Effect of Thyrotropin-Releasing Hormone (TRH) on Motor Performance of Hemiparetic Stroke Patients

RYUICHI NAKAMURA and MASAOKI FUJITA

*Institute of Rehabilitation Medicine, Tohoku University
School of Medicine, Narugo 989-68*

NAKAMURA, R. and FUJITA, M. *Effect of Thyrotropin-Releasing Hormone (TRH) on Motor Performance of Hemiparetic Stroke Patients*. Tohoku J. Exp. Med., 1990, **160** (2), 141-143 — The maximum walking speed, the stability of standing balance, and isokinetic strength for knee extension on the both sides were examined in 7 hemiparetic stroke patients before and 10-20 min after intravenous administration of 2-mg TRH. The maximum walking speed, the stability of standing balance and the strength of the affected side increased significantly with TRH but the strength of the non-affected side did not change. It seems that TRH enables functionally depressed areas to resume activity. — stroke; biomechanics; thyrotropin-releasing hormone

Considerable progress has been made over the past few decades on neuropharmacological modification of motor recovery after cerebral insults in both animal experiments and clinical studies (cf: Stein and Sabel 1988). For instance, α -receptor agonists, e.g., norepinephrine (NE), accelerate recovery of motor function and its antagonists retard or reinstate motor deficit in rats or cats with unilateral ablation of the motor cortex (Feeney et al. 1982; Hodva and Feeney 1984). According to a pilot study examining the effect of amphetamine on motor recovery of stroke patients, a single dose of amphetamine combined with physical therapy increased the recovery compared with results in patients receiving physical therapy alone (Davis et al. 1987). It seems that acceleration of motor recovery induced by amphetamine is independent of any arousing effect of the drug. Our previous study indicated that thyrotropin releasing hormone (TRH) facilitated functional recovery of stroke patients examined by behavioral measures such as activities of daily living (ADL) and social maturation scale, and shortened their hospital stay for medical rehabilitation (Chida et al. 1987). Takahashi and Saito (1986), examining the effect of TRH on amplitudes of cerebral evoked potentials in normal subjects and patients with spinocerebellar degeneration, reported that TRH activated the central nervous system diffusely. Also Yanagisawa et al. (1986) wrote that the improvement of standing balance and visuomotor tracking performance with TRH in patients with cerebellar ataxia might be attributable to

Received January 9, 1990; revision accepted for publication January 22, 1990.

TABLE 1. Means and standard deviation (in parenthesis) of the biomechanical variables

Variables	Before	After	Difference
A-IK (Ft • 1b)	60.1(57.5)	62.3(58.1)	2.1(2.1)*
N-IK (Ft • 1b)	104.0(50.1)	104.7(50.8)	0.7(6.3)
Body sway (cm/10 sec)	26.8(13.9)	20.8(7.9)	-6.0(6.1)*
Walking speed (m/min)	81.9(49.0)	84.0(48.0)	3.1(1.8)*

A-IK, isokinetic strength of the affected side; N-IK, isokinetic strength of the non-affected side. $n = 7$; * $p < 0.05$.

general activation or an arousing effect. There remains a question whether the improvement of motor performance with TRH in stroke patients is only due to non-specific arousing effect or not. In this report we made comparison of gross motor performance before and after TRH administration in hemiparetic stroke patients.

Seven hemiparetic stroke patients aged from 23 to 74 years participated in this study. The time since stroke onset to examination was 8 to 54 weeks (mean : 20 weeks). They could stand and walk without cane and brace. Gross motor performance, before and 10-20 min after injecting a single 2-mg dose of TRH intravenously, was examined using following variables: the maximum walking speed for 10 m distance; the maximum isokinetic strength for knee extension on the both sides starting from 90° flexion with a constant velocity of 30°/sec; and the body sway, i.e., total length of the sway path of center of foot pressure, for 10 sec at standing posture. The method and apparatus to measure the variables were previously reported (Nakamura et al. 1985; Mojica et al. 1988).

Table 1 presents the means and S.Ds. of the variables examined. The isokinetic strength of the affected side increased and the body sway decreased significantly after TRH administration ($p < 0.05$, respectively), resulting in the increase of maximum walking speed ($p < 0.05$). However, the isokinetic strength of non-affected side did not change with TRH.

The results showed that TRH specifically improved the impaired motor functions of stroke patients, but did not enhance the unimpaired motor functions. It seems that TRH, facilitating the turnover of NE in the brain (Keller et al. 1974) and directly acting on NE sensitive neurons (Winokur and Beckman 1978), enables functionally depressed areas involved in motor performance to resume activity and to aid functional recovery (cf: Bach-y-Rita et al. 1988).

References

- 1) Bach-y-Rita, P., Lazarus J.C., Boyeson, M.G., Balliet, R. & Myers, T.A. (1988) Neural aspects of motor function as a basis of early and post-acute rehabilitation. In: *Rehabilitation Medicine*, edited by J.A. DeLisa, Lippincott, Philadelphia, pp. 175-195.

- 2) Chida, T., Abe, S., Nakamura, R. & Kosaka, K. (1987) Effect of thyrotropin releasing hormone on stroke rehabilitation. *J.J.A. Phys. M. Baln. Clim.*, **50**, 175-181. (Japanese)
 - 3) Davis, J.N., Crisostomo, E.A., Duncan, P., Propst, M. & Feeney, D.M. (1987) Amphetamine and physical therapy facilitate recovery from stroke: Correlative animal and human studies. In: *Cerebrovascular Diseases*, edited by M.E. Rachle & W.J. Powers, Raven Press, New York, pp. 297-306.
 - 4) Feeney, D.M., Gonzalez, A.L. & Law, W.A. (1982) Amphetamine, haloperidol, and experience interact to affect rate of recovery after motor cortex injury. *Science*, **217**, 855-857.
 - 5) Hodva, D.A. & Feeney, D.M. (1984) Amphetamine with experience promotes the rate of recovery of locomotor function after unilateral cortex injury in the cat. *Brain Res.*, **298**, 358-361.
 - 6) Keller, H.H., Bartholoni, G. & Pletscher, A. (1974) Enhancement of cerebral noradrenalin turnover by thyrotropin releasing hormone. *Nature*, **248**, 528-529.
 - 7) Mojica, J.A.P., Nakamura, R., Kobayashi, T., Handa, T., Morohashi, I. & Watanabe, S. (1988) Effect of ankle-foot orthosis (AFO) on body sway and walking capacity of hemiparetic stroke patients. *Tohoku J. Exp. Med.*, **156**, 395-401.
 - 8) Nakamura, R., Hosokawa, T. & Tsuji, I. (1985) Relationship of muscle strength for knee extension to walking capacity in patients with spastic hemiparesis. *Tohoku J. Exp. Med.*, **145**, 335-340.
 - 9) Stein, D.G. & Sabel, B.A. (Eds) (1988) *Pharmacological Approaches to the Treatment of Brain and Spinal Cord Injury*. Plenum Press, New York.
 - 10) Takahashi, K. & Saito, J. (1986) Effect of TRH on cerebral evoked potentials. In: *TRH and Spinocerebellar Degeneration*, edited by I. Sobue, Elsevier, Amsterdam, pp. 221-225.
 - 11) Winokur, A. & Beckman, A.L. (1978) Effect of thyrotropin releasing hormone, noradrenalin and acetylcholine on the activity of neurones in the hypothalamus, septum and cerebral cortex. *Brain Res.*, **150**, 205-209.
 - 12) Yanagisawa, N., Fujimoto, S. & Nakano, T. (1986) Effect of TRH on maintenance of standing equilibrium and on voluntary activity in SCD. In: *TRH and Spinocerebellar Degeneration*, edited by I. Sobue, Elsevier, Amsterdam, pp. 237-246.
-