Pediatric Pain Letter

Commentaries on pain in infants, children, and adolescents

April 2008

Vol. 10 No. 1

www.pediatric-pain.ca/ppl

Editor: Carl L. von Baeyer, carl.vonbaeyer@usask.ca

© 2008, Patrick J. McGrath & G. Allen Finley

Please visit the website for information on submission and review

Commentary The paradox of physical activity and pain for children with juvenile idiopathic arthritis

Susan Tupper

For children with juvenile idiopathic arthritis (JIA), physical activity occupies a paradoxical relationship with pain. Participating in physical activity can make pain worse and pain is often cited as a barrier to activity participation. However, regular physical activity over the longer term has been shown to help reduce pain, fatigue and disability and to improve quality of life. Patients beginning an exercise program struggle with this apparent contradiction especially during the first several weeks until functional improvements are observed. It is the role of clinicians to support patients to remain active and explain the possible harms and benefits of physical activity. Patients must continually strive for a level of exercise that stresses their systems sufficiently to improve function yet avoid a level that causes an excessive symptom reaction, signalling that the patient has exceeded a safe limit. It is important to understand the relationship between physical activity and pain in order to support children in pursuing increased activity levels, both as a pain management method and for their general health. This commentary will explore the relationship between physical activity and pain: (a) by summarizing the evolutionary, physiological and psychological processes that contribute to avoidance of physical activity when in pain, and (b) by reviewing the current literature on the benefits of physical activity for children with JIA.

Juvenile Idiopathic Arthritis

JIA encompasses seven distinct subtypes of childhood arthritis with international prevalence that ranges from 0.07 to 4.01 per 1,000 children (Manners & Bower, 2002). Although the clinical presentation varies by subtype, pain is a common experience for children with JIA. In a study by Sherry et al. (1990), 86% of children with arthritis reported pain during a routine clinic visit. Schanberg et al. (2003) found that children with polyarticular juvenile arthritis followed daily for two months reported pain on 73% of days.

Physical activity impairments are also common in children with arthritis. Children with JIA demonstrate lower daily activity levels compared to healthy controls and report lower participation in leisure time physical activity (Henderson et al., 1995; Takken et al., 2003a). Cardiovascular fitness levels are significantly reduced in children with both active disease and those in remission, with JIA groups exhibiting 22% lower cardiovascular fitness than healthy peers (Takken et al., 2002; Paap et al., 2005). Muscle strength is also significantly lower in children with JIA (Fan et al., 1998; Takken et al., 2003b; Broström et al., 2004).

Pain-related activity interference

Schanberg et al. (2003) found significant associations between functional disability and higher levels of daily pain (r = 0.44) and higher

percentage of days with pain (r = 0.42) in children with arthritis. This study also found that higher pain intensity and higher numbers of painful locations predicted reduced participation in school and social activity in children with arthritis. Adults with arthritis cite pain as a primary barrier to physical activity (Wilcox et al., 2006). Randomized controlled trials of physical activity interventions report dropouts due to pain exacerbation with exercise in children with JIA (Singh-Grewal et al., 2006).

Although it may seem intuitive, it is worth questioning why individuals in pain restrict physical activity participation. Pain behaviors typically include guarding and avoiding use of the symptomatic body part. These behaviors are thought to be an evolutionary mechanism to communicate distress and danger while at the same time protecting the injured area from further harm (Williams, 2002). Archetypal avoidance behaviors can not fully explain why children with arthritis pain avoid activity. Avoidance behaviors are adaptive when pain is acute. However, when pain persists, activity avoidance becomes maladaptive and can contribute to a cycle of muscle and cardiovascular deconditioning and loss of joint or muscle range of motion leading to a reduced capacity for physical activity and subsequent disability.

Physiological bases for reduced physical activity

in muscle Impairments strength and cardiovascular fitness are thought to result in part reduced activity participation due to pain from and limited joint range of motion (Bar-Or, 1986; Klepper, 2003). However. disease-related pathophysiological changes such as changes in muscle and nerve activity and organization further contribute to the challenge of remaining active with arthritis.

In the presence of persistent inflammation, thresholds for afferent nociceptive fibers are lower than normal due to peripheral biochemical mediators acting both directly and indirectly on the cell membranes (Dray, 1995). Therefore, normally innocuous events such as daily physical activity or exercise can cause pain. Likewise, central sensitization contributes to lower pain thresholds (Hogeweg et al., 1995).

Physical activity, even in the absence of tissue damage, can cause a proliferation of chemical mediators known to affect nociception. For example, interleukin 6 (IL-6), a proinflammatory cytokine, is produced by contracting skeletal muscle tissue in proportion to the intensity of physical activity performed (Moldoveanu et al., 2001; Shephard, 2002). Further research is needed to determine the cytokine response to physical activity in healthy children and those with pathology and the implications for the role of cytokines produced during physical activity on disease symptoms. An example of such a study would be a comparison of the cytokine response to activity between healthy children and children with arthritis to determine whether the arthritis group has a greater expression of pro-inflammatory cytokines with activity or whether the cytokine cascade has a similar timing in response to physical activity. Do children with elevated baseline levels of IL-6 have a parallel pattern of cytokine expression to healthy children or is the anti-inflammatory response delayed or suppressed? It is unlikely that increased levels of IL-6 act alone to heighten the pain response following exercise; however, if different patterns of immune response exist this could have implications for the intensity of exercise prescribed.

Lindehammar and Bäckman (1995) found that muscles around an inflamed joint produced only 45-65% of expected strength whereas there was only a slight reduction (10%) of strength around unaffected joints in children with arthritis. Muscle atrophy (wasting) and changes to muscle composition also contribute to reduced strength and fitness (Lindehammar & Bäckman, 1995; Klepper, 2003; Lindehammar & Lindvall, 2004).

Psychological and social bases for physical activity avoidance

Bio-behavioral models of chronic pain purport that activity avoidance is a learned or conditioned response (Turk & Marcus, 1994; Flor & Hermann, 2004). For example, when a child with arthritis experiences pain from climbing stairs, his memory of the pain may inhibit him from performing that activity for fear of harming himself or experiencing pain again. He may develop fear-avoidance of climbing stairs and avoid them whenever possible (Vlaeyen & Linton, 2000).

A recent study by Feldman et al. (2007) on adherence to prescribed exercise revealed that children with JIA reported only moderate (54-64%) adherence. In this study, parent beliefs of treatment helpfulness were significantly associated with adherence to prescribed exercises. An exacerbation of a child's pain either during or shortly following exercise may have a strong influence on the parent's or child's belief in the potential harm of the activity.

Social modeling and reinforcement by parents, teachers and peers affect both physical activity choices (Gyurcsik et al., 2006) and avoidance behaviors (Reid et al., 2005). Children without pathology report numerous intrapersonal, interpersonal (social) and environmental barriers to physical activity (Gyurcsik et al., 2006). Further qualitative studies are needed to identify barriers to physical activity specific to children with JIA. Factors worth investigating for their influence on adherence to exercise include fatigue (as a side effect of medications or sleep disturbance due to pain), short-term symptom response with daily activities or prescribed exercises, fear-avoidance of activity, and parental belief in the harm or benefit of activity. This knowledge will help clinicians target intervention strategies and support children with JIA as they pursue increased levels of activity.

Patterns of pain response

Temporal relationships must be explored in order to identify patterns of pain response to activity in children with JIA. These patterns of response will contribute to the knowledge of causal mechanisms between physical activity and pain. For example, in healthy individuals, pain from physical activity results from acute injury, delayed onset muscle soreness, mechanical inefficiencies, or overuse; however, pain can also be a signal of achieving maximal exertion that results in a training effect. Much of the pain response to physical activity in children with JIA follows similar patterns to healthy individuals, albeit with altered pain perception due to physiological and psychological processes.

Sorting through the various manifestations of pain in response to exercise can be confusing for children who may have had limited previous exposure. Children with arthritis need instructions and supervision for a safe introduction to exercise to help them distinguish between the sensations produced by the innocuous "hurt" of reactivating unconditioned muscles or the beneficial end range stretch of a restricted joint and the "harm" of excessive activity that results in tissue damage or aggravation of inflammation. Understanding temporal patterns of pain response to activity as well as the different qualities of sensation (e.g. aching versus burning) will help patients comprehend the complex web of acute on chronic pain.

Benefits of physical activity

The known health benefits of regular physical activity are well documented. These include improved cardiovascular conditioning, strength, flexibility, and balance (proprioception) as well as social and psychological benefits. Regular physical activity is also known to reduce the risk of obesity, osteoporosis, and mortality and morbidity from some cancers, diabetes, and cardiovascular disease (Warburton et al., 2006). For children with JIA, regular physical exercise is a primary treatment recommendation for general health and disease management and is essential in light of the low levels of physical activity participation (Simon et al., 2002).

A number of recent studies have found that regular physical activity results in reduced pain in children with arthritis. Singh-Grewal et al. (2007), in a randomized controlled trial comparing vigorous and gentle exercise over an eight-week period, demonstrated benefits for disease symptoms in both treatment arms, despite the lack of a significant change in cardiovascular fitness. Pilot studies have found similar results with a 15-week long aquatic exercise program (Takken et al., 2001) and a 12week land and water based exercise program (Singh-Grewal et al., 2006).

The beneficial impact of regular exercise on disease symptoms has been attributed to improved capacity for exercise; however, the reduction of disease symptoms in the absence of significant changes in cardiovascular conditioning or muscle strength points to the need to look for alternate causal mechanisms. Recent changes in the

understanding of causes of physiological fatigue may inform this argument. Traditional theories of physiological fatigue claim that fatigue from maximal exercise occurs when the body reached a physiological end point due to overwhelming the body's ability to meet the demands of working muscles (Noakes & St Clair Gibson, 2004). This claim does not stand up to current research that demonstrates a closely regulated reserve of muscle capacity with high intensity exercise. New models suggest that the sensation of fatigue is regulated by the central nervous system through redundant central and peripheral neurologic and metabolic mechanisms. Fatigue is thought to be "an interpretation of the effect of the current level of activity on future exercise capacity and any threats that immediate and future events pose to the maintenance of homeostasis" (Noakes et al., 2004, p. 513). Likewise, regular exercise may act to reduce symptoms through redundant physiological and psychological mechanisms; possibly through a "recalibration" of the central nervous system's interpretation of the potential threat of an activity in relationship to successful exercise exposure. If exercise is considered to be a form of systematic desensitization, the implications are that symptom reduction can occur with very gentle and gradual exposures, as the study by Singh-Grewal et al. (2007) would seem to suggest. Depending on the needs of the child, alternate exercise goals may be to improve cardiovascular condition or muscle strength, and these would require a more exhaustive exercise.

Activity recommendations

Research to date has varied widely in the length, intensity, frequency and types of exercises studied. Despite these variations, there are consistent trends for reduced symptoms with regular exercise and a general tolerance of many types of exercise by children with arthritis (Takken et al., 2001; Klepper, 2003, 2007; Singh-Grewal et al., 2006, 2007). It should be emphasized that these studies included small samples and may not generalize to the entire JIA population. In the absence of definitive guidelines for best practice it would seem that any activity that is tolerated and acceptable to the child would be appropriate with adequate supervision and monitoring for exacerbation. Further research is needed to determine patient characteristics that predict poor response to physical activity so that education and exercise prescription can be appropriately tailored. As research develops toward identifying the most effective exercise protocols for children with arthritis, clinicians must seek to match the activities to the needs of the child by keeping in mind the treatment goal, be it pain relief, strengthening, cardiovascular conditioning or range of motion. Most importantly, treatment goals must be balanced with the activity preferences of the child.

Conclusion

Although children with arthritis struggle to remain active and to understand the contradictory effects that physical activity can have on pain, it is a struggle worth pursuing. Evolutionary protective mechanisms, physiological changes due to inflammation and psychological processes all contribute to activity avoidance for the child in pain. However, regular physical activity is used as a therapeutic tool in the treatment of arthritis pain. Further research is needed to understand the role that physiological, psychological and social factors play in both activity avoidance due to pain and the contribution to reduced pain with exercise. This research will contribute to a better understanding of the interaction between pain and physical activity in order that clinicians and parents may support children with arthritis in pursuing increased activity levels as a pain management method and for their long-term health and well-being.

Susan Tupper, BScPT

PhD student, Department of Community Health and Epidemiology, University of Saskatchewan, Saskatoon, Canada email: susan.tupper@usask.ca

Acknowlegdement

The author is supported by *Pain in Child Health*, a Strategic Training Initiative in Health Research of the Canadian Institutes of Health Research, and by the University of Saskatchewan College of Medicine. The author thanks the Research Group on Pain in Childhood at the University of Saskatchewan for their feedback on this manuscript.

References

Bar-Or O. Pathophysiological factors which limit the exercise capacity of the sick child. Med Sci Sports Exerc 1986;18:276-282.

www.ncbi.nlm.nih.gov/pubmed/3724407

Broström E, Nordlund MM, Cresswell AG. Plantar- and dorsiflexor strength in prepubertal girls with juvenile idiopathic arthritis. Arch Phys Med Rehabil 2004;85:1224-1230.

www.ncbi.nlm.nih.gov/pubmed/15295744

Dray A. Inflammatory mediators of pain. Br J Anaesth 1995;75:125-131.

www.ncbi.nlm.nih.gov/pubmed/7577246

Fan J, Wessel J, Ellsworth J. The relationship between strength and function in females with juvenile rheumatoid arthritis. J Rheumatol 1998:25:1399-1405. www.ncbi.nlm.nih.gov/pubmed/9676775

Feldman DE, de Civita M, Dobkin PL, Malleson P, Meshefedjian G, Duffy CM. Perceived adherence to prescribed treatment in juvenile idiopathic arthritis over a one-year period. Arthritis Rheum 2007;57:226-233. www.ncbi.nlm.nih.gov/pubmed/17330298

Flor H, Hermann C. Biopsychosocial models of pain. In: Dworkin RH, Breitbart W, editors. Psychosocial aspects of pain: a handbook for health care providers. Seattle, WA: IASP Press, 2004. pp 47-75.

Gyurcsik NC, Spink KS, Bray SR, Chad K, Kwan M. An ecologically based examination of barriers to physical activity in students from grade seven through first-year university. J Adolesc Health 2006;38:704-711. www.ncbi.nlm.nih.gov/pubmed/16730599

Henderson CJ, Lovell DJ, Specker BL, Campaigne BN. Physical activity in children with juvenile rheumatoid arthritis: quantification and evaluation. Arthritis Care Res 1995;8:114-119.

www.ncbi.nlm.nih.gov/pubmed/7794985

Hogeweg JA, Kuis W, Huygen AC, de Jong-de Vos van Steenwijk C, Bernards AT, Oostendorp RA, et al. The pain threshold in juvenile chronic arthritis. Br J Rheumatol 1995:34:61-67. www.ncbi.nlm.nih.gov/pubmed/7881842

Klepper SE. Exercise and fitness in children with arthritis: evidence of benefits for exercise and physical activity. Arthritis Rheum 2003;49:435-443.

Klepper S. Making the case for exercise in children with juvenile idiopathic arthritis: what we know and where we go from here. Arthritis Rheum 2007;57:887-890.

Lindehammar H. Bäckman E. Muscle function in juvenile chronic arthritis. J Rheumatol 1995;22:1159-1165.

www.ncbi.nlm.nih.gov/pubmed/7674247

Lindehammar H, Lindvall B. Muscle involvement in juvenile idiopathic arthritis. Rheumatology 2004;43:1546-1554. www.ncbi.nlm.nih.gov/pubmed/15342926

Manners PJ, Bower C. Worldwide prevalence of juvenile arthritis why does it vary so much? J Rheumatol 2002:29:1520-1530.

www.ncbi.nlm.nih.gov/pubmed/12136914

Moldoveanu AI, Shephard RJ, Shek PN. The cytokine response to physical activity and training. Sports Med 2001:31:115-144.

www.ncbi.nlm.nih.gov/pubmed/11227979

Noakes TD, St Clair Gibson A. Logical limitations to the "catastrophe" models of fatigue during exercise in humans. Br J Sports Med 2004;38:648-649. www.ncbi.nlm.nih.gov/pubmed/15388560

Noakes TD, St Clair Gibson A, Lambert EV. From catastrophe to complexity: a novel model of integrative central neural regulation of effort and fatigue during exercise in humans. Br J Sports Med 2004;38:511-514. www.ncbi.nlm.nih.gov/pubmed/15273198

Paap E, van der Net J, Helders PJ, Takken T. Physiologic response of the six-minute walk test in children with juvenile idiopathic arthritis. Arthritis Rheum 2005;53:351-356.

www.ncbi.nlm.nih.gov/pubmed/15934128

Reid GJ, McGrath PJ, Lang BA. Parent-child interactions among children with juvenile fibromyalgia, arthritis, and healthy controls. Pain 2005;113:201-210. www.ncbi.nlm.nih.gov/pubmed/15621381

Schanberg LE, Anthony KK, Gil KM, Maurin EC. Daily pain and symptoms in children with polyarticular arthritis. Arthritis Rheum 2003;48:1390-1397. www.ncbi.nlm.nih.gov/pubmed/12746912

Shephard R. Cytokine responses to physical activity, with particular reference to IL-6: sources, actions, and clinical implications. Crit Rev Immunol 2002;22:165-182.

www.ncbi.nlm.nih.gov/pubmed/12498381

Sherry DD, Bohnsack J, Salmonson K, Wallace CA, Mellins E. Painless juvenile rheumatoid arthritis. J Pediatr 1990:116:921-923.

Simon LS, Lipman AG, Caudill-Slosberg M, Gill LH, Keefe FJ, Kerr KL, et al. Guideline for the management of pain in osteoarthritis, rheumatoid arthritis, and juvenile chronic arthritis. No. 2. Glenview, IL: American Pain Society, 2002.

www.ampainsoc.org/pub/arthritis.htm

Singh-Grewal D, Wright V, Bar-Or O, Feldman BM. Pilot study of fitness training and exercise testing in polyarticular childhood arthritis. Arthritis Rheum 2006;55:364-372.

www.ncbi.nlm.nih.gov/pubmed/16739204

Singh-Grewal D, Schneiderman-Walker J, Wright V, Bar-Or O, Beyene J, Selvadurai H, et al. The effects of vigorous exercise training on physical function in children with arthritis: a randomized, controlled, singleblinded trial. Arthritis Rheum 2007;57:1202-1210. www.ncbi.nlm.nih.gov/pubmed/17907238

Takken T, Hemel A, van der Net J, Helders PJ. Aerobic fitness in children with juvenile idiopathic arthritis: a systematic review. J Rheumatol 2002;29:2643-2647. www.ncbi.nlm.nih.gov/pubmed/12465166

Takken T, van der Net J, Helders PJ. Do juvenile idiopathic arthritis patients benefit from an exercise program? A pilot study. Arthritis Rheum 2001;45:81-85.

Takken T, van der Net J, Helders PJ. Relationship between functional ability and physical fitness in juvenile idiopathic arthritis patients. Scand J Rheumatol 2003b;32:174-178.

www.ncbi.nlm.nih.gov/pubmed/12892255

Takken T, van der Net J, Kuis W, Helders PJ. Physical activity and health related physical fitness in children with juvenile idiopathic arthritis. Ann Rheum Dis 2003a;62:885-889.

www.ncbi.nlm.nih.gov/pubmed/12922964

Turk DC, Marcus DA. Assessment of chronic pain patients. Semin Neurol 1994;14:206-212.

Vlaeyen JW, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. Pain 2000;85:317-332. www.ncbi.nlm.nih.gov/pubmed/10781906

Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: the evidence. CMAJ 2006;174:801-809.

www.ncbi.nlm.nih.gov/pubmed/16534088

Wilcox S, Der Ananian C, Abbott J, Vrazel J, Ramsey C, Sharpe PA, et al. Perceived exercise barriers, enablers, and benefits among exercising and non-exercising adults with arthritis: results from a qualitative study. Arthritis Rheum 2006;55:616-627.

www.ncbi.nlm.nih.gov/pubmed/16874785

Williams AC. Facial expression of pain: an evolutionary account. Behav Brain Sci 2002;25:439-488. www.ncbi.nlm.nih.gov/pubmed/12879700