Cross-education of strength and skill: an old idea with applications in the aging nervous system

Trevor S. Barss\textsuperscript{a, h, c, d}, Gregory E.P. Pearcey \textsuperscript{a, h, c, d}, and E. Paul Zehr\textsuperscript{a, h, c, d, e}\textsuperscript{*}

\textsuperscript{a}Rehabilitation Neuroscience Laboratory, University of Victoria, Victoria, BC, Canada; \textsuperscript{b}Human Discovery Science, International Collaboration on Repair Discoveries (ICORD), Vancouver, BC, Canada; \textsuperscript{c}Centre for Biomedical Research, University of Victoria, Victoria, BC, Canada; \textsuperscript{d}School of Exercise Science, Physical, and Health Education, University of Victoria, Victoria, BC, Canada; \textsuperscript{e}Division of Medical Sciences, University of Victoria, Victoria, BC, Canada.

Edward Wheeler Scripture’s 1894 work out of the Yale Psychological Laboratory has been influential in identifying the nervous system’s contribution to the bilateral improvements that are seen with unilateral strength and skill training. Scripture coined the term “cross-education” to describe this improvement in the untrained contralateral limb. While physiological changes accompany aging that may negatively affect the performance of physical tasks, far too much credit has been given to the natural aging process rather than the effects of inactivity. Emerging evidence indicates strength or skill training interventions induce significant neuroplasticity in an aging population. The model of unilateral training provides a unique approach in which to elicit such plasticity. This brief review highlights the innate ability of the nervous system to adapt to unilateral strength and skill training interventions, regardless of age, and provides a novel perspective on the robust plastic ability of the aging nervous system.

“Thus, training of one portion of the body trains at the same time the symmetrical part and also neighboring parts. … The training seems to be of a psychical rather than of a physical order and to lie principally in steadiness of attention.”
--- Edward Wheeler Scripture, 1894

INTRODUCTION

Can you gain strength and skill in a limb that you do not train? This question was answered when Edward Wheeler Scripture published his seminal paper, “On the education of muscular control and power” in 1894 out of the Yale Psychological Laboratory. Although the true merits of this paper would not be recognized for more than a century, its novel findings, describing adaptations resulting from physical and skilled training, continue to influence scientific literature to this day.

Most notably, Scripture coined the term “cross-education,” describing the improvement in performance of not only the trained limb, but also in the untrained contralateral limb, now commonly known as the “cross-transfer” effect. While these terms continue to be used interchangeably, cross-education will be used throughout this review for historical context.

Recent evidence from both clinical and basic science experiments support Scripture’s original work and highlight the immense ability for the nervous system to adapt to physical training [1-15]. The opening quote highlights Scripture’s hypothesis that the contralateral training effect was of a “psychical” rather than a “physical” order, which describes early evidence for training-induced changes in the nervous system (neuroplasticity).

Neuroplasticity remains a key feature across the lifespan, allowing individuals to improve movement skills continuously.

\*To whom all correspondence should be addressed: E. Paul Zehr, P.O. Box 3010 STN CSC, University of Victoria, Victoria, BC V8W 3P1, Canada. Tel: 250-721-8379; Fax: 250-472-5063; Email: pzehr@uvic.ca.

\ddagger Abbreviations: BDNF, brain derived neurotropic factor; ROM, range of motion

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Yet, while the nervous system can adapt in response to physical training to produce positive results, the nervous system can also become maladaptive when not adequately stressed on a regular basis. In this case, the old adage firmly applies in that “if you don’t use it, you lose it.”

While physiological changes accompany aging and can negatively affect the performance of physical tasks, far too much credit is given to the natural aging process, rather than inactivity [16]. Over the past 30 years, evidence for cross-education suggests a manifestation arising from small changes occurring simultaneously at multiple levels of the nervous system including cortical, sub-cortical, and spinal reflex pathways.

While neural mechanisms are not the focus of this article, a number of excellent reviews have been published on the topic [1,3,11,17].

The intent of this brief review is to highlight the innate ability of the nervous system to adapt across the lifespan through a model of cross-education.

Exploring the historical context through which cross-education was identified provides a clear perspective on the robust ability for change while providing a novel rehabilitation strategy that may be employed when one side of the body is more affected than the other, such as in the case of surgery, immobilization, stroke, multiple sclerosis, or spinal cord injury.

**19TH-CENTURY EVIDENCE FOR CROSS-EDUCATION**

Scripture’s approach was guided by two earlier studies using entirely different modalities exploring skill specific adaptation with training. Gustav Fechner was a philosopher, physicist, and experimental psychologist whose formative work in 1857 documented how training a task could increase performance.

In his report (in which he was the lead author and sole participant), Fechner lifted two dumbbells (~9 lbs in each hand) up over his head as many times as he could, every day, for 60 consecutive days [18]. Fechner performed 104 and 692 repetitions on days 1 and 55, respectively (Figure 1). While the result is quite underwhelming based on our current understanding of training adaptation, the detailed time-course that was documented has rarely been explored or detailed even to this day.

While Fechner’s work clearly illustrated that motor performance improvements to strength training existed in the trained limbs, further work by Alfred Wilhelm Volkmann, a physiologist, anatomist, and philosopher who specialized in the nervous system, revealed that training of a single limb can also affect an untrained limb. The focus of his work attempted to uncover whether perceptual tactile sensitivity could be improved by training.

A paper in 1858 showed that training the ability to detect touch of only the left fingertip for several weeks resulted in an improved ability to perceive tactile sensation not only of the trained finger, but also of the right, contralateral fingertip despite not using it at any point in the training protocol [19]. Further experiments also found that practice on the third phalanx increased touch sensitivity on the first phalanx.

Because of work by Fechner and Volkmann, Scripture recognized a relation between training and cross-limb tactile effects and decided to explore the effects of strength or skill training with only one limb. In a similar fashion to the Fechner paper, Scripture had two co-authors of his work perform training with a single arm [20].

The first participant, identified as Miss Brown, completed a strength training (“muscular power”) task by squeezing a rubber bulb, similar to that of the end of a blood pressure cuff. The second participant was identified as Miss Smith, and she completed a skill training (“muscular control”) protocol by trying to put a needle through
an electrified drill board with holes of decreasing diameter. If the needle touched the metal on the board, the trial ended. The task appears to be similar to the modern board game “Operation” (Hasbro Inc.).

Unsurprisingly, Miss Smith improved her percentage of successful trials by ~40 percent, while Miss Brown increased strength by almost 70 percent in the trained right limb, both results being referred to as effects of “practice.” Interestingly, results in the untrained limbs showed that Miss Smith increased accuracy by 50 percent, and Miss Brown got ~43 percent stronger. Scripture suggested that these effects were due to “indirect practice.”

After 1894, the idea of cross-education laid dormant for close to a century until researchers began exploring the functional properties in many different muscles and tasks while using advanced methodologies, including imaging to explore locus and mechanism. Only recently has its possible use in rehabilitation from unilateral injuries received noteworthy consideration [12,21].

MODERN INTERPRETATIONS OF CROSS-EDUCATION

Recent review papers have highlighted cross-education for its potentially relevant use as a rehabilitation tool for unilateral injuries [12,21]. A series of pseudo-clinical studies indicated that strength in an immobilized limb can be maintained by strength training the free limb [22-25].

Cross-education, or the cross-transfer effect, has come to be defined as an improvement in strength or skill performance of the untrained contralateral limb after unilateral training of the opposite homologous limb [26] and these training effects appear to be independent of gender [1,17,27].

Meta-analyses have determined the strength increases in the untrained contralateral limb are about 35 percent of the strength that is gained in the trained limb [28,29], and on average, represents an ~8 percent increase in strength from baseline in the untrained contralateral limb. Skilled task performance also shows bilateral improvements as a result of unilateral training [30], which may provide similar neural mechanisms that allow the cross-transfer effect to occur similarly between tasks.

In recent years, the mechanistic understanding of cross-education has increased substantially [1,3,9,17,30], and although many details have yet to be identified, it is clear that the effect is due to changes within the nervous system. There appear to be many small contributions at multiple levels of the nervous system including cortical, sub-cortical, and spinal reflex pathways, which produce the contralateral increases in strength or performance [23,25,31-33].

Two main theories, which are not mutually exclusive, have been proposed to explain how unilateral training can produce bilateral changes in the cortex of the brain. They include the “cross-activation” and “bilateral access” hypotheses [3]. The cross-activation theory suggests that bilateral activation of the motor pathways occurs during unilateral movement tasks, which in turn produces bilateral increases in corticospinal excitability. The bilateral access model proposes that motor engrams formed during unilateral movements may be used bilaterally during future movements.

However, there is no empirical evidence to identify if either or both of these hypotheses are the sole contributors to the cross-education effect.

Early experiments observing the effects of unilateral training on reflex pathways suggested that there were little to no contralateral effects on the spinal circuitry in response to unilateral training [34,35]. However, when more sensitive measures, (which included recruitment thresholds in both agonist and antagonist muscles) were employed by Dragert and Zehr [36], evidence for bilateral alterations in spinal reflex excitability was found.

Since it is clear that cross-education is due to changes in the nervous system, it provides an excellent model to explore whether similar improvements are seen with aging. An aging nervous system that can improve skill or strength bilaterally by training only one limb would highlight an innate ability for neuroplasticity, regardless of age.

TRAINING-INDUCED PLASTICITY OF THE NERVOUS SYSTEM DOES NOT EXPIRE

It is commonly assumed that decreased muscular strength and endurance accompany the aging process. In fact, muscular strength has been documented to begin declining in the fifth decade [37-39], and this decrease in strength accelerates as individuals reach their 70s [37,38]. Many neural mechanisms have been associated with this decrease in muscular strength as people age. These changes have included: decreased motor unit discharge rates [40,41], alterations in reflex excitability [42], increased antagonist muscle co-activation [10,43-45], decreased maximal voluntary muscle activation [42,46-48], increased intra-cortical inhibition and decreased intra-cortical facilitation [49], decreased excitability of both excitatory and inhibitory spinal pathways [50], and decreased excitability of the corticospinal pathway [51].

However, resistance training reduces the rate of decline and even increases strength in the elderly due to improvements in many of the same pathways that are thought to decline with age [52]. Recent work by various groups has identified many neural mechanisms that contribute to the maintenance or increase in strength after intervention [7,10,53-55].

Neural adaptations to resistance training interventions documented in the elderly include: increased muscular strength [7,10,53-55], alterations of voluntary muscle activation and co-activation patterns [10], increased circulating levels of brain-derived neurotropic factor (BDNF) [54], altered cortical inhibition processes [7], altered descending drive to muscles [53], increased volume of white matter in the brain [55], and improved memory [55].
These studies clearly indicate that changes within the aging nervous system can occur with training to produce significant increases in strength.

Interestingly, recent studies indicate age is not a limiting factor to strength increases transferred to the untrained limb [5,6,13,27,56]. Evidence of cross-education occurring across the lifespan provides a novel perspective on training-induced neuroplasticity.

**TRANSFERRING NEW TRICKS TO TWO SIDES OF AN AGING BRAIN**

A large body of work has documented cross-education in a predominantly younger population; however, this does not mean that the aging population cannot benefit from unilateral training to induce contralateral adaptations when appropriate. Asymmetries occur in a variety of circumstances within elderly populations and may result from neurological impairment and/or lateral immobilization requiring rehabilitation. In these situations, it may be difficult or impossible to train the injured limb due to the severity of disability.

Previous experiments have suggested that same-day inter-limb transfer of ballistic motor-skill training is less prominent in older individuals compared to younger individuals [57,58].

However, a number of strength-training interventions within an elderly population have demonstrated significant neuroplasticity via the cross-education effect.

Tracy et al. [27] examined whether unilateral training of the quadriceps three times per week for nine weeks produced bilateral increases in strength in an older population. Twelve men (ages 65 to 75) and 11 women (ages 65 to 73) were recruited for the study. After training, there were similar increases in strength in the trained limb for both men (27±3%) and women (29±4%). There were also significant increases in the untrained quadriceps for both men (10±3%) and women (12±4%), indicating neither gender nor age played a role in the strength transfer.

Bemben et al. [56] examined whether age affected the transfer of strength from the trained right to the untrained left limb after elbow flexion training each day for two weeks. Twenty females were divided into a young (n = 10; 20.8±0.1 years) or an older (n = 10; 58.1±0.14 years) group. After completing the same training regime, both the young and older groups exhibited similar increases in strength of both the trained (28 percent) and untrained (12 percent to 15 percent) elbow flexors, indicating age had relatively little effect on cross-education.

A more recent study by Ehsani et al. [59] also compared the cross-education effect between a group of young individuals (28.3±3.1 years) and older individuals (73.1±5.3 years). Participants completed elbow flexion exercises each day for two weeks, which led to significant increases in both the trained (young 31 percent; older 52 percent) and untrained (young 24 percent; older 39 percent) limbs for both groups. While the elderly groups within these studies have lower absolute strength, their ability to increase strength (percentage) in response to resistance exercise appears very similar across lifespan.

Recently, three studies have explored the possible clinical applications of cross-education within an aging population. Magnus et al. [5] explored whether an at-home resistance tubing strength-training program on one shoulder would produce strength increases in the trained and untrained shoulder. Twenty-seven participants were recruited in the training group (63.3±10.2 years), while 24 participants (62.7±10.2 years) were recruited to the control group. The training group completed multiple shoulder exercises during an at-home resistance tubing program three days a week, for four weeks. Training produced increases in external (10.9 percent; 12.7 percent) and internal (14.8 percent; 14.6 percent) rotator strength in the trained and untrained limbs, respectively, while the control group showed no changes.

Thus, an at-home resistance tubing training program in one limb, provided to individuals ages 44 to 77, produced significant contralateral increases in strength.

A randomized controlled trial by Magnus et al. [6] explored whether cross-education could be applied during recovery after unilateral distal radius fractures on muscle strength and range of motion (ROM). Thirty-one women older than 50 (63.0±10.1 years) with a unilateral distal radius fracture were recruited to participate in the study. Participants were randomized to a standard rehabilitation group or standard rehabilitation plus strength training in the non-fractured hand. Training was completed at home three times a week, for 26 weeks.

The fractured hand was significantly stronger (17.3±7.4 kg Vs. 11.8±5.8 kg) and the ROM was increased (100.5°±19.2° Vs. 80.2°±18.7°) in the training group compared to the control group at 12 weeks post-fracture. This indicates that a group of women (ages 48 to 84) who sustained a wrist fracture recovered strength significantly faster when they completed resistance training on their non-fractured free limb.

Another recent study by Dragert and Zehr [13] explored whether those with chronic stroke are able to increase strength and muscle activation of their more affected side by training only the less-affected side. Nineteen participants (58.3±12.2 years), who were on average 84.1±77.6 months post-infarct, completed six weeks of unilateral dorsi-flexion resistance training on their less-affected side.

Although the focus was on stroke, these participants were mainly elderly with the oldest being 81 years old.

Large contralateral increases in strength and muscle activation were observed. Remarkably, four participants who were unable to produce any measurable force or muscle activity at baseline were able to functionally dorsiflex after the intervention. These changes can have a meaningful effect on quality of life for individuals with significant impairment.
CONCLUSIONS

Taken together, these studies indicate a profound ability of the nervous system to continue to adapt late in the aging process. Although the magnitudes of improvement may not be equi-vocal, there does not appear to be an age ceiling preventing benefit from skill or strength-training interventions across the human lifespan.

Furthermore, while the concept of neuroplasticity across the lifespan is not unique to movement paradigms, cross-education has substantial potential for implications in rehabilitation from injuries or pathology, to which the elderly tend to be more prone. This includes not only limb immobilization and post-stroke weakness, but also where other asymmetries may be present (post-surgery, multiple sclerosis, spinal cord injury, etc.).

Future research is needed in both animal and human models to differentiate the aging-specific from the inactivity-specific changes within the nervous system. Regardless, this review provides empirical evidence to support the idea that cross-education and neuroplasticity has no expiry date in the aging human nervous system.

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