Spinal Cord (2010) 48, 734–739

www.nature.com/sc

ORIGINAL ARTICLE

Impaired immune response to voluntary arm-crank ergometer exercise in patients with cervical spinal cord injury

M Yamanaka[1], K Furusawa[2], H Sugiyama[2], M Goto[1], T Kinoshita[1], N Kanno[1], K Takaoka[3] and F Tajima[1]

[1]Department of Rehabilitation Medicine and Nachi-Katsuura Research Center of Sports Medicine and Balneology, Wakayama Medical University, Wakayama-shi, Japan; [2]Department of Rehabilitation Medicine, Kibikogen Rehabilitation Center for Employment Injuries, Kaga-gun, Kibichuo-cho, Okayama, Japan and [3]Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine, Abeno-ku, Osaka-shi, Japan

Study design: Non-randomized study.
Objective: The mechanism underlying exercise-induced argumentation of natural killer cell cytotoxic activity (NKCA) in humans remains unclear. To address this, NKCA responses were studied during and after exercise in persons with cervical spinal cord injury (CSCI) and dysfunctional sympathetic nervous system.
Setting: Kibikogen Rehabilitation Center for Employment Injuries.
Methods: We examined the NKCA responses to 20-min arm-crank ergometer exercise at 60% of maximum oxygen consumption in eight persons with CSCI (between C6 and C7) and six able-bodied subjects. NKCA, adrenaline, and cortisol were measured before, immediately after exercise, 1 h after exercise, and 2 h after exercise.
Results: In able-bodied subjects, NKCA increased immediately after exercise ($P<0.01$) and then decreased to below the pre-exercise level 1 h after exercise, before recovering to the baseline level at 2 h after exercise. Plasma adrenaline concentrations increased significantly immediately after exercise ($P<0.01$) and returned to the baseline level 1 h after exercise. The plasma cortisol level did not change throughout the study. In contrast, NKCA, plasma concentrations of adrenaline, and cortisol did not change throughout the study in subjects with CSCI.
Conclusion: In subjects with CSCI, the lack of response in NKCA throughout the experiment is probably mainly due to a dysfunctional sympathetic nervous system.
Spinal Cord (2010) **48,** 734–739; doi:10.1038/sc.2010.13; published online 23 March 2010

Keywords: sympathetic nervous system; adrenaline; natural killer cells

Introduction

Clinical data indicate that patients with spinal cord injury (SCI) suffer from profound immunological impairment at rest,[1] probably due to autonomic dysfunction, physical inactivity, and selected medications.[1] Numerous studies have investigated the immune responses after exercise in able-bodied (AB) persons. It is well known that strenuous exercise suppresses, whereas moderate exercise activates various immune parameters.[2] Natural killer (NK) cell cytotoxic activity (NKCA) is commonly measured to assess the immune response because of its sensitivity to physiological and psychological stress.[3] Most researchers agree that the immediate post-exercise increase in NKCA reflects the recruitment of NK cells into the circulation, mediated by sympathetic outflow and catecholamine action.[4] However, there is disagreement about the reasons for the transient NKCA decrease during recovery.[5]

Very few studies have examined the immunological changes after exercise in SCI.[6–10] We reported previously that competitive wheelchair athletes with paraplegia show decreased peripheral NK cell numbers and NKCA immediately after a full marathon race and recovery to baseline values after just one night of rest.[6] However, NKCA increased significantly in paraplegics immediately after a wheelchair half-marathon and remained so during the next day of recreational athletics.[7] We hypothesized that the decrease in NK cell function immediately after a full marathon might reflect the immune response to prolonged and intensive exercise. However, there are no studies on NKCA during voluntary exercise specifically in persons with cervical SCI (CSCI).

Correspondence: Dr F Tajima, Department of Rehabilitation Medicine, Wakayama Medical University, 811-1 Kimiidera, Wakayama City, Wakayama prefecture 641-8509, Japan.
E-mail: fumi@wakayama-med.ac.jp
Received 5 August 2009; revised 17 November 2009; accepted 11 January 2010; published online 23 March 2010

Klokker *et al*.[9] studied NK cells in six subjects with CSCI after 30 min of electrically stimulated cycling exercise. No NK changes were seen in the quadriplegic group. Blood adrenaline concentrations increased during exercise in all subjects, although the rise was more pronounced in paraplegic than in quadriplegic subjects, indicating a difference between the groups in sympathetic nervous system integrity.[9] The authors concluded that sympathoadrenal activity resulted in the recruitment of NK cells to the circulation during exercise.[9] However, it is possible that electrically stimulated cycling exercise does not activate the pyramidal tract and medullary cardiovascular center in persons with CSCI. Furthermore, the extent of the NKCA response depends on the intensity and duration of exercise.[5,11,12] Thus, further studies need to be conducted under physiological and clinically relevant conditions. To investigate the role of sympathoadrenal activity in increased NKCA during voluntary exercise, the intensity and duration of the exercise must be tightly controlled to levels that increase blood adrenaline level in AB but not in CSCI.

In general, the higher the level of the SCI, the more profound the effects of sympathetic nervous dysfunction below the level of the injury.[13] Therefore, we were interested in the immunological changes induced during and after exercise in CSCI. To our knowledge, no studies have examined these immunological parameters during voluntary exercise of well-controlled duration and intensity in subjects with dysfunction of the sympathetic nervous system. This study investigated the effect of cervical transection on activation of immune parameters induced by voluntary exercise. Specifically, we compared the NKCA and adrenaline responses to arm-crank ergometer exercise in subjects with chronic CSCI and AB.

Materials and methods

Subjects

The Research Ethics Committee of Kibikogen Rehabilitation Center for Employment Injuries approved the experimental protocol and all subjects provided written informed consent. The study included eight persons with CSCI who were involved in a regular physical training program and six AB subjects as controls. The selection criteria for the study were as follows: (1) male (no females to exclude the effects of menstrual cycle-related hormone changes), (2) chronic injury state (58–64 months), (3) complete CSCI (ASIA Impairment Scale A), and (4) excellent current health and on no medications that would affect the immune and endocrine responses. Table 1 lists the subjects' characteristics. There were no differences between CSCI and AB with respect to age, height, and weight. The mean VO_2max of control subjects was higher than CSCI. Of the eight CSCI persons studied, seven used clean intermittent catheterization and one used indwelling supra-pubic catheter.

Table 1 Anthropometric data of participating subjects

	CSCI subjects	*Able-bodied subjects*
Number	8	6
Age (years)	35.3 ± 3.4	34.3 ± 3.2
Height (cm)	175.5 ± 2.6	174.8 ± 1.3
Weight (kg)	61.9 ± 3.5	68.5 ± 2.8
VO_2max (ml kg^{-1} min^{-1})	20.0 ± 1.1	32.9 ± 1.6
Spinal lesion	C6–C7	—
AIS	A	—

Abbreviations: AIS, ASIA Impairment Scale; CSCI, cervical spinal cord injury. Values are expressed as means ± s.e.m.

Study protocol

In this study, we selected an arm-crank ergometer exercise because all subjects with CSCI suffered from complete tetraplegia. Two weeks before the scheduled start of the study, subjects performed a progressive VO_2max test on an arm-crank ergometer (818E, Hand ergometer, Monark, Sweden). The test protocol required the subjects to maintain a target cadence of 60 r.p.m. After a 15-min rest period, subjects performed unloaded exercise for 3 min. The power output of the ergometer was subsequently increased by 10 W every minute. The test was terminated when the subjects reached exhaustion, or if the cadence fell below 60 r.p.m. O_2 uptake and ventilation were measured using a respiratory metabolic cart (WLCU-5207A, Westron, Japan) and EKG was monitored continuously (BP unit, PB14-136, NEC, Japan).

All subjects indicated that they had avoided intensive exercise for at least 24 h before the test and they were healthy and free of symptoms associated with respiratory or urinary tract infections. The subjects had their regular breakfast before 0900 hours and then refrained from eating, but were allowed to drink tap water *ad libitum* until the end of experiment. They reported to the Human Performance Laboratory between 1000 and 1100 hours and were outfitted with electrodes for EKG recording. Before the resting period, the subject emptied the bladder to eliminate possible autonomic dysreflexia induced by bladder distension. After resting in a quiet room for 30 min, subjects started to exercise on an arm-crank ergometer for 20 min at intensities of 60% VO_2max; the power output was increased progressively from 0 W to the desired level over 3 min.

Blood samples were collected from the antecubital vein into heparinized tubes and EDTA-2K-containing tubes before, immediately after, 1 h after, and 2 h after completion of exercise. Total blood volume in each sampling period was 15 ml. Six AB subjects performed the same experiment as the control group.

NKCA assays and measurement of NK cell number

NKCA was assayed as described earlier.[6,7] Three-color flow cytometry was used to determine the total number of NK cells (CD3−CD16+CD56+). Briefly, 50 μl of whole blood was incubated at room temperature for 20 min with 10 μl of antibody cocktail in a polypropylene tube. Antibodies were purchased from Becton-Dickinson (San Jose, CA, USA). Erythrocytes were then lysed with 1 ml FACSlyse and incubated for a further 9 min. Finally, the tube was centrifuged at 2500 r.p.m. for 3 min before the supernatant was removed, and cells were then resuspended in 250 μl 1%

formalin until analysis. Samples were sent to a commercial pathology laboratory (Sullivan Nicolaides, Taringa, Queensland, Australia) for analysis by a FACScan flow cytometer (Becton-Dickinson). The flow cytometer was calibrated daily by using different microbeads (QC Windows and Quantum 1000 (Flow Cytometry Standards, San Juan, Puerto Rico) and CaliBRITE (Becton-Dickinson)), as per standard methods for quantifying cellular antigens by flow cytometry. A total of 20 000 events were collected and the data recorded as percentage of positive cells. The total number of lymphocytes determined from a full blood count was multiplied by the percentage of CD3−CD16 + CD56 + cells.

Other blood tests

Total blood cell counts, hematocrit, the percentage of neutrophils, total lymphocytes, and monocytes, plasma catecholamines, and cortisol levels were measured using the methods described earlier.[10]

Statistical analysis

Data were expressed as mean ± standard error of the mean (s.e.m.) and analyzed using a 2×4 repeated measures analysis of variance (ANOVA). When the results of ANOVA tests were significant ($P<0.05$), we used Scheffe's test to determine differences between pre-exercise levels and each time period, and between two groups (control and exercise). A P-value <0.05 denoted the presence of a significant difference between the two groups.

Results

Blood parameters

Table 2 lists the blood cell counts of participants at four different time points: before exercise, immediately after exercise, 1 h after, and 2 h after exercise. Red blood cell (RBC) counts, absolute leukocyte numbers, hemoglobin levels, and hematocrit did not change in CSCI, whereas in AB, all four values increased immediately after exercise compared with the pre-exercise measurements, and then returned to the baseline levels by 1 h after exercise. In both groups, the absolute number of peripheral neutrophils was higher at immediately, 1 and 2 h after exercise, compared with baseline, but reached significance only at 2 h post-exercise in the CSCI.

NK cell count and NKCA

Figure 1 displays the number of peripheral NK cells at the aforementioned time intervals in CSCI and AB. In CSCI, the absolute numbers of NK cells remained constant throughout the study, whereas in AB, NK cell counts increased immediately after exercise then returned to the baseline, pre-exercise level by 1 h after exercise. However, the absolute numbers of

Table 2 Changes in blood cell count, hemoglobin, hematocrit, and leukocyte subpopulations in cervical spinal cord injury subjects (CSCI) and able-bodied subjects (AB) during 20 min arm ergometer exercise at 60% VO_2max

	Before exercise	*Immediately after exercise*	*1 h after exercise*	*2 h after exercise*	P-*value*
RBC ($\times 10^{10}$ per l)					
CSCI	498 ± 8.9	498 ± 12.0	483 ± 12.4	483 ± 12.0	NS
AB	507 ± 7.6	530 ± 6.1#	510 ± 5.7	511 ± 3.8	
Hemoglobin ($\times 10\,g\,l^{-1}$)					
CSCI	15.5 ± 0.2	15.6 ± 0.4	15.2 ± 0.4	15.2 ± 0.3	NS
AB	15.8 ± 0.3	16.6 ± 0.3*	15.9 ± 0.2	15.9 ± 0.2	
Hematocrit (%)					
CSCI	45.5 ± 0.6	45.6 ± 1.0	44.1 ± 1.0	44.1 ± 1.0	NS
AB	46.6 ± 0.7	49.7 ± 1.0#	46.8 ± 0.8	46.9 ± 0.6	
Leukocytes ($\times 10^{9}$ per l)					
CSCI	6.5 ± 0.5	7.2 ± 0.6	7.4 ± 0.5	8.0 ± 0.5	NS
AB	6.0 ± 0.5	7.7 ± 0.6#	6.3 ± 0.4	8.2 ± 0.6#	
Lymphocytes ($\times 10^{9}$per l)					
CSCI	2.1 ± 0.2	2.1 ± 0.3	1.8 ± 0.2	1.8 ± 0.1	NS
AB	2.1 ± 0.2	2.9 ± 0.2*	1.7 ± 0.1	2.1 ± 0.1	
Monocytes ($\times 10^{6}$ per l)					
CSCI	366 ± 41	383 ± 37	381 ± 38	349 ± 35	NS
AB	371 ± 66	267 ± 70	212 ± 37	373 ± 59	NS
Neutrophils ($\times 10^{9}$ per l)					
CSCI	3.8 ± 0.3	4.4 ± 0.5	5.0 ± 0.5	5.6 ± 0.6*	
AB	3.4 ± 0.5	4.3 ± 0.4	4.2 ± 0.4	5.6 ± 0.6#	

Abbreviations: RBC, red blood cells; NS, no significant differences between values at all phases.
Values are expressed as mean ± s.e.m. P-value is for time × group interaction.
*$P<0.05$, #$P<0.01$, compared with baseline.

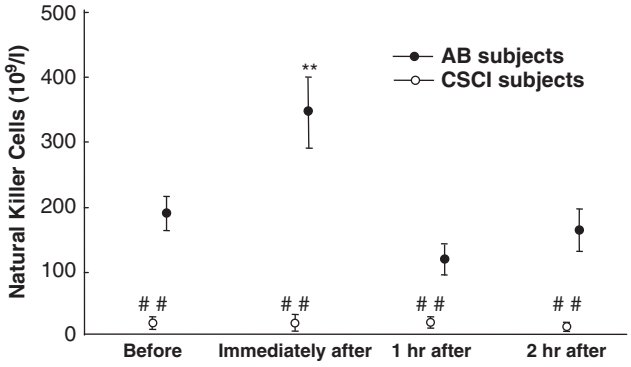

Figure 1 Number of NK cells during physical exercise (arm ergometer, 60% of VO_2max, 20 min) in cervical spinal cord injury subjects (CSCI) and AB subjects (AB). Data are expressed as mean ± s.e.m. $^{*}P<0.01$, compared with baseline (before exercise). $^{\#\#}P<0.01$, compared with the control.

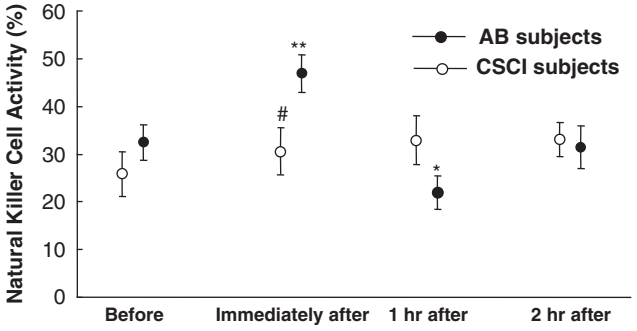

Figure 2 NK cells activity after acute physical exercise (arm ergometer, 60% of VO_2max, 20 min) in cervical spinal cord injury subjects (CSCI) and able-bodied subjects (AB). Data are expressed as mean ± s.e.m. $^{**}P<0.01$, $^{*}P<0.05$, compared with baseline (before exercise). $^{\#}P<0.05$, compared with the control.

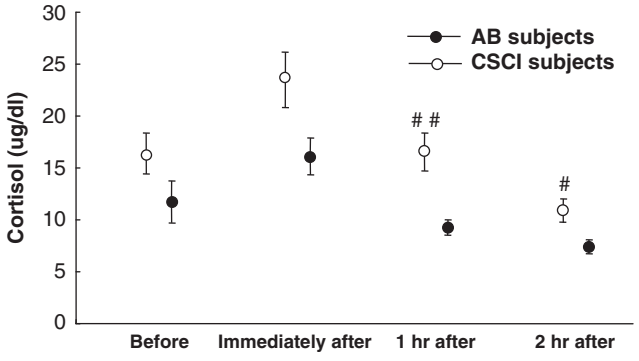

Figure 3 Plasma cortisol response to acute physical exercise (arm ergometer, 60% of VO_2max, 20 min) in cervical spinal cord injury subjects (CSCI) and able-bodied (AB) subjects. Data are expressed as mean ± s.e.m. $^{\#}P<0.05$, $^{\#\#}P<0.01$, compared with the control.

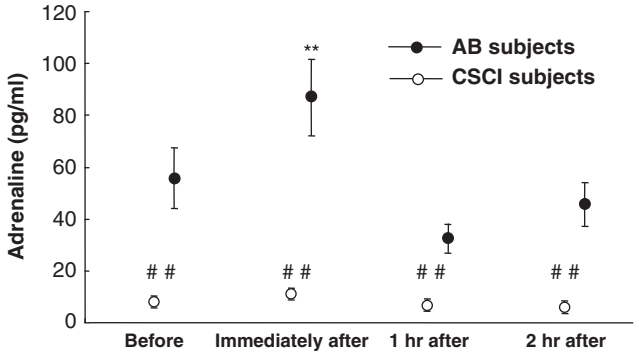

Figure 4 Plasma adrenaline response to acute physical exercise (arm ergometer, 60% of VO_2max, 20 min) in cervical spinal cord injury subjects (CSCI) and able-bodied (AB) subjects. Data are expressed as mean ± s.e.m. $^{**}P<0.01$, compared with baseline (before exercise). $^{\#\#}P<0.01$, compared with the control.

NK cells at all time points were significantly lower in CSCI than AB.

Pre-exercise NKCA was not significantly different between AB and CSCI. In controls, NKCA increased immediately after exercise and decreased below the pre-exercise level 1 h after exercise, before returning to pre-exercise values by 2 h after exercise. However, NKCA in CSCI remained constant throughout the study (Figure 2).

Cortisol and adrenaline

The mean pre-exercise concentrations of cortisol were not significantly different between AB and CSCI, but were higher in CSCI than in AB at 1 and 2 h after exercise (Figure 3). In both groups, the plasma cortisol remained constant throughout the study, with a trend toward an increase immediately after exercise (Figure 3).

Plasma adrenaline concentrations were significantly and markedly lower in CSCI than AB before exercise. Exercise significantly increased these concentrations in AB, but no change was observed in CSCI throughout the study (Figure 4). The exercise-induced increase in plasma adrenaline was reversed to pre-exercise levels at 1 h after exercise in AB.

Discussion

This study is the first to examine changes in NKCA during voluntary arm-crank ergometer exercise for 20 min at 60% of VO_2max in CSCI. We showed that exercise of well-controlled duration and intensity significantly increased plasma adrenaline concentrations and NKCA in AB, whereas these parameters did not change in CSCI either during or after exercise.

Patients with high-level CSCI have impaired sympathetic nervous system and thereby a reduced catecholamine response to exercise, compared with both normal healthy subjects and to some extent subjects with lower thoracic-level SCI.[14] This study also showed that plasma adrenaline concentrations in AB increased significantly immediately after exercise, whereas that of CSCI did not change throughout the experiment. Exercise-induced factors other than adrenaline might be similar in CSCI and AB, as the

duration and intensity of the exercise were fixed. An impaired sympathetic nervous system might therefore also have a major function in the unchanged adrenaline response in CSCI.

Both the number and activity of circulating NK cells fluctuate greatly during and after exercise, as well as in response to other stressors.[4] NK cells are rapidly mobilized into the peripheral circulation most likely via multiple mechanisms including: a catecholamine-induced downregulation of adhesion molecule expression and shear stress due to a substantial increase in peripheral blood flow.[15]

NK cells derive mainly from the spleen and are recruited into the circulation by sympathetic outflow and catecholamine action.[4] We speculated that the increases of RBC, absolute leukocyte numbers, hemoglobin levels, and hematocrit immediately after exercise in only AB would be induced by a blood shift from the spleen. NK cells attached to vascular endothelial cells *in vitro* detach after brief incubations (as short as 5 min) with catecholamines, in a dose-dependent manner.[16] The addition of a selective β-2 adrenoreceptor antagonist is reported to block this catecholamine-dependent detachment of NK cells.[17] Compared with noradrenaline, adrenaline was more effective in inducing detachment of the NK cells, which correlates with the higher affinity of β-2 adrenoreceptors for adrenaline.[4] A more recent report has emphasized that exercise-induced catecholamines modulate the expression of adhesion molecules on NK cells, resulting in the mobilization of NK cells into the circulation.[18] Furthermore, plasma catecholamines may mobilize leukocytes by increasing cardiac output and thus intravascular shear forces.[19] In this study, persistent changes in adrenaline levels, NK cell numbers, and NKCA in CSCI were observed during voluntary exercise. These findings strongly suggest that the increased NKCA during exercise was inhibited in CSCI mainly due to impaired sympathetic nervous system.

In an earlier study, we compared the immune responses to 2 h of arm-crank ergometer exercise at 60% of VO_2max between seven subjects with SCI at Th11-L4 and six AB persons.[10] NKCA increased significantly in AB immediately after exercise, but decreased significantly in SCI immediately after exercise.[10] Cortisol levels remained constant throughout the experiment in all subjects. In this study, with substantially shorter exercise duration, NKCA in CSCI did not decrease immediately after exercise.

Klokker *et al*.[9] showed that the increase in circulating NK cells after 30 min of electrically stimulated cycling exercise was lower in subjects with cervical spinal cord injuries, whose spinal injuries were at higher levels of the spinal cord affecting the sympathetic outflow, compared with paraplegics. This study required subjects with SCI to perform voluntary arm-crank ergometer exercise, as electrically stimulated cycling exercise might not activate the pyramidal tract and medullary cardiovascular center. In addition, our aim was to study subjects under physiological conditions that are more clinically relevant. With the fixed duration and intensity of the described voluntary arm exercise, circulating concentrations of adrenaline and NKCA remained constant in subjects with CSCI. These subjects have transected sympathetic nerve activities at cervical lesions connecting the peripheral and central nervous systems instead of normal activations in AB with unimpaired sympathetic nerve function. Therefore, it seems that NKCA increases through sympathoadrenal activity, mainly by increasing adrenaline, during voluntary exercise in humans.

There are two reasons for selecting 20 min for exercise duration and 60% of VO_2max for exercise intensity. First, as sympathetic innervation in CSCI is terminated at the cervical lesion, the peak heart rate of CSCI was limited and the subjects could not complete either greater intensity or longer duration exercise than those selected in this study. In a series of preliminary studies, we selected the maximal workload that could be completed during the exercise task by the majority of CSCI subjects because both the intensity and duration of the exercise seem to influence the scale of the NK mobilization. Second, earlier studies reported an increase in NKCA and the proportion of NK cells after 6-min cycling exercise at 55% of VO_2max in AB persons,[20] indicating that short-duration low-intensity exercise can significantly increase NK cell number and activity. Therefore, we expected an increase in NKCA in the selected exercise, which was in fact observed in our AB subjects.

Conclusion

NKCA in AB increases significantly during and after 20-min arm exercise conducted at 60% of maximum oxygen consumption, whereas CSCI did not show increased NKCA. These findings probably reflect an impaired sympathetic nervous system in CSCI.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We are grateful to Drs Hiroyuki Okawa, Atsushi Ikeda, Tomoyuki Ito, and Yoshiki Akatsu for the clinical assistance. We also thank Dr Faiq G Issa for the careful reading and editing of the manuscript. This project was supported by the Japanese National Foundation for Scientific Research.

References

1 Nash MS. Known and plausible modulators of depressed immune functions following spinal cord injuries. *J Spinal Cord Med* 2000; **23**: 111–120.
2 Shephard RJ, Rhind S, Shek PN. Exercise and the immune system. Natural killer cells, interleukins and related responses. *Sports Med* 1994; **18**: 340–369.
3 Hoffman-Goetz L, Pedersen BK. Exercise and the immune system: a model of the stress response? *Immunol Today* 1994; **15**: 382–387.
4 Nagatomi R. The implication of alterations in leukocyte subset counts on immune function. *Exerc Immunol Rev* 2006; **12**: 54–71.
5 Nieman DC, Nehlsen-Cannarella SL. The immune response to exercise. *Semin Hematol* 1994; **31**: 166–179.
6 Furusawa K, Tajima F, Tanaka Y, Ide M, Ogata H. Short-term attenuation of natural killer cell cytotoxic activity in wheelchair

marathoners with paraplegia. *Arch Phys Med Rehabil* 1998; **79**: 1116–1121.
7 Furusawa K, Tajima F, Umezu Y, Ueta M, Ide M, Mizushima T *et al*. Activation of natural killer cell function in recreational athletes with paraplegia during a wheeelchair half-marathon race. *Arch Phys Med Rehabil* 2003; **84**: 706–711.
8 Kawashima N, Nakazawa K, Ishii N, Akai M, Yano H. Potential impact of orthotic gait exercise on natural killer cell activities in thoracic level of spinal cord-injured patients. *Spinal Cord* 2004; **42**: 420–424.
9 Klokker M, Mohr T, Kjaer M, Galbo H, Pedersen BK. The natural killer cell response to exercise in spinal cord injured individuals. *Eur J Appl Physiol Occup Physiol* 1998; **79**: 106–109.
10 Ueta M, Furusawa K, Takahashi M, Akatsu Y, Nakamura T, Tajima F. Attenuation of natural killer cell activity during two-hour exercise in individuals with spinal cord injuries. *Spinal Cord* 2008; **46**: 26–32.
11 Shek PN, Sabiston BH, Buguet A, Radomski MW. Strenuous exercise and immunological changes: a multi-time-point analysis of leukocyte subsets, CD4/CD8 ration, immunoglobulin production and NK cell response. *Int J Sports Med* 1995; **16**: 466–474.
12 Pedersen BK, Hoffman-Goetz L. Exercise and immune system: regulation, integration and adaptation. *Physiol Rev* 2000; **80**: 1055–1081.
13 Teasell RW, Arnold JM, Krassioukov A, Delaney GA. Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. *Arch Phys Med Rehabil* 2000; **81**: 506–516.
14 Kjaer M, Pollack SF, Mohr T, Weiss H, Gleim GW, Bach FW *et al*. Regulation of glucose turnover and hormonal responses during electrical cycling in tetraplegic humans. *Am J Physiol* 1996; **271**: R191–R199.
15 Timmons BW, Cieslak T. Human natural killer cell subsets and acute exercise: a brief review. *Exerc Immunol Rev* 2008; **14**: 8–23.
16 Benschop RJ, Oostveen FG, Heijnen CJ, Ballieux RE. Beta 2-adrenergic stimulation causes detachment of natural killer cells from cultured endothelium. *Eur J Immunol* 1993; **23**: 3242–3247.
17 Benschop RJ, Nijkamp FP, Ballieux RE, Heijnen CJ. The effects of beta-adrenoceptor stimulation on adhesion of human natural killer cells to cultured endothelium. *Br J Pharmacol* 1994; **113**: 1311–1316.
18 Nagao F, Suzui M, Takeda K, Yagita H, Okumura K. Mobilization of NK cells by exercise: downmodulation of adhesion molecules on NK cells by catecholamines. *Am J Physiol Regulatory Integrative Comp Physiol* 2000; **279**: R1251–R1256.
19 Shephard RJ. Exercise under hot conditions: a major threat to the immune response? *J Sports Med Phys Fitness* 2002; **42**: 368–378.
20 Moyna NM, Acker GR, Weber KM, Fulton JR, Robertson RJ, Goss FL *et al*. Exercise-induced alterations in natural killer cell number and function. *Eur J Appl Physiol Occup Physiol* 1996; **74**: 227–233.

EDITORIAL NOTE

Editorial Note on: Impaired immune response to voluntary arm crank ergometer exercise in patients with spinal cord injury

Spinal Cord (2010) **48,** 739; doi:10.1038/sc.2010.27; published online 30 March 2010

Editorial Note on: *Spinal Cord* (2010) **48,** 734–739; doi:10.1038/sc.20010.13; published online 23 March 2010

Medical professionals who deal with spinal cord injuries recognize that their clients are always at risk for infectious complications. Thus, it is entirely appropriate to state that medical management of spinal cord injury is always accompanied by medical management of infections, regardless of whether the client is in the emergency room or living in the community.

A published report recently found that the immune function of patients with spinal cord injuries is reduced compared with able-bodied individuals.[1] However, there has been little discussion of rehabilitation programs and sport activities in this patient population from the view of the immune system.

The research group of this paper have chosen natural killer cell activity and interleukin-6 in blood samples as the indicators of immune function.[2] The former indicator is a type of lymphocyte and the latter is a 'cytokine' produced by skeletal muscles. Both of these indicators reflect the degree of physical stress. Many medical professionals consider immune responses in physically handicapped patients only at the time an infectious disease appears. This paper offers some new concepts in this field. In particular, the study design contains several valuable approaches. First, study participants included both able-bodied persons and tetraplegic patients. Second, exercise was conducted using a hand-ergometer. The first approach should provide some understanding of the 'influence of the autonomic nervous system on immune function'. The second approach should allow the standardization and quantification of physical stress on the physically handicapped, thereby providing improved insight into future studies in this area.

M Ide
Rehabilitation Centre, St Mary's Hospital, Fukuoka Prefecture, Japan
E-mail: VZA07307@nifty.ne.jp

References

1 Campagnolo DI, Dixon D, Schwartz J, Bartlett JA, Keller SE. Altered innate immunity following spinal cord injury. *Spinal Cord* 2008; **46**: 477–481.
2 Ueta M, Furusawa K, Takahashi M, Akatsu Y, Nakamura T, Tajima F. Attenuation of natural killer cell activity during 2 h exercise in individual with spinal cord injury. *Spinal Cord* 2008; **46**: 26–32.