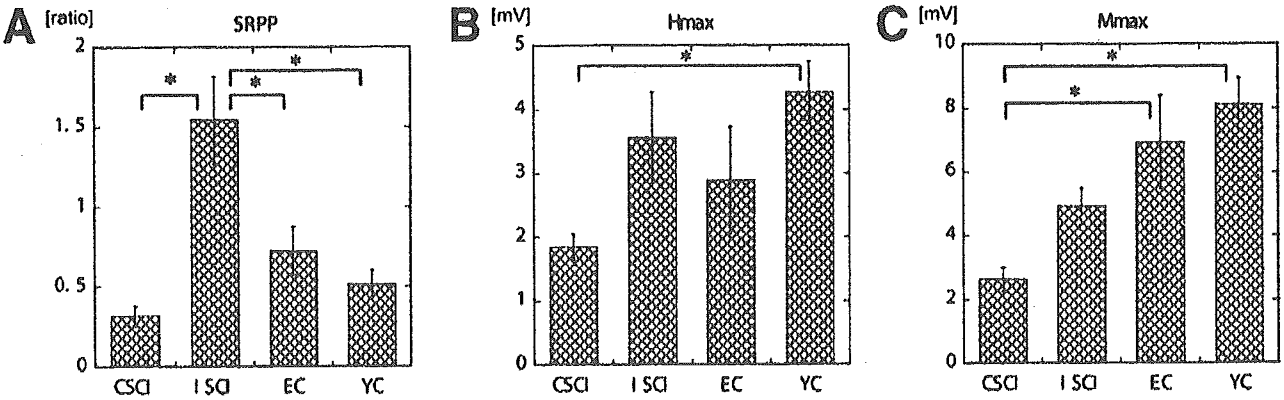

Fig 2. Summary of absolute peak-to-peak reflex electromyographic amplitude (SRPP), absolute Hmax value, and Mmax of each subject group. Bar heights show mean and error bars represent the SEM. ANOVA indicated there were statistically significant intergroup differences in the absolute reflex electromyographic amplitude, Hmax, and Mmax. Abbreviations: CSCI, complete spinal cord injury; EC, elderly healthy subjects; ISCI, incomplete spinal cord injury; YC, young health subjects. *Significant between-group differences revealed by Scheffé post hoc comparison (*P*<.05).

showed that there were statistically significant differences in the group means of the stretch reflex amplitudes among the 4 groups ($F=12.735$, $P<.05$). Scheffé post hoc multiple comparisons further revealed that the stretch reflex of the incomplete SCI group was significantly greater ($P<.05$) than those of the other groups, indicating that the absolute reflex electromyographic amplitude was the greatest in the motor-incomplete SCI group.

Maximum H-Reflex Amplitude

Figure 1 shows typical examples of H-reflex and M response. The mean latencies of H-reflex and M responses ± SEM were 11.52±0.15ms and 30.83±0.50ms, respectively.

The maximum H-reflex amplitude (Hmax) differed significantly among the groups ($F=3.653$, $P<.05$). The group mean of Hmax was greatest in the young healthy group, whereas the stretch reflex amplitude was greatest in the incomplete SCI group. There was a significant difference in the group means of Hmax between complete SCI and young healthy ($P<.05$).

Maximum Motor Potential

The Mmax differed significantly among the groups ($F=8.843$, $P<.05$; fig 2C). Mmax values were generally larger in the younger and elderly subject groups, indicating greater maximum motor potentials in the non-SCI groups. Statistically, the Mmax of the complete SCI group was significantly smaller than those of the elderly and younger subject groups ($P<.05$).

Relative Stretch Reflex and Hmax Sizes to the Mmax

To test whether the reflex electromyographic response relative to the Mmax is different among the 4 groups, the stretch reflex and Hmax were normalized to the Mmax. Figure 3 summarizes those results. There were still statistically significant differences in the relative sizes of the stretch reflex electromyographic amplitude among the groups ($F=5.900$, $P<.05$), with that of incomplete SCI showing the highest value (see fig 3A). The intergroup relation of the H/M size represented in figure 3B was not identical to that of the stretch reflex (see fig 3A). The H/M ratios were greater in the SCI groups, suggesting an enhanced H-reflex excitability in both the complete and incomplete SCI groups. Statistically, there were significant differences among the group means of the H/M ratio ($F=3.920$, $P<.05$), although the post hoc test indicated no significant differences between any pairs of groups.

Effects of Postinjury Time on Stretch Reflex Excitability

There was substantial variability in postinjury time in the subjects with SCI (see table 1). Therefore we tested whether the postinjury time had a significant influence on the stretch reflex and H-reflex variables.

Figure 4 depicts the relationships between the reflex-related variables and postinjury time for both the complete and incomplete SCI subjects. There were no statistically significant correlations in the relations of the Hmax and Mmax and postinjury time only in the incomplete SCI subjects (Hmax: $r=.723$, $P<.05$; Mmax: $r=.671$, $P<.05$). Both the Hmax and Mmax increased with postinjury time in the incomplete SCI subjects, whereas in the complete SCI group there were no such relations. For the other variables there were no statistically significant relations with postinjury time in the both subject groups.

DISCUSSION

In this study, we compared both mechanically and electrically induced reflex electromyographic responses among 4 different subject groups: complete and incomplete SCI subjects, and elderly and young healthy subjects. The main findings from the intergroup comparisons were: (1) the absolute stretch reflex electromyographic amplitude and its relative value to the Mmax were markedly greater in the incomplete SCI group; and

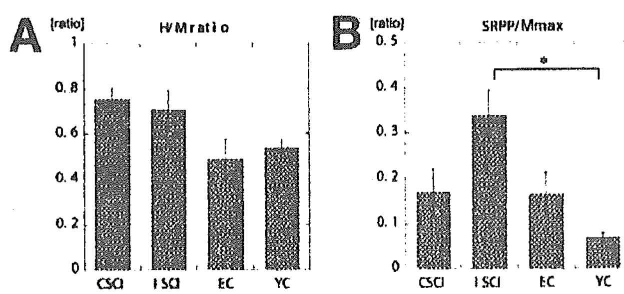

Fig 3. Summary of relative peak-to-peak stretch reflex sizes and H/M ratios for each subject group. Bar heights show mean and error bars represent the SEM. There were statistically significant intergroup differences in the relative peak-to-peak stretch reflex sizes and H/M. *Significant (*P*<.05) between-group differences revealed by Scheffé post hoc comparison (*P*<.05).

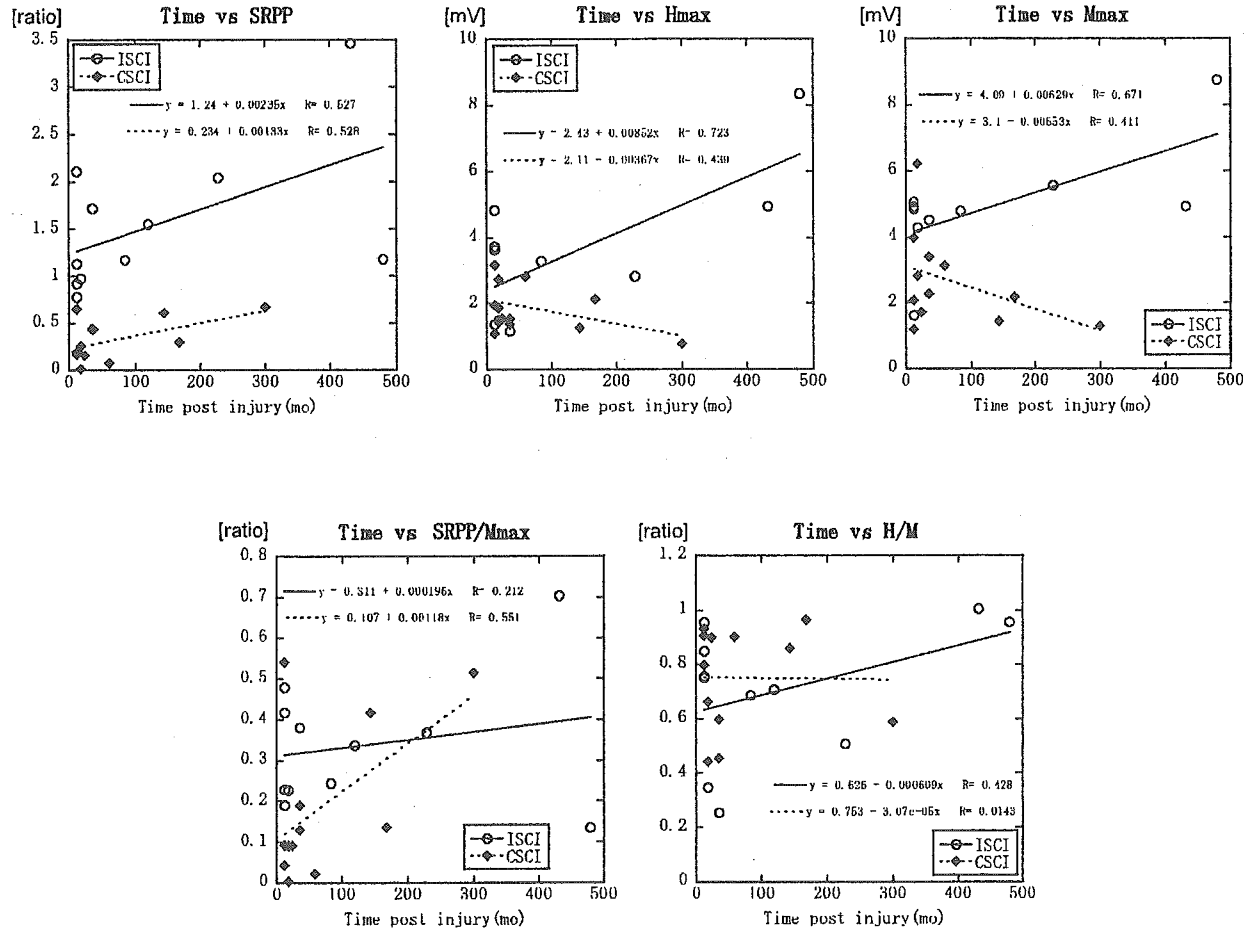

Fig 4. Relations between postinjury time and reflex-related variables evaluated in incomplete SCI and complete SCI subjects. Plots represent individual data from all SCI subjects.

(2) no significant differences were found in the H/M ratios in any pairs of groups, although those of the SCI groups were greater than those of the healthy groups. Possible neural mechanisms explaining the results are discussed below.

H-Reflex Excitability

The H/M ratios of both SCI groups and those of the able-bodied subjects were, respectively, within the ranges of previously reported values.[3,4,7,8,10,14] Noteworthy was that both SCI groups showed comparable values, indicating that at least among those incomplete SCI subjects whose American Spinal Injury Association grades were C and D, H/M ratios did not differ significantly from the ratios of complete SCI subjects. These results suggest that the fraction of motoneurons that can be activated via Ia pathways, which is evaluated using the H/M ratio, is not markedly altered in incomplete SCI subjects as compared with complete SCI subjects. The similarity in H/M ratios between the 2 SCI groups leads us to conclude that the supposed differences in descending inhibitory inputs associated with complete and incomplete spinal cord lesions have no detectable effects on H/M ratios. In other words, the marked differences in motor functions between the complete and incomplete SCI groups were not associated with the difference in H-reflex excitability assessed using H/M ratios.

On the Difference in Stretch Reflex Excitability Between the 2 SCI Groups

The results of mechanically induced stretch reflex indicated that stretch reflex excitability assessed in both absolute and relative terms was markedly enhanced in the incomplete SCI subjects. Also, the relative stretch reflex of the complete SCI subjects was higher than that of the younger subjects, although the difference was not statistically significant. The greater stretch reflex of the motor-incomplete subjects is consistent with the larger muscle responses to patellar and Achilles' tendon taps reported by Calancie et al.[13] They noted that "At a more chronic stage, persons with incomplete SCI tend to have enhanced spinal cord excitability, characterized by frequent spasms, enlarged tendon response amplitude, and recruitment of heteronymous muscles following tendon taps, compared to subjects with complete injury."[13(p2359)] No other study has reported quantitatively the larger stretch reflex responses of incomplete SCI persons.

Why, then, was the mechanically induced stretch reflex more facilitated in the motor-incomplete SCI subjects in this study? Our results alone cannot provide a definitive answer to this question. However, considering reported results, it is possible that differences in descending neural tracts severed[13,15] and/or alteration in mechanical property of muscles and tendons[7,16] are related to the elevated stretch reflex in the motor-incomplete SCI subjects.

In short, lesion of the lateral corticospinal tract is suggested to play a critical role in elevating the reflex excitability of motor-incomplete SCI[13] as a neural factor. As a mechanical factor, alteration in muscles and tendons after SCI also possibly explains the higher stretch reflex in the motor-incomplete SCI subjects. After SCI, a significant amount of muscle atrophy takes place.[16-19] This decrease in muscle fiber size might be more prominent in complete SCI subjects because of disuse, as suggested by the relation between the Mmax size and postinjury time (see fig 4). This hypothesis is supported by the fact that we found no such decrease with postinjury time for the Mmax of incomplete SCI subjects. Together with the H/M result that demonstrated no large difference in reflex excitability at the spinal motoneuron level, it is possible that alteration in the muscle proprioceptors and in the muscle mechanical properties played the major role in the higher relative stretch reflex amplitudes of both SCI groups. The relatively higher stretch reflex and similar H/M ratio of the elderly subjects in comparison with those of the younger subjects also support this idea (see figs 3A, 3B).

CONCLUSIONS

Our results in this study demonstrated that stretch reflex excitability after SCI differed markedly in chronically motor-complete and incomplete SCI subjects. Regardless of the underlying neuronal mechanisms, the difference most probably reflects unique neurologic and histologic reorganization processes taking place after complete or incomplete SCI. Specifically, the elevated reflex excitability in people with incomplete SCI is said to be closely related to their motor recovery with and without training such as unloaded body weight–supported treadmill (BWST) training.[20] Future studies will focus on the effects of sensorimotor interventions such as BWST on the competitive relation between central inputs via spared pathways and peripheral afferents mediated by reflex pathways at spinal motoneurons.

References

1. Raineteau O, Schwab ME. Plasticity of motor systems after incomplete spinal cord injury. Nat Neurosci Rev 2001;2:263-73.
2. Ashby P, Verrier M, Lightfoot E. Segmental reflex pathways in spinal shock and spinal spasticity in man. J Neurol Neurosurg Psychiatry 1974;37:1352-60.
3. Calancie B, Broton J, Klose K, Traad M, Difini J, Ayyar D. Evidence that alterations in presynaptic inhibition contribute to segmental hypo- and hyperexcitability after spinal cord injury in man. Electroencephalogr Clin Neurophysiol 1993;89:177-86.
4. Nielsen J, Petersen N, Ballegaard M, Biering-Sorensen F, Kiehn O. H-reflexes are less depressed following muscle stretch in spastic spinal cord injured patients than in healthy subjects. Exp Brain Res 1993;97:173-6.
5. Taylor S, Ashby P, Verrier M. Neurophysiological changes following traumatic spinal lesions in man. J Neurol Neurosurg Psychiatry 1984;47:1102-8.
6. Schindler-Ivens SM, Shields RK. Low frequency depression of H-reflexes in humans with acute and chronic spinal-cord injury. Exp Brain Res 2000;133:233-41.
7. Schindler-Ivens SM, Shields RK. Soleus H-reflex recruitment is not altered in persons with chronic spinal cord injury. Arch Phys Med Rehabil 2004;85:840-7.
8. Boorman G, Hulliger M, Lee RG, Tako K, Tanaka R. Reciprocal Ia inhibition in patients with spinal spasticity. Neurosci Lett 1991;127:57-60.
9. Hiersemenzel LP, Curt A, Dietz V. From spinal shock to spasticity: neuronal adaptations to a spinal cord injury. Neurology 2000; 54:1574-82.
10. Little J, Halar E. H-reflex changes following spinal cord injury. Arch Phys Med Rehabil 1985;66:19-22.
11. Schmit BD, Benz EN, Rymer WZ. Afferent mechanisms for the reflex response to imposed ankle movement in chronic spinal cord injury. Exp Brain Res 2002;145:40-9.
12. Leis AA, Kronenberg MF, Stetkarova I, Paske WC, Stokic DS. Spinal motoneuron excitability after acute spinal cord injury in humans. Neurology 1996;47:231-7.
13. Calancie B, Molano MR, Broton JG. Tendon reflexes for predicting movement recovery after acute spinal cord injury in humans. Clin Neurophysiol 2004;115:2350-63.
14. Diamantopoulos E, Zander OP. Excitability of motor neurons in spinal shock in man. J Neurol Neurosurg Psychiatry 1967;30:427-31.
15. Quencer RM, Bunge RP, Egnor M, et al. Acute traumatic central cord syndrome: MRI-pathological correlations. Neuroradiology 1992;34:85-94.
16. Castro MJ, Apple DF Jr, Staron RS, Campos GE, Dudley GA. Influence of complete spinal cord injury on skeletal muscle within 6 months of injury. J Appl Physiol 1999;86:350-8.
17. Martin TP, Stein RB, Hoeppner PH, Reid DC. Influence of electrical stimulation on the morphological and metabolic properties of paralyzed muscle. J Appl Physiol 1992;72:1401-6.
18. Scelsi R, Marchetti C, Poggi P, Lotta S, Lommi G. Muscle fiber type morphology and distribution in paraplegic patients with traumatic cord lesion. Histochemical and ultrastructural aspects of rectus femoris muscle. Acta Neuropathol (Berl) 1982;57:243-8.
19. Round JM, Barr FM, Moffat B, Jones DA. Fibre areas and histochemical fibre types in the quadriceps muscle of paraplegic subjects. J Neurol Sci 1993;116:207-11.
20. Little JW, Ditunno JF, Stiens SA, Harris RM. Incomplete spinal cord injury: neuronal mechanisms of motor recovery and hyperreflexia. Arch Phys Med Rehabil 1999;80:587-99.

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