Physiology in Health and Disease
Published on behalf of The American Physiological Society by Springer

J. Andrew Taylor *Editor*

The Physiology of Exercise in Spinal Cord Injury

Springer

Physiology in Health and Disease

Published on behalf of The American Physiological Society by Springer

Physiology in Health and Disease

This book series is published on behalf of the American Physiological Society (APS) by Springer. Access to APS books published with Springer is free to APS members.
APS publishes three book series in partnership with Springer: *Physiology in Health and Disease* (formerly *Clinical Physiology*), *Methods in Physiology*, and *Perspectives in Physiology* (formerly *People and Ideas*), as well as general titles.

More information about this series at http://www.springer.com/series/11780

J. Andrew Taylor
Editor

The Physiology of Exercise in Spinal Cord Injury

Springer

Editor
J. Andrew Taylor
Physical Medicine & Rehabilitation
Harvard Medical School
Spaulding Hospital Cambridge
Cambridge, Massachusetts
USA

Physiology in Health and Disease
ISBN 978-1-4939-6662-2 ISBN 978-1-4939-6664-6 (eBook)
DOI 10.1007/978-1-4939-6664-6

Library of Congress Control Number: 2016960324

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer Science+Business Media LLC
The registered company address is 233 Spring Street, New York, NY 10013, U.S.A

Contents

Chapter 1
The Physiology of Exercise in Spinal Cord Injury (SCI): An Overview of the Limitations and Adaptations

Hannah W. Mercier and J. Andrew Taylor

Abstract For all human beings, exercise is vital to living well. Exercise promotes physical and psychological health across the lifespan, reducing risk for mortality and decreasing prevalence of health complications which contribute to chronic disease. Exercise requires integrated physiologic responses across the musculoskeletal, cardiovascular, autonomic, pulmonary, thermoregulatory, and immunologic systems. However, persons living with spinal cord injury (SCI) have difficulty achieving the minimal exercise requirements for health benefits since paralyzed skeletal muscles cannot contribute to overall oxygen consumption. Moreover, SCI can be considered as an accelerated systemic form of aging due to the severely restricted physical inactivity imposed, usually at an early age. Indeed, persons with SCI experience profound declines in function across many physiological systems and are considered, as a group, to be sedentary and among the least fit individuals. And, there are numerous considerations for exercise in those with an SCI. Alterations in function across almost all the physiological systems engaged by exercise may be compromised or altered. Nonetheless, exercise can still confer significant benefits and may be among the most important components of a healthy lifestyle for this population.

After SCI, the motor, sensory, and autonomic deficits limit not only the convenience of exercising, but notably the capacity to exercise. Due to the decreased ability to ventilate independently and limited innervated skeletal muscle, 6 % of persons with tetraplegia are unable to achieve aerobic exercise after discharge

H.W. Mercier, Ph.D. • J. A. Taylor, Ph.D. (✉)
Cardiovascular Research Laboratory, Spaulding Hospital Cambridge, 1575 Cambridge St, Cambridge, MA 02138, USA

Department of Physical Medicine & Rehabilitation, Harvard Medical School, Cambridge, MA, USA
e-mail: jandrew_taylor@hms.harvard.edu

J.A. Taylor (ed.), *The Physiology of Exercise in Spinal Cord Injury*, Physiology in Health and Disease, DOI 10.1007/978-1-4939-6664-6_1

(National Spinal Cord Injury Statistical Center 2015). Apart from this small percentage, research has documented that exercise can result in notable training adaptations and clearly protects against risk of death and disease, and reduces the limits that SCI imposes on the body (Huonker et al. 1996; Washburn and Figoni 1998; Knutsson et al. 1973). As physiological changes unique to SCI become better understood, innovative technological solutions for exercise interventions and tailored methods for measuring the effects of training will become increasingly available. This chapter provides an overview to the limitations on exercise physiology for those living with SCI, as well as considerations and current challenges for facilitating exercise performance.

1.1 Motor Limitations and Potential Adaptations

Among the physiological changes in SCI most apparent is reduced or complete loss of volitional muscular control below the level of injury. This limited motor control results from cessation, partial or complete, of supraspinal input to the spinal cord. There is a potential for motor recovery in the lower extremities, however the spinal cord can generate automatic movements without conscious or volitional control (Roy et al. 2012). Spinal circuitry "learns" what motor action (standing, stepping) is taught and practiced (de Leon et al. 1998a, b), and it can "forget" the movement when practice is ceased (de Leon et al. 1999; Cha et al. 2007). Furthermore, there is evidence that the spinal circuitry can alter motor actions in response to the sensory input received at a given moment, even "predicting" subsequent motor actions through central pattern generation (Roy et al. 2012; Edgerton et al. 2004). The spinal cord demonstrates plasticity in generating motor control when it is trained repetitively. Remarkably, even those with motor complete SCI, via electrical stimulation and repetitive training, can exert control on lower extremity motor action based on proprioceptive information (Harkema et al. 1997; Grillner and Zangger 1979; Roy et al. 2012). Finally, pharmacological and epidural stimulation interventions can amplify residual descending input to facilitate motor recovery (de Leon et al. 1998a, b). Recognizing these adaptations and spinal circuitry resiliency, rehabilitation has advanced motor function recovery after SCI using assisted motor training, spinal cord epidural stimulation, and/or pharmacological agents in recent years (Roy et al. 2012). These opportunities for regaining lower extremity motor function present even more reason to exercise and thus prevent secondary health complications that would complicate participation in locomotor training.

Within 6 weeks of SCI, paralyzed skeletal muscles atrophy significantly (Gorgey et al. 2015). They convert to fast-type muscle fibers, becoming weak and highly fatigable (Scott et al. 2006). In addition to limiting exercise performance, the loss of skeletal muscle mass and extreme lower limb physical inactivity in SCI induce structural and functional changes in the heart and circulatory system which lead to increased cardiovascular disease risk. There is strong evidence for the beneficial

effects of functional electrical stimulation (FES) to activate larger amounts of muscle mass and achieve the benefits of regular aerobic exercise, including muscular hypertrophy (Crameri et al. 2002; Gerrits et al. 2001; Pollack et al. 1989; Goss et al. 1992; Deley et al. 2015; Panisset et al. 2016). Hybrid FES exercise, which incorporates volitional contractions of the upper body in synchrony with FES to paralyzed muscles, also serves as a total body exercise (Krauss et al. 1993). Though evidence of comparative effectiveness is limited, greater gains in aerobic capacity have been found using hybrid FES exercise compared to upper body exercise alone (Verellen et al. 2007). Activating the paralyzed muscles with FES during exercise also has benefits to cardiac output as the lower limb contractions act as a muscle pump (Davis et al. 1990). In addition, abdominal binding (West et al. 2012), compression garments, and anti-gravity suits (Hopman et al. 1992) can be used to counteract the lack of sympathetically mediated vasoconstriction that lead to blood pooling in inactive and splanchnic areas.

1.2 Cardiovascular Implications

An accelerated age-related decline in the cardiovascular system occurs after SCI (Phillips et al. 2012; Miyatani et al. 2009), resulting in risk for cardiovascular disease three times greater than the able-bodied and risk for stroke approximately four times greater (Cragg et al. 2013). Factors contributing to this increased physiological risk for cardiovascular disease include autonomic dysfunction, physical inactivity, and poor metabolic profile. Exercise can induce cardiac remodeling which diminishes the functional and structural deficits after SCI (Brown and Weaver 2011; Gibbons et al. 2016). Moreover, arterial cross sectional area is larger among athletes with paraplegia compared to those who are sedentary (Huonker et al. 1998). In fact, increases in arterial diameter have been noted after just two weeks of FES cycling exercise (Thijssen et al. 2006) and arterial wall stiffness may be reversed by exercise (de Groot et al. 2005).

Autonomic dysfunction after SCI produces an unstable cardiovascular system and diminished blood pressure and heart rate responses to exercise. Low resting blood pressure and orthostatic hypotension are related to impaired cerebrovascular and cognitive function, syncope, fatigue, and nausea (Phillips et al. 2014a, b; Claydon, Steeves et al. 2006). Though the symptoms are not distinct from those in able bodied persons (Cleophas et al. 1986; Frisbie and Steele 1997; Sclater and Alagiakrishnan 2004), orthostatic hypotension may limit the positions possible for exercise in persons with SCI. In contrast, autonomic dysreflexia occurs in response to noxious afferent stimuli below the level of lesion, such as bowel or bladder distention, tight clothing, pressure ulcers, or even standard therapeutic electrical stimulation, and can lead to dangerously high blood pressure. Exercise has been shown to be a safe therapeutic approach for attenuating the severity of autonomic dysreflexia (DiCarlo et al. 1994; Halliwill 2001), though interestingly, athletes with

SCI have induced autonomic dysreflexia to generate increased blood pressure and improve exercise performance (Harris 1994).

1.3 Ventilatory Limitations

An SCI results in frequent respiratory problems due to lesser innervated respiratory musculature. For example, the capacity to generate cough is compromised due to impaired innervation of the abdominal muscles at most SCI levels. On the other hand, less active muscle mass, especially in individuals with high level SCI may not impose enough stress on the respiratory system to elicit ventilatory constraint or inspiratory muscle fatigue during exercise. Indeed, athletes with high level SCI may demonstrate lung hyperinflation during exercise without increased ventilatory constraint or inspiratory muscle fatigue. This may permit increased expiratory flow and reduced airway resistance, but also increase diaphragmatic fatigue and impede venous return. There is evidence that various exercise modalities can improve respiratory function among those with SCI (Sheel et al. 2008; Silva et al. 1998; Phillips et al. 1989; Terson de Paleville et al. 2013). The positive effects of exercise training in SCI may reside in an increase in respiratory muscle strength and endurance in addition to adjacent effects of reduced ventilatory demand during exercise via peripheral adaptations. If ventilatory response could be improved, higher intensities which are more effective at improving cardio-metabolic risk may be achievable (Kemi et al. 2005; Swain and Franklin 2006). However, it should be noted that hybrid FES exercise that results in greater skeletal muscle work may allow for oxygen demand that exceeds respiratory capacity in high level SCI (Brurok et al. 2011; Qui et al. 2016).

1.4 Thermoregulatory Considerations

Impaired thermoregulation occurs both at rest and during exercise after SCI, due to a loss of sympathetic innervation and decreased ability to vasoconstrict or shiver below the level of injury. Persons with SCI have a greater risk of heat-related illness, though some cooling technologies used with able bodied persons have been successfully applied to SCI athletes. Cooling of the hands and feet have been used to direct blood flow to the active muscles and facilitate exercising at higher aerobic demands (Griggs et al. 2014). In contrast to the peripheral “detraining” of sweat glands among those with SCI (Ogawa and Asayama 1978), exercise training enhances nitric oxide-dependent vasodilation (Thijssen et al. 2007; Green et al. 2004) and thus the ability to thermoregulate.

1.5 Alterations in Body Composition and Inflammation

Persons with SCI at the same BMI as able-bodied individuals are approximately 13 % fatter due to loss of skeletal muscle and characteristic increases in adipose tissue after injury (Spungen et al. 2003). Adipose has a profound influence on metabolic syndrome (Grundy 2008), chronic low grade inflammation, and cardiovascular disease. However, beneficial changes in body composition can result from various forms of exercise (electrical stimulation, arm crank ergometry, resistance training, and combinations of these). Following the decreased physical activity and obesity that often occur with SCI is greater risk for a state of chronic low grade inflammation (Myers et al. 2007). Persons with SCI have higher inflammatory markers, such as resting cortisol levels (Campagnolo et al. 1999) which in turn increases their propensity to develop cardiovascular disease and diabetes (Gleeson et al. 2011). While acute inflammatory responses are worse for those with high cervical SCI, the anti-inflammatory effects of exercise are attainable for both persons with tetraplegia and paraplegia (Bakkum et al. 2015; Griffin et al. 2009, Turiel et al. 2011; Rosety-Rodriguez et al. 2014). Indeed, exercise holds benefits for lowering BMI, fat mass, and inflammation even at levels that would be considered recreational (Paulson et al. 2013; Kouda et al. 2012; Yamanaka et al. 2010).

1.6 Impact on Bone Fracture Risk

Inactivity and less weight bearing after SCI profoundly limit the mechanical stimulus to bone and increase the risk for low-load fractures during daily living (Lala et al. 2014). Furthermore, poor fracture healing leads to further complications such as deconditioning and pressure ulcers from bed rest (Gifre et al. 2014; Frotzler et al. 2008). Bone loss is greatest in long bones below the level of injury, and is most treatable during the acute phases of SCI. In fact, present literature suggests that there are limited effective interventions to prevent or restore bone loss in those with chronic SCI. Though they involve some component of weight bearing, FES rowing (Gibbons et al. 2014), FES cycling (Frotzler et al. 2008; Lai et al. 2010), and activity-based training (Astorino et al. 2013) demonstrate only modest benefits to bone mineral density specific to the area trained, but with no lasting effects. Furthermore, both increases and decreases in bone mineral density have been identified with the use of electrical stimulation (Gorgey et al. 2015; Gater et al. 2011). Mechanical stresses placed on skeletal muscles during exercise should stimulate osteoblast activity and bone formation. However, load has rarely been quantified during specific exercises and this would assist in developing interventions that would maximize fracture prevention, minimize bone resorption, and promote bone growth.

1.7 Pain

Eighty percent of persons with SCI experience chronic pain, with a third having levels of pain that interfere with activities of daily living and work (Cardenas et al. 2004; Dijkers et al. 2009). A significantly greater proportion of those with SCI, compared to able bodied persons, are prescribed more than one analgesic-narcotic medication and are five and-a-half times more likely to be issued two or more analgesic-narcotics (Kitzman et al. 2016). Considering these rates of use and the high rates of potential adverse events (Kitzman et al. 2016), exercise may be a relatively affordable, safe, and empowering method of reducing pain. However, pain is also a barrier to exercise (Ditor et al. 2003; Hicks et al. 2003; Subbarao et al. 1995). Nonetheless, if psychological and behavioral means are available to support exercise participation, those with SCI may experience lesser pain. For example, regular aerobic exercise decreases pain after just three months, and with greater effects after nine months (Hicks et al. 2003; Martin-Ginnis et al. 2003). Indeed, when those with SCI ceased participating in an exercise program, they experienced increased pain (Ditor et al. 2003). Those who self-propel wheelchairs and transfer numerous times daily (Morrow et al. 2010) typically have weak posterior shoulder muscle strength (Mulroy et al. 1996; Wilbanks and Bickel 2016; Olenik et al. 1995). Strong evidence supports exercise as an intervention to decrease shoulder pain, one of the common chronic pain conditions among persons with SCI. In fact, by decreasing pain even just marginally, exercise also improves psychological well-being and decreases the severity of depression (Stanton and Reaburn 2014).

1.8 Conclusion

As elegantly stated by Henry Barcroft, “the condition of exercise is not a mere variant of the condition of rest, it is the essence of the machine.” Indeed, across the systems impacted by SCI, exercise offers at least modest adaptations to the physiological limitations of injury. Those with SCI who exercise achieve a variety of benefits related to lifelong health and wellness goals: from the cellular level to more distal functional and psychosocial outcomes. Discussed more in detail in the forthcoming chapters are the challenges in measuring these physiological changes which may have relatively large impact in the lives of persons with SCI. Although regular exercise is important for more complete recovery, more than half of those with an SCI experience barriers to exercising, and many do not meet criteria to induce significant health benefits. Given that exercise is unique as rehabilitative for bodily function and as representative of integrated physiological control, the fields of rehabilitation and physiology should work together to develop innovative solutions for those with SCI to optimize exercise interventions.

References

Astorino TA, Harness ET, Witzke KA (2013) Effect of chronic activity-based therapy on bone mineral density and bone turnover in persons with spinal cord injury. Eur J Appl Physiol 113:3027–3037

Bakkum AJ, Paulson TA, Bishop NC et al (2015) Effects of hybrid cycle and handcycle exercise on cardiovascular disease risk factors in people with spinal cord injury: a randomized controlled trial. J Rehabil Med 47(6):523–530

Brown A, Weaver LC (2011) The dark side of neuroplasticity. Exp Neurol 235(1):133–141

Brurok B, Helgerud J, Karlsen T, Leivseth G, Hoff J (2011) Effect of aerobic high-intensity hybrid training on stroke volume and peak oxygen consumption in men with spinal cord injury. Am J Phys Med Rehabil 90(5):407–414

Campagnolo DI, Bartlett JA, Chatterton R et al (1999) Adrenal and pituitary hormone patterns after spinal cord injury. Am J Phys Med Rehabil 78(4):361–366

Cardenas DD, Bryce TN, Shem K et al (2004) Gender and minority differences in the pain experience of people with spinal cord injury. Arch Phys Med Rehabil 85:1774–1781

Cha J, Heng C, Reinkensmeyer DJ, Roy RR, Edgerton VR, de Leon RD (2007) Locomotor ability in spinal rats is dependent on the amount of activity imposed on the hindlimbs during treadmill training. J Neurotrauma 24:1000–1012

Claydon VE, Steeves JD, Krassioukov A (2006) Orthostatic hypotension following spinal cord injury: understanding clinical pathophysiology. Spinal Cord 44:341–351

Cleophas TJM, Kauw FHW, Bijl C, Meijers J, Stapper G (1986) Effects of beta adrenergic receptor agonists and antagonists in diabetics with symptoms of postural hypotension: a double-blind, placebo-controlled study. Angiology 37:855–862

Cragg JJ, Noonan VK, Krassioukov A, Borisoff J (2013) Cardiovascular disease and spinal cord injury: results from a national population health survey. Neurology 81:723–728

Crameri RM, Weston A, Climstein M, Davis GM, Sutton JR (2002) Effects of electrical stimulation-induced leg training on skeletal muscle adaptability in spinal cord injury. Scand J Med Sci Sport 12:316–322

Davis GM, Servedio FJ, Glaser RM, Gupta SC, Suryaprasad AG (1990) Cardiovascular responses to arm cranking and FNS-induced leg exercise in paraplegics. J Appl Physiol 69(2):671–677

de Groot P, Crozier J, Rakobowchuk M, Hopman M, MacDonald M (2005) Electrical stimulation alters FMD and arterial compliance in extremely inactive legs. Med Sci Sports Exerc 37:1356–1364

de Leon RD, Hodgson JA, Roy RR, Edgerton VR (1998a) Locomotor capacity attributable to step training versus spontaneous recovery after spinalization in adult cats. J Neurophysiol 79:1329–1340

de Leon RD, Hodgson JA, Roy RR, Edgerton VR (1998b) Full weightbearing hindlimb standing following stand training in the adult spinal cat. J Neurophysiol 80:83–91

de Leon RD, Hodgson JA, Roy RR, Edgerton VR (1999) Retention of hindlimb stepping ability in adult spinal cats after the cessation of step training. J Neurophysiol 81:85–94

Deley G, Denuziller J, Babault N (2015) Functional electrical stimulation: cardiorespiratory adaptations and applications for training in paraplegia. Sports Med 45(1):71–82

DiCarlo SE, Collins HL, Howard MG, Chen C-Y, Scislo TJ, Patil RD (1994) Postexertional hypotension: a brief review. Sports Med Train Rehab 5:17–27

Dijkers M, Bryce T, Zanca J (2009) Prevalence of chronic pain after traumatic spinal cord injury: a systematic review. J Rehabil Res Dev 46:13–29

Ditor DS, Latimer AE, Ginis KA et al (2003) Maintenance of exercise participation in individuals with spinal cord injury: effects on quality of life, stress and pain. Spinal Cord 41:446–450

Edgerton VR, Tillakaratne NJ, Bigbee AJ, de Leon RD, Roy RR (2004) Plasticity of the spinal neural circuitry after injury. Annu Rev Neurosci 27:145–167

Frisbie JH, Steele DJ (1997) Postural hypotension and abnormalities of salt and water metabolism in myelopathy patients. Spinal Cord 35:303–307
Frotzler A, Coupaud S, Perret C, Kakebeeke TH, Hunt KJ, Donaldson NN, Eser P (2008) High-volume FES-cycling partially reverses bone loss in people with chronic spinal cord injury. Bone 43:169–176
Gater DR Jr, Dolbow D, Tsui B, Gorgey AS (2011) Functional electrical stimulation therapies after spinal cord injury. NeuroRehabilitation 28(3):231–248
Gerrits HL, de Haan SJ, van Langen H, Hopman MT (2001) Peripheral vascular changes after electrically stimulated cycle training in people with spinal cord injury. Arch Phys Med Rehabil 82:832–839
Gibbons RS, McCarthy ID, Gall A, Stock CG, Shippen J, Andrews BJ (2014) Can FES-rowing mediate bone mineral density in SCI: a pilot study. Spinal Cord 52(Suppl 3):S4–S5
Gibbons RS, Stock CG, Andrews BJ, Gall A, Shave RE (2016) The effect of FES-rowing training on cardiac structure and function: pilot studies in people with spinal cord injury. Spinal Cord 54(10):822–829
Gifre L, Vidal J, Carrasco J, Portell E, Puig J, Monegal A, Guañabens N, Peris P (2014) Incidence of skeletal fractures after traumatic spinal cord injury: a 10-year follow-up study. Clin Rehabil 28:361–369
Gleeson M, Bishop NC, Stensel DJ et al (2011) The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. Nat Rev Immunol 11(9):607–615
Gorgey AS, Dolbow DR, Dolbow JD, Khalil RK, Gater DR (2015) The effects of electrical stimulation on body composition and metabolic profile after spinal cord injury–Part II. J Spinal Cord Med 38(1):23–37
Goss FL, McDermott A, Robertson RJ (1992) Changes in peak oxygen uptake following computerized functional electrical stimulation in the spinal cord injured. Res Q Exerc Sport 63 (1):76–79
Green DJ, Maiorana A, O'Driscoll G, Taylor R (2004) Effect of exercise training on endothelium-derived nitric oxide function in humans. J Physiol 561(Pt 1):1–25
Griffin L, Decker MJ, Hwang JY et al (2009) Functional electrical stimulation cycling improves body composition, metabolic and neural factors in persons with spinal cord injury. J Electromyogr Kinesiol 19(4):614–622
Griggs KE, Price MJ, Goosey-Tolfrey VL (2014) Cooling athletes with a spinal cord injury. Sports Med 45(1):9–21
Grillner S, Zangger P (1979) On the central generation of locomotion in the low spinal cat. Exp Brain Res 34:241–261
Grundy SM (2008) Metabolic syndrome pandemic. Arterioscler Thromb Vasc Biol 28(4):629–636
Halliwill JR (2001) Mechanisms and clinical implications of post-exercise hypotension in humans. Exerc Sport Sci Rev 29:65–7057
Harkema SJ, Hurley SL, Patel UK, Requejo PS, Dobkin BH, Edgerton VR (1997) Human lumbosacral spinal cord interprets loading during stepping. J Neurophysiol 77:797–811
Harris P (1994) Self-induced autonomic dysreflexia ('boosting') practised by some tetraplegic athletes to enhance their athletic performance. Paraplegia 32:289–291
Hicks AL, Martin KA, Ditor DS et al (2003) Long-term exercise training in persons with spinal cord injury: effects on strength, arm ergometry performance and psychological well-being. Spinal Cord 41:34–43
Hopman MT, Oeseburg B, Binkhorst RA (1992) The effect of an anti-G suit on cardiovascular responses to exercise in persons with paraplegia. Med Sci Sports Exerc 24(9):984–990
Huonker M, Halle M, Keul J (1996) Structural and functional adaptations of the cardiovascular system by training. Int J Sports Med 17(Suppl 3):S164–S172

Huonker M, Schmid A, Sorichter S, Schmidt-Trucksab A, Mrosek P, Keul J (1998) Cardiovascular differences between sedentary and wheelchair-trained subjects with paraplegia. Med Sci Sports Exerc 30(4):609–613

Kemi OJ, Haram PM, Loennechen JP et al (2005) Moderate vs. high exercise intensity: differential effects on aerobic fitness, cardiomyocyte contractility, and endothelial function. Cardiovasc Res 67:161–172

Kitzman P, Cecil D, Kolpek JH (2016) The risks of polypharmacy following spinal cord injury. J Spinal Cord Med 9:1–7

Knutsson E, Lewenhaupt-Olsson E, Thorsen M (1973) Physical work capacity and physical conditioning in paraplegic patients. Spinal Cord 11(3):205–216

Kouda K, Furusawa K, Sugiyama H et al (2012) Does 20-min arm crank ergometer exercise increase plasma interleukin-6 in individuals with cervical spinal cord injury? Eur J Appl Physiol 112(2):597–604

Krauss JC, Robergs RA, Depaepe JL, Kopriva LM, Aisenbury JA, Anderson MA, Lange EK (1993) Effects of electrical stimulation and upper body training after spinal cord injury. Med Sci Sports Exerc 25(9):1054–1061

Lai C, Chang W, Chan W, Peng C, Shen L, Chen J, Chen S (2010) Effects of functional electrical stimulation cycling exercise on bone mineral density loss in the early stages of spinal cord injury. J Rehabil Med 42:150–154

Lala D, Craven BC, Thabane L, Papaioannou A, Adachi JD, Popovic MR, Giangregorio LM (2014) Exploring the determinants of fracture risk among individuals with spinal cord injury. Osteoporos Int 25:177–185

Martin Ginis K, Latimer A, McKecknie K et al (2003) Using exercise to enhance subjective well-being among people with spinal cord injury: the mediating influences of stress and pain. Rehab Psychol 48:157–164

Miyatani M, Masani K, Oh PI, Miyachi M, Popovic MR, Craven BC (2009) Pulse wave velocity for assessment of arterial stiffness among people with spinal cord injury: a pilot study. J Spinal Cord Med 32:72–78

Morrow MMB, Hurd WJ, Kaufman KR (2010) An KN. Shoulder demands in manual wheelchair users across a spectrum of activities. J Electromyogr Kinesiol 20(1):61–67

Mulroy SJ, Gronley JK, Newsam CJ, Perry J (1996) Electromyographic activity of shoulder muscles during wheelchair propulsion by paraplegic persons. Arch Phys Med Rehabil 77 (2):187–193

Myers J, Lee M, Kiratli J (2007) Cardiovascular disease in spinal cord injury: an overview of prevalence, risk, evaluation, and management. Am J Phys Med Rehabil 86(2):142–152

National Spinal Cord Injury Statistical Center, Complete Public Version of the 2015 Annual Statistical Report for the Spinal Cord Injury Model Systems (2015). University of Alabama at Birmingham

Ogawa T, Asayama M (1978) Frequency of sweat expulsion as indicator of sudomotor neural activity. In: Houdas Y, Guieu JD (eds) Trends in thermal physiology. Masson, Paris, pp. 105–107

Olenik LM, Laskin JJ, Burnham R, Wheeler GD, Steadward RD (1995) Efficacy of rowing, backward wheeling and isolated scapular retractor exercise as remedial strength activities for wheelchair users: application of electromyography. Spinal Cord 33(3):148–152

Panisset MG, Galea MP, El-Ansary D (2016) Does early exercise attenuate muscle atrophy or bone loss after spinal cord injury? Spinal Cord 54(2):84–92

Paulson TAW, Goosey-Tolfrey VL, Lenton JP et al (2013) Spinal cord injury level and the circulating cytokine response to strenuous exercise. Med Sci Sports Exerc 45(9):1649–1655

Phillips CA, Danopulos D, Kezdi P et al (1989) Muscular, respiratory and cardiovascular responses of quadriplegic persons to an F. E. S. bicycle ergometer conditioning program. Int J Rehabil Res 12:147–157

Phillips AA, Cote AT, Bredin SS, Krassioukov AV, Warburton DE (2012) Aortic stiffness increased in spinal cord injury when matched for physical activity. Med Sci Sports Exerc 44:2065–2070

Phillips AA, Krassioukov AV, Ainslie PN, Warburton DER (2014a) Perturbed and spontaneous regional cerebral blood flow responses to changes in blood pressure after high level spinal cord injury: the effect of midodrine. J Appl Physiol 116:645–665

Phillips AA, Warburton DE, Ainslie PN, Krassioukov AV (2014b) Regional neurovascular coupling and cognitive performance in those with low blood pressure secondary to high-level spinal cord injury: improved by alpha-1 agonist midodrine hydrochloride. J Cereb Blood Flow Metab 34:794–801

Pollack SF, Axen K, Spielholz N, Levin N, Haas F, Ragnarsson KT (1989) Aerobic training effects of electrically induced lower extremity exercises in spinal cord injured people. Arch Phys Med Rehabil 70(3):214–219

Qui S, Alzhab S, Picard G, Taylor JA (2016) Ventilation limits aerobic capacity after functional electrical stimulation row training in high spinal cord injury. Med Sci Sport Exerc 48 (6):1111–1118

Rosety-Rodriguez M, Camacho A, Rosety I et al (2014) Low-grade systemic inflammation and leptin levels were improved by arm cranking exercise in adults with chronic spinal cord injury. Arch Phys Med Rehabil 95(2):297–302

Roy RR, Harkema SJ, Edgerton VR (2012) Basic concepts of activity-based interventions for improved recovery of motor function after spinal cord injury. Arch Phys Med Rehabil 93:1487–1497

Sclater A, Alagiakrishnan K (2004) Orthostatic hypotension. A primary care primer for assessment and treatment. Geriatrics 59:22–27

Scott WB, Lee SCK, Johnston TE, Binkley J, Binder-Macleod SA (2006) Contractile properties and the force-frequency relationship of the paralyzed human quadriceps femoris muscle. Phys Ther 86:788–799

Sheel AW, Reid WD, Townson AF et al (2008) Effects of exercise training and inspiratory muscle training in spinal cord injury: a systematic review. J Spinal Cord Med 31:500–508

Silva AC, Neder JA, Chiurciu MV et al (1998) Effect of aerobic training on ventilatory muscle endurance of spinal cord injured men. Spinal Cord 36:240–245

Spungen AM, Adkins RH, Stewart CA, Wang J, Pierson RN, Waters RL, Bauman WA (2003) Factors influencing body composition in persons with spinal cord injury: a cross-sectional study. J Appl Phys. 95(6):2398–2407

Stanton R, Reaburn P (2014) Exercise and the treatment of depression: a review of the exercise program variables. J Sci Med Sport 17(2):177–182

Subbarao JV, Klopfstein J, Turpin R (1995) Prevalence and impact of wrist and shoulder pain in patients with spinal cord injury. J Spinal Cord Med 18(1):9–13

Swain DP, Franklin BA (2006) Comparison of cardioprotective benefits of vigorous versus moderate intensity aerobic exercise. Am J Cardiol 97:141–147

Terson de Paleville D, McKay W, Aslan S et al (2013) Locomotor step training with body weight support improves respiratory motor function in individuals with chronic spinal cord injury. Respir Physiol Neurobiol 189:491–497

Thijssen DH, Ellenkamp R, Smits P, Hopman MT (2006) Rapid vascular adaptations to training and detraining in persons with spinal cord injury. Arch Phys Med Rehabil 87:474–481

Thijssen DH, Ellenkamp R, Kooijman M, Pickkers P, Rongen GA, Hopman MT et al (2007) A causal role for endothelin-1 in the vascular adaptation to skeletal muscle deconditioning in spinal cord injury. Arterioscler Thromb Vasc Biol 27(2):325–331

Turiel M, Sitia S, Cicala S et al (2011) Robotic treadmill training improves cardiovascular function in spinal cord injury patients. Int J Cardiol 149(3):323–329

Verellen J, Vanlanderijck Y, Andrews B, Wheeler GD (2007) Cardiorespiratory responses during arm ergometry, functional electrical stimulation cycling, and two hybrid exercise conditions in spinal cord injured. Disabil Rehabil Assist Technol 2(2):127–132

Washburn RA, Figoni SF (1998) Physical activity and chronic cardiovascular disease prevention in spinal cord injury: a comprehensive literature review. Top Spinal Cord Injury Rehabil 3:16–32

West CR, Campbell IG, Shave RE et al (2012) Effects of abdominal binding on cardiorespiratory function in cervical spinal cord injury. Respir Physiol Neurobiol 180:275–282

Wilbanks SR, Bickel CS (2016) Scapular stabilization and muscle strength in manual wheelchair users with spinal cord injury and subacromial impingement. Top Spinal Cord Injury Rehabil 22 (1):60–70

Yamanaka M, Furusawa K, Sugiyama H et al (2010) Impaired immune response to voluntary arm-crank ergometer exercise in patients with cervical spinal cord injury. Spinal Cord 48 (10):734–739

Chapter 2
Physiology of Motor Deficits and the Potential of Motor Recovery After a Spinal Cord Injury

V. Reggie Edgerton and Roland R. Roy

Abstract The focus of this chapter is to highlight some fundamental concepts on the physiology of movement control after a spinal cord injury (SCI). We will discuss how these concepts are defined by the order of motor unit recruitment within a motor pool and how the relative recruitment across multiple motor pools defines the movements performed. We then will describe how these factors are affected by SCI. Understanding how these particular "neural decisions" might be modified by SCI will provide greater insight in assessing the etiology of the movement dysfunctions and thus in finding potential resolutions in a given individual at a given time post-injury (Fig. 2.1).

2.1 Introduction

The focus of this chapter is to highlight some fundamental concepts on the physiology of movement control after a spinal cord injury (SCI). We will discuss how these concepts are defined by the order of motor unit recruitment within a motor pool and how the relative recruitment across multiple motor pools defines the movements performed. We then will describe how these factors are affected by SCI. Understanding how these particular "neural decisions" might be modified by SCI will provide greater insight in assessing the etiology of the movement dysfunctions and thus in finding potential resolutions in a given individual at a given time post-injury (Fig. 2.1).

V.R. Edgerton, Ph.D. (✉) • R.R. Roy, Ph.D.
Department of Integrative Biology and Physiology, University of California, Los Angeles, Terasaki Life Sciences Building, 610 Charles E. Young Drive East, Los Angeles, CA 90095-1527, USA

University of California, Los Angeles, CA 90095, USA

Brain Research Institute, University of California, Los Angeles, CA 90095, USA
e-mail: vre@ucla.edu; rrr@ucla.edu

J.A. Taylor (ed.), *The Physiology of Exercise in Spinal Cord Injury*, Physiology in Health and Disease, DOI 10.1007/978-1-4939-6664-6_2

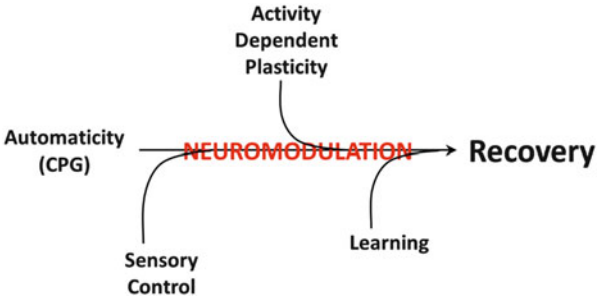

Fig. 2.1 Schematic that emphasizes the importance of multiple physiological concepts being combined in efforts to enhance the recovery of function after a SCI. Each of these concepts is discussed in some detail in the text

An initially useful perspective in understanding what is lost and what potentially can be recovered after a SCI is to consider the different sources and kinds of control of different types of motor tasks as occurs normally compared to the sources and kinds of control after a SCI. One useful general principle to consider is that the sources of control of movement are remarkably redundant. Another useful concept in understanding the potential for recovery is the dominance of the automaticity of the control strategies that are built into our nervous system, even for very complex movements. Although the level of automaticity that persists in routine movements is generally not recognized, the pervasiveness of this phenomenon can be readily understood when considering the persistent conservation of basic evolutionary mechanisms within the neuromotor systems. For example, we routinely and continuously assess the extensive details of every aspect of our movements in the context of what has occurred only a few milliseconds beforehand to essentially those that occurred probably even prenatally. In a sense our nervous system takes advantage of many different types of mechanisms that have evolved and have been conserved in our species. One might view this process as "evolutionary learning" and explain why the automaticity of control is such a pervasive and important feature of our control systems. Undoubtedly there are multiple mechanisms of learning and forgetting within the sensorimotor system that function within a wide range of time frames, all of which may be retaining some aspect of the experience of movement. It seems likely that these learning and forgetting processes occur throughout the neural networks that sense and control movement.

What are the sources of control of movement that are lost in part or in total after a SCI? After a complete separation of the caudal and rostral segments of the spinal cord, the lost sources of control certainly include the supraspinal centers in the brain that normally play a predominant role in these processes. In this context, all sensory information plays an important role in the control of movement. Stated another way, all sensory systems at some point project directly or indirectly to the motor networks. For example, sensory information related to vision, hearing, odor, and taste are normally available. After a SCI, however, there is some degree or even total loss of "*direct*" control of these systems innervated by the spinal segments distal to the lesion. Thus these physiological systems must rely on the processing

and translation of proprioception and cutaneous sensory input derived from the more caudal spinal segments, i.e., those below the level of the lesion. But additionally a paralyzed individual with a lesion at a mid-thoracic level may have lost normal access to multiple sensory modalities, although vision can remain a critical source of control of the upper body and thus enable the individual to ski and sail. An example of the level of redundancies in the neural control of movement has been demonstrated in an individual who is blind and paralyzed but can still walk proficiently with the aid of an exoskeletal device combined with transcutaneous spinal cord stimulation (Gad et al. 2015). This fact leads back to the importance of the plasticity within and among the different networks that can contribute to the control of movement after a SCI.

The experimental evidence is clear, however, that the potential control mechanisms that remain most important after a SCI is proprioception and cutaneous input. "Potential" is a key word here because to reclaim this source of control, significant plasticity must occur via a range of neuromodulatory interventions, including activity-dependent rehabilitation. This activity-dependent rehabilitation provides the opportunity for the spinal networks to learn what it practices, e.g., stepping and standing (Edgerton et al. 1997). The precision in movement that can be observed based on the neural networks that receive, process, and translate proprioceptive and cutaneous input in real-time is embedded within the sensorimotor networks throughout the spinal cord. Given the redundancy in the sources of control of movement, the loss of vision, hearing, taste and even equilibrium are much less prohibitive in one's level of mobility given that proprioception and cutaneous information is usually preserved after a SCI.

What, then, are the challenges in regaining motor function after a SCI? There is a severe loss in the ability to respond directly and precisely to the routine, ongoing, but highly comprehensive, sensing of the environmental surroundings. As noted above, proprioception and cutaneous inputs caudal to the lesion provide the information needed to assess the kinetics environment and to recognize the consequences of these kinetics. The robust feed-forward mechanisms within that spinal circuitry make it possible to translate this information in real time to generate the appropriate kinetics and kinematics of the complex musculoskeletal system without any input from supraspinal sources. A second factor is that the spinal circuitry can learn and improve motor skills with practice. Thus it appears that for rehabilitative strategies to be effective for recovering sensorimotor function they must (1) reengage the sensorimotor networks that generate a movement and (2) provide the opportunity to repeatedly engage the circuitry so that it can learn the task that it is being trained.

2.2 Adaptation of Neuromuscular Properties After a SCI

After a SCI, there are dramatic changes in the neuromotor units below the level of the lesion. In this section related to animal studies we will focus primarily on the effects of a complete spinal cord transection or spinal cord isolation, i.e., complete spinal cord transections at a mid-thoracic and a high sacral level plus bilateral deafferentation between the transection sites resulting in electrical silencing of the muscles innervated by the motoneurons located in the isolated spinal cord segment (Roy et al. 2007a). For the human we will focus on studies involving a severe SCI. In both cases we then will highlight activity-dependent rehabilitation strategies that influence the recovery of function at the neuromotor level.

2.3 Animal Studies

2.3.1 Adaptations Post-injury

Motoneurons located below the lesion after a complete spinal cord transection or within the isolated region of the spinal cord after spinal cord isolation have lower rheobase currents and higher spike after hyperpolarization amplitudes and input resistances compared to motoneurons in control animals (Button et al. 2008). In addition, these motoneurons also show depolarization of the resting membrane potential and voltage threshold (Beaumont et al. 2004; Cope et al. 1986; Hochman and McCrea 1994), decreased after hyperpolarization duration (Cope et al. 1986; Hochman and McCrea 1994; Czeh et al. 1978), and a rightward shift in the frequency–current relationship (Beaumont et al. 2004). Interestingly, the soma size and oxidative capability as reflected by quantitative histochemical determinations of succinic dehydrogenase activity are unaffected even months after either spinal cord transection or isolation (Roy et al. 2007b; Chalmers et al. 1992; Krikorian et al. 1982). There is some disassembly of neuromuscular synapses and a mild decrement in neuromuscular junction function after a spinal cord transection and, although transmission remains largely intact for supramaximal stimulation, these decrements could be related to the increased fatigue observed under non-supramaximal stimulation conditions (Burns et al. 2007; Ollivier-Lanvin et al. 2009). In addition, a slight increase (Cope et al. 1986) or no change (Mayer et al. 1984; Munson et al. 1986) in motor axon conduction velocity after a spinal cord transection has been reported.

There are a number of morphologic, phenotypic, and mechanical changes in the skeletal muscles below the level of the lesion. The muscles and muscle fibers atrophy, lose force capacity, show an increase in myosin ATPase activity, become "faster" phenotypically and mechanically, and have a decrease in fatigue resistance (Edgerton et al. 1996; Roy et al. 1991). After spinal cord transection there is an increase in the expression of the fastest MHC isoforms in both predominantly slow

and fast muscles, but with the response being more robust in slow muscles (Roy et al. 1991, 1999; Roy and Acosta 1986; Talmadge 2000). In general, the muscles also show a lower oxidative capacity, although the predominantly slow soleus muscle in cats and rats maintains its oxidative capacity as reflected by the staining patterns of succinate dehydrogenase and the levels of citrate synthase and resistance to fatigue.

Similar changes have been observed at the motor unit level. In general a higher percentage of motor units produce less force (Cope et al. 1986; Mayer et al. 1984; Gallego et al. 1978; Celichowski et al. 2006), have faster twitch mechanical properties (Cope et al. 1986; Mayer et al. 1984; Talmadge et al. 2002), show reduced levels of oxidative enzymes (Pierotti et al. 1994) and higher levels of glycolytic enzymes (Pierotti et al. 1994), and are more fatigable (Mayer et al. 1984; Munson et al. 1986; Celichowski et al. 2006) after either spinal cord transection or isolation. In addition, the motor units change towards a faster phenotype (Cope et al. 1986; Talmadge 2000; Gallego et al. 1978) and this is reflected in an increase in the percentage of fast motor units post-injury (Pierotti et al. 1994). The fibers comprising a single motor unit post-injury are of the same myosin immunohistochemical type and show a similar range in oxidative and glycolytic enzyme activities as in intact animals (Pierotti et al. 1994; Roy et al. 2008).

Combined all of these changes result in the neuromuscular system becoming weaker and less resistant to fatigue. Thus the strategy from a therapeutic and rehabilitation viewpoint is to counter or minimize these deficits.

2.3.2 Rehabilitation Strategies

Several forms of motor training have been somewhat successful in ameliorating the deficits in the neuromuscular system after a complete SCI in animals. For example, treadmill training (Roy et al. 1998a), "passive" cycling exercise (Dupont-Versteegden et al. 1998), stand training (Roy et al. 1998a; Jiang et al. 1990), and robotic loading during a step cycle (Nessler et al. 2011) have reduced the amount of atrophy and phenotypic changes in the muscles below a complete mid-thoracic spinal cord transection. Several motoneuron properties affected after a SCI such as depolarization of the resting membrane potential and voltage threshold, decrease in the excitability for rhythmic firing, increased amplitude of both the action potential after-hyperpolarization and synaptic input to motoneurons are normalized by either step training (Petruska et al. 2007) or cycling using a motorized ergometer (Beaumont et al. 2004; Gardiner 2006).

We have used the spinal cord isolation model to begin to determine the optimal type, duration, and frequency of contractile activity for maintaining muscle properties post-injury. This model has allowed us to impose a known amount and type of contractile activity on the otherwise silent muscles. The hindlimbs of spinal cord isolated cats were moved through a simulated step cycle and the soleus muscle was stimulated while being lengthened, shortened, or during an isometric phase for

30 min/day, 5 days/week for 6 months: isometric contractions was the most effective mode for maintaining the muscle properties close to normal (Roy et al. 2002). Interestingly, passive cycling thorough the same range of movement ameliorated the effects of spinal cord isolation on the soleus mass, force capability, and maximum shortening velocity (Roy et al. 1998b). Using the same model in rats, we then showed that the same amount of daily contractile activity distributed at 2–3 intervals during the day was more effective in maintaining the properties of the soleus and medial gastrocnemius muscles than one bout per day (Kim et al. 2007, 2010; Haddad et al. 2003a, b).

2.4 Human Studies

2.4.1 Adaptations Post-injury

Human studies generally have reported similar changes as those observed in animals in the neuromuscular system post-injury. Compared to normal controls, there is a decrease in muscle cross sectional area (Shah et al. 2006; Mohr et al. 1997; Ragnarsson 1988) and peak torque (Krieger et al. 2005; Jayaraman et al. 2008; Lotta et al. 1991; Castro et al. 1999a, b), lower oxidative capacity (Gerrits et al. 2003; Rochester et al. 1995), and a decrease in fatigue resistance to repetitive activation reflecting a decrease in the percentage of slow fatigue resistant fibers in the muscle groups below the lesion (Talmadge 2000; Mohr et al. 1997; Rochester et al. 1995; Grimby et al. 1976; Martin et al. 1992; Olsson et al. 2006; Gerrits et al. 1999, 2001; Shields et al. 1997; Gaviria and Ohanna 1999; Butler and Thomas 2003).

In chronic SCI, the muscles below the lesion generally have faster contractile properties, e.g., a shorter contraction and half-relaxation time, most likely reflecting changes in muscle fiber composition toward a predominance of fast glycolytic fibers (Rochester et al. 1995; Gerrits et al. 1999, 2001; Shields et al. 1997). Single fiber analyses from chronic spinal cord injured subjects also show an increased contraction velocity (Malisoux et al. 2007).

There is a high incidence of diabetes in individuals with a SCI (Duckworth et al. 1980; Bauman et al. 1999; Lavela et al. 2006). Functional electrical stimulation (FES) paradigms help regulate common pathways involved with glucose metabolism (Petrie et al. 2014). For example, FES during exercise can decrease blood glucose levels and improve glucose utilization (Jeon et al. 2002) resulting in a decrease in the glucose intolerance and insulin resistance associated with paralysis (Bauman and Spungen 1994).

2.4.2 Rehabilitative Strategies

A variety of functional electrical stimulation (FES) modalities with some form of loading on the musculature have been somewhat effective in restoring the neuromuscular deficits associated with a SCI. FES paradigms involving isometric resistance training (Dudley et al. 1999), cycling (Duffell et al. 2008; Crameri et al. 2002; Baldi et al. 1998; Scremin et al. 1999), and lifting ankle weights with isotonic contractions (Rodgers et al. 1991; Mahoney et al. 2005; Gorgey and Shepherd 2010) have resulted in improvement in neuromuscular function. For example, training programs involving FES cycling (Mohr et al. 1997; Liu et al. 2007; Pacy et al. 1988; Hjeltnes et al. 1997; Sloan et al. 1994), FES ambulation (Klose et al. 1997; de Abreu et al. 2009), FES resistance training, and vibration exercise (Melchiorri et al. 2007) produced significant increases in muscle mass, with training frequencies ranging from 2–7 per week, for 8–52 weeks duration.

The contractile properties also revert toward normal values. The muscles become slower contracting (Rochester et al. 1995; Harridge et al. 2002), there is an increase in muscle force (Crameri et al. 2002; Gerrits et al. 2002; Hartkopp et al. 2003), an increased fatigue resistance (Rochester et al. 1995; Martin et al. 1992; Harridge et al. 2002; Gerrits et al. 2002; Hartkopp et al. 2003; Shields and Dudley-Javoroski 2006, 2007), and half-relaxation time returns to normal (Rochester et al. 1995). Electrically induced stimulation increases the glycolytic and mitochondrial oxidative enzyme levels (Kjaer et al. 2001) and there is an increase in both SDH activity (Rochester et al. 1995; Martin et al. 1992) and citrate synthase activity (Mohr et al. 1997; Crameri et al. 2002; Chilibeck et al. 1999).

Chronic FES training regulates metabolic gene signaling pathways in human paralyzed muscle (Petrie et al. 2014). Although acutely paralyzed muscles in humans appear to be fatigue resistant and oxidative, they transform into highly fatigable, glycolytic muscle after one year of paralysis (Shields 1995). Long term studies have shown that the size, fatigue resistance, oxidative enzyme levels, and contractile speed can be sustained using FES that includes loading of the musculature (Shields and Dudley-Javoroski 2006, 2007; Shields et al. 2006; Adams et al. 2011). It appears that variable frequency trains are more effective than constant frequency trains because they are less fatiguing (Deley et al. 2015) and that the inclusion of doublets enhances the torque production (Chang and Shields 2011).

Body weight support treadmill training has been shown to be very effective in recovering locomotor function (Roy et al. 2012), and there is some indication that this may be related to changes in the neuromuscular properties. Recently, it has even been shown that body weight–supported treadmill training (without FES) can increase muscle cross-sectional area (Giangregorio et al. 2005, 2006) and muscle fiber size and oxidative capacity in incomplete SCI subjects (Stewart et al. 2004; Adams et al. 2006).

FES also has a profound effect on fiber phenotype: there have been reports of a decrease in the proportion of type IIX fibers (the fastest fiber phenotype) and type II