뇌신경재활
발표일시 및 장소 : **10 월 26 일(금) 13:25-13:35 Room C(5F)**

OP2-1-2

A pilot study to evaluate the safety and efficacy of cord blood therapy in stroke patients

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Introduction
Stroke causes significant neurological sequelae, however, perfect treatment is not available yet. In previous researches, stem cells therapy decreased infarction volume and ameliorated inflammation-related mechanisms. Although it cannot explain all therapeutic mechanisms, the Results provide a positive perspective on the effects of stem cell therapy and directions of subsequent studies. In this pilot study, we aimed to confirm the safety and efficacy of allogeneic umbilical cord blood (UCB) therapy for patients with stroke.

Methods
Five patients with stroke within 1 to 6 months after the onset were included. A single intravenous infusion of UCB selected by criteria of immune compatibility and cell number was performed. All patients received oral immunosuppressant for 2 weeks. Adverse events were monitored closely for safety. To measure the efficacy, functional outcomes were assessed at baseline, 4, 12 and 20 weeks after UCB therapy. To assess therapeutic mechanism, functional magnetic resonance imaging (fMRI) was performed in 20 weeks post-infusion. And gene expression related to inflammation was conducted using peripheral blood samples.

Results
The demographic characteristics of subjects are summarized in Table. As a safety issue, there was no serious adverse event and only mild symptoms were reported which were associated with immunosuppressant. As for the efficacy, muscle strength, Berg Balance Scale, Trunk Impairment Scale, Fugl-Meyer Assessment, Functional Independence Measure, Modified Barthel Index and Motor-free Visual Perception Test-3 scores showed improvement after UCB treatment (Figure 1). Patients who had good function showed near normal status from the baseline. Follow up fMRI of patient 1 showed localized activation of ipsilateral M1 cortex. And in patient 3 and 4, follow up fMRI showed cortical reorganization with deactivation of contralateral M1 cortex (Figure 2). In serologic study,

gene expression levels of tumor necrosis factor-α and interleukin-1β were down-regulated after UCB treatment except patient 4 who had common cold (Figure 3).

Conclusions

We could observe improvement in motor function after UCB treatment in the subjects without significant side effect. In cases of very good initial function, the ceiling effect of each score may have concealed therapeutic effect. Early bilateral activation of the motor network and later localized ipsilateral activation of the motor cortex were found. These findings were similar to previous study Results that showed neuroplasticity and it could be interpreted that ipsilateral motor pathways may play a role in motor recovery. And after the intervention, inflammatory markers were suppressed significantly, that could be supported by various studies demonstrating anti-inflammatory effects of UCB. We believe that this pilot study could be a useful reference for future development of stem cell therapy protocols.

Table. Patients characteristics

	Age	Sex	Brain lesion	Type of stroke	From onset to treatment (months)	UCB cell count
Patient 1	43	M	Right thalamus	Hemorrhage	1	$2.0X10^7$/kg
Patient 2	49	M	Right basal ganglia	Hemorrhage	1	$2.5X10^7$/kg
Patient 3	53	M	Left frontal lobe	Hemorrhage	2	$2.5X10^7$/kg
Patient 4	52	M	Right pons	Hemorrhage	2	$2.7X10^7$/kg
Patient 5	41	M	Left fronto-parietal lobe	Hemorrhage	4	$2.3X10^7$/kg

UCB, Umbilical Cord Blood

Figure 1. Changes in functional evaluation after UCB administration

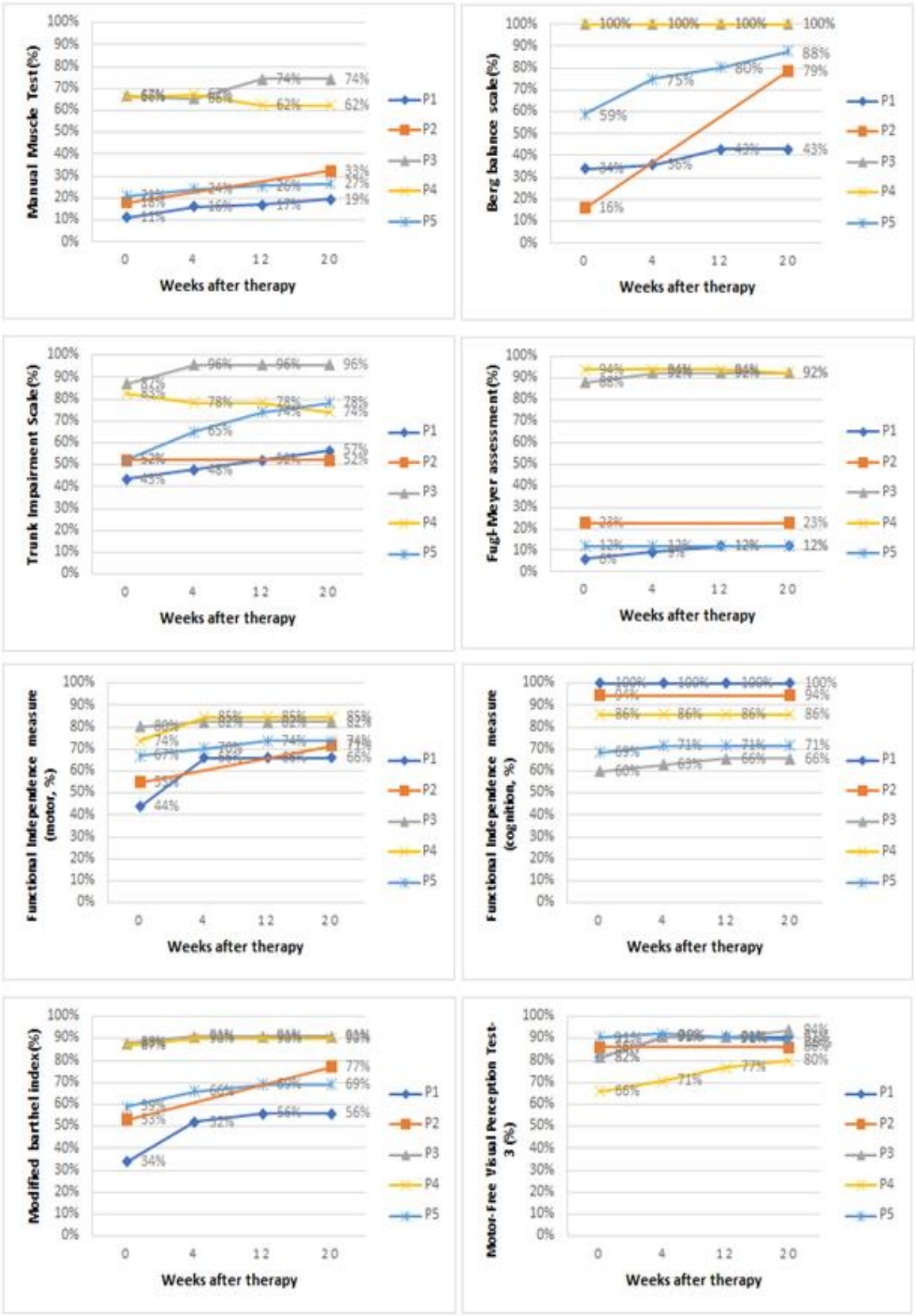


Figure 2. Changes in fMRI by UCB administration while hand movement of affected side

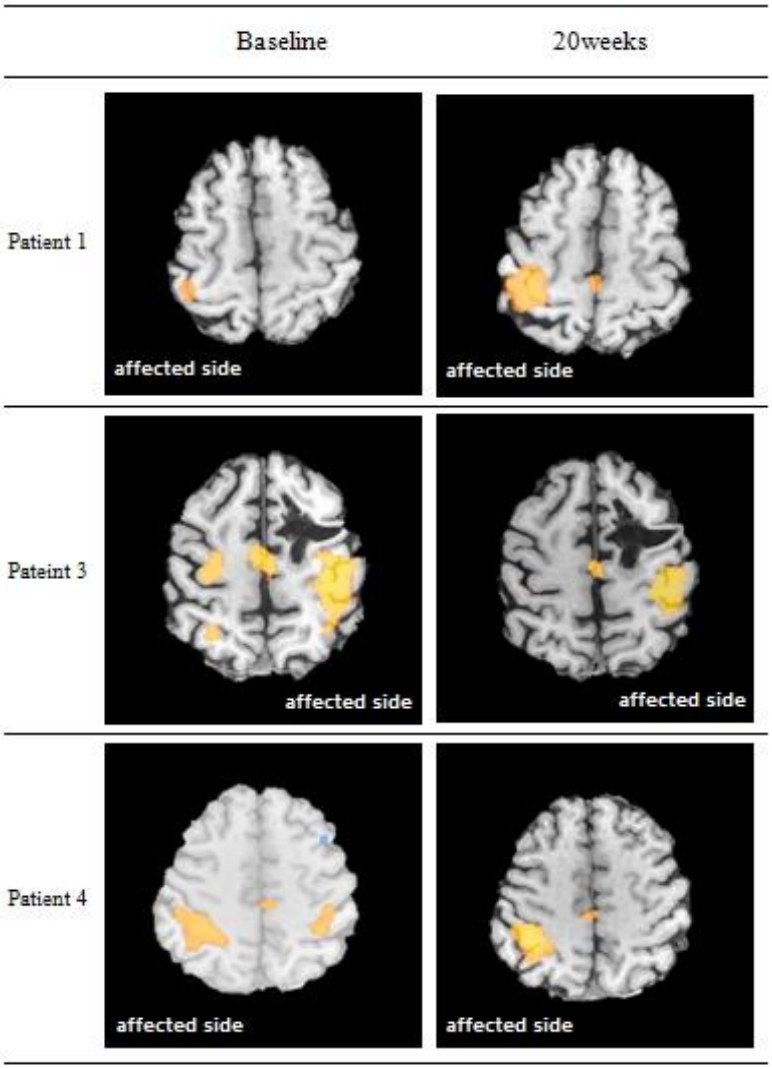
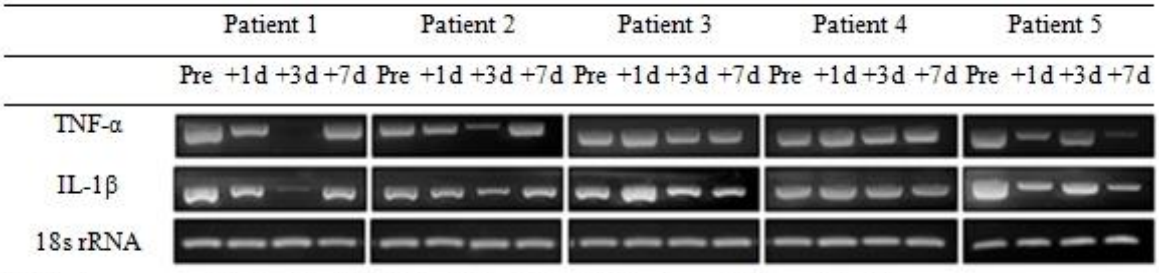


Figure 3. Changes of TNF-α, IL-1β by UCB administration



TNF-α; tumor necrosis factor alpha, IL-1β; interleukin 1 beta, rRNA; ribosomal ribonucleic acid

Gene expression levels related to inflammation in peripheral blood samplings within 10days before UCB administration and at 1 day, 3 days and 7 days after UCB administration by RT-PCR