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WE describe a patient who in 1983 suffered a stroke which resulted in severe hemiplegia and somatosensory loss. His neurological condition remained stable until January 1996, when, because of a myocardial infarction, the patient underwent systemic thrombolytic therapy which led to a remarkable improvement of both motor and somatosensory functions. This finding suggests the existence of 'idling neurons' which remain viable for a long time after stroke, and opens a fascinating window on the therapeutic potential of thrombolytic therapy in chronic stroke patients. *NeuroReport* 9: 2643–2645 © 1998 Rapid Science Ltd.

Neurological recovery after systemic thrombolytic therapy in a chronic stroke case

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Introduction

A stroke lesion usually consists of a densely ischaemic focus and a perifocal area which is marginally supplied with oxygen, the so called ischaemic penumbra.¹ This is potentially salvageable tissue, and the restoration of a normal perfusion within a few hours may prevent its recruitment in the infarction process, thus reducing the clinical expression of the stroke. Otherwise, left to its destiny, the infarction expands with time at the expense of the ischaemic penumbra. This gradual pattern represents the rationale for thrombolytic therapy in acute ischaemic stroke: the recanalization of the occluded vessel is followed by a progressive recovery of motor function. However, to the extent that it depends on a restoration of normal perfusion of the ischaemic penumbra, thrombolytic treatment is not indicated beyond a time window of 3–6 h.

We report on a patient who in October 1983 suffered a stroke leading to severe hemiplegia and somatosensory loss. The neurological condition remained stable until January 1996, when, because of a myocardial infarction, the patient underwent systemic thrombolytic therapy. This brought about a remarkable improvement of both motor and somatosensory functions, suggesting that thrombolytic therapy may have some use in chronic stroke patients, in addition to cardiopathic and acute stroke patients.

Materials and Methods

A.R., born in 1921, is a right-handed retired workman, with 5 years of schooling. He had no history of neurological or psychiatric disturbances, and no such diseases were present in his family. A.R. was in good health until September 1983 when he suddenly exhibited motor and sensory defects in his right hemisoma. Since he was absolutely unable to move his right limbs spontaneously, his motor impairment, assessed according to the four-point scale of Bisiach and co-workers,² was maximal for both upper and lower limb (score 3). Tendon reflexes of right limbs were very brisk and Babinsky's sign was elicitable on the right foot. Sensations of light touch, deep pressure and joint position were practically abolished in both upper and lower right limb. Cranial nerves I–XII were intact. No instability of mood, aphasia or other cognitive deficits were recorded. Sphincter control was normal.

Following his discharge from the hospital the patient underwent no rehabilitation treatments and needed almost full assistance in daily life activities. In October 1991, because of a lipothymia, he was readmitted to the hospital. His neurological condition was stable, and a CT scan failed to show any cerebral lesion. In September 1994, he complained of a headache followed by temporary blindness and speech difficulties. By the time of hospital admission, the symptoms had cleared up. Motor and sensory

impairments were stable. In February 1995 he suffered a drop attack and was admitted to hospital. Once again, his neurological condition was stable, and a diagnosis of generalized small vessels disease in a patient with chronic hemiplegia was made.

On 6 January 1996, more than 12 years after the stroke, the patient suffered a myocardial infarction. Immediately after being admitted to hospital, he underwent intravenous thrombolytic therapy with Alteplasi (Actilyse, 15 + 50 + 35 ml). A few hours after infusion, he felt pain at the site of injections in the right arm and noticed the re-appearance of some movements in the previously paralysed limbs. Such a surprising improvement of his neurological condition was also noticed by the physicians in charge, who referred the patient to us.

The patient gave informed consent to the present study.

Results

The patient's performance on the MMSE³ (score 27; cut-off 23) demonstrated the preservation of his intellectual abilities. According to Bisiach *et al.*,² a significant recovery of motor functions in both the lower (score 1) and, to a lesser extent, the upper (score 2) limb was recorded. Functional motor skills were further assessed by means of the European Stroke Scale⁴ and compared with the patient's performance before myocardial infarction rated retrospectively from the patient's history and from the medical records. Several motor abilities were remarkably improved (Table 1); however, the patient was still unable to perform finger movements with the right hand. The patient's answers to a behavioral questionnaire demonstrated a clear amelioration of somatosensory functions (Table 2). Finally, the patient's wife, asked to estimate the degree of care needed by him before and after the myocardial infarction, reported a significant improvement of his capacities in several daily life activities (Table 3).

Table 2. Behavioural questionnaire on somatosensory functions. The patient was asked to score on a four point scale (0–3) the sensation evoked on the right side of the body by the following activities.

Activities	Before thrombolytic therapy	After thrombolytic therapy
Shaving	3	3
Wearing gloves	0	2
Wearing socks	0	2
Cutting nails	0	2
Having injections	0	2
Combing his hair	3	3
Getting scalded	1	3

Score: 0 = No sensation; 1 = Minimal sensation; 2 = A sensation less vivid than that on the left; 3 = A sensation as vivid as that on the left.

Table 3. Degree of care needed by the patient. The patient's wife was asked to score on a four point scale (0–3) the degree of care needed by the patient as regards the following activities.

Activities	Before thrombolytic therapy	After thrombolytic therapy
Feeding	1	1
Transferring from bed to wheelchair	2	1
Locomotion	2	0
Toileting	2	1
Dressing	2	1
Bathing	3	2

Score: 3 = Totally disabled; 2 = Needs much help; 1 = Needs some help; 0 = Fully independent.

On a follow-up examination carried out in July 1996, the neurological improvement was found to be stable. At that time, an MRI examination documented an ischaemic lesion involving the corona radiata and the anteriormost part of the posterior limb of the internal capsule on the left (Fig. 1). Multiple small ischaemic subcortical lesions were also evident in both hemispheres.

Table 1. Assessment of patient's motor impairment according to the European Stroke Scale.

Impaired functions	Before thrombolytic therapy	After thrombolytic therapy	Maximum
1 Arm (maintain outstretched position)	0	1	4
2 Arm (raise)	0	2	4
3 Extension of the wrist	0	2	8
4 Fingers	0	0	8
5 Leg (maintain position)	0	4	4
6 Leg (flex)	0	2	4
7 Dorsiflexion of the foot	2	6	8
8 Gait	2	6	10

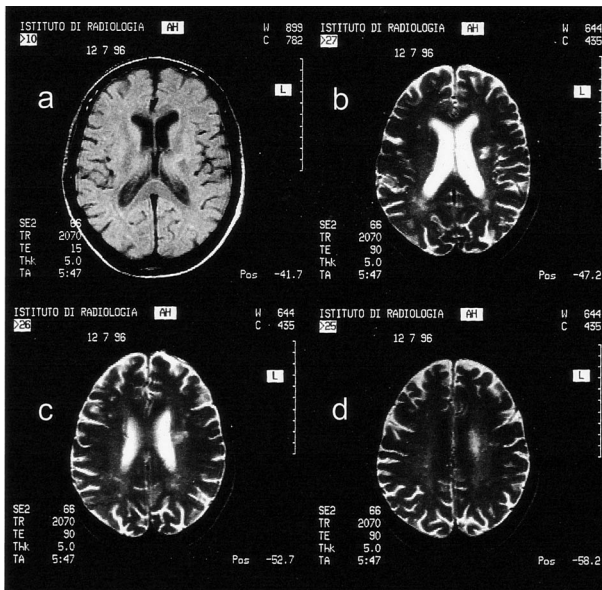


FIG. 1. Selected magnetic resonance images. (a) Proton density; (b,c,d) T2 weighted, showing the patient's lesion. Damaged areas appear lighter than does the normal brain tissue. The left hemisphere is represented on the right. The examination was performed at the Policlinico 'Borgo Roma', Verona, on July 12th, 1996. See text for details.

Discussion

For almost 13 years, our patient exhibited dense right motor and sensory hemiplegia of both limbs. As documented by several examinations, this neurological condition remained stable until thrombolytic therapy for a myocardial infarction suddenly improved it. Some voluntary movements re-appeared, and the patient re-experienced previously lost sensations. A neurological examination demonstrated a remarkable recovery of strength in the right lower limb and, to a lesser degree, in the right upper limb, as well as a dramatic improvement of the ability to detect tactile, painful and thermal stimuli in those limbs. As a result, the patient's ability to perform daily life activities improved significantly.

Two possible interpretations of this functional recovery can be proposed. First, the return of neuronal function depends on a restoration of a normal perfusion in areas surrounding the focal lesion. It seems plausible that 'idling neurons' remain viable, although not functional, in peri-infarctional zones, and appropriate treatments may lead to their functional recuperation, even many years after stroke onset;⁵⁻⁷ alternatively, there may be a return of neuronal function following restoration of normal

perfusion in undamaged areas. Recent positron emission tomography (PET) studies demonstrate that motor recovery after a stroke is due to the extension of motor areas in the affected hemisphere, as well as to the recruitment of ipsilateral motor pathways from the other hemisphere.⁸⁻¹⁰ In addition, PET examination of chronic stroke patients with absent or partial recovery showed remote depressions of regional cerebral blood flow and oxygen metabolism in many cerebral areas outside the structural lesion.^{11,12} In our case, since these possibilities can co-exist, it can be assumed that the clinically significant improvement of neuronal function paralleled the regression of the hypoperfusion in both peri-infarctional and previously ischaemic remote regions.

Conclusions

These findings corroborate the idea that the outcome of a stroke depends on the functional impact of brain damage on the remaining networks, rather than on the amount of neural tissue destroyed. As claimed by Franz and co-workers¹³ as early as 1915, 'Lesions of the motor cortex do not (necessarily) abolish function, but put the function in abeyance until such a time as the appropriate condition is present for production of movement'. In conclusion, although a single case does not allow us to draw any definite conclusions, we think that our data show a promise for encouraging adequate trials which can assess the benefits and risks of thrombolytic therapy in chronic stroke patients.

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