

back pain and which can be used to predict which patients will respond to placebo. A pure placebo and brain imaging study found the same results in OA patients.

Using brain coordinates from a chronic back pain study, the investigators were able to identify a prefrontal circuit that differentiates and predicts placebo responders from nonresponders with >95% accuracy. Thus, there is a brain circuit that indicates which patients will be placebo responders. “The brain predicts the future, and this may be a critical tool for future decisions about the patient,” Dr. Apkarian concluded.

N-3 Fatty Acids at the Intersection of RA and CV Morbidity

Written by Rita Buckley

A meta-analysis of 17 randomized, controlled trials suggests that supplementation with oral n-3 fatty acids improves patient-assessed pain, duration of morning stiffness, and number of painful and/or tender joints in patients with rheumatoid arthritis (RA) [Bahadori B et al. *JPEN J Parenter Enteral Nutr* 2010; Kremer JM. *Am J Clin Nutr* 2007; Goldberg RJ, Katz J. *Pain* 2007]. Joel M. Kremer, MD, Albany Medical College and the Center for Rheumatology, Albany, New York, USA, reviewed studies on the efficacy of fish oil in the treatment of RA and its cardiovascular (CV) benefits.

A 24-week, prospective, double-blind, randomized trial of high and low doses of fish oil and olive oil showed significant improvements from baseline in the number of tender joints ($p=0.05$ for the high dose; $p=0.04$ with the low dose) and morning stiffness ($p\leq 0.01$) and significant decreases in leukotriene B₄ and macrophage IL-1 production, especially in the high-dose n-3 fatty acid group [Kremer JM et al. *Arthritis Rheum* 1990].

A 12-month, double-blind, randomized study [Geusens P et al. *Arthritis Rheum* 1994] compared supplementation with either 2.6 gm of n-3 fatty acids or 1.3 gm of n-3 fatty acids+3 gm of olive oil. Findings indicated that 2.6 gm/day of n-3 fatty acids led to significant clinical benefit and may have reduced the need for concomitant antirheumatic medication.

According to Dr. Kremer, more than 20 peer-reviewed, blinded studies have demonstrated a consistent amelioration of tender joints in patients who have been given n-3 fatty acids versus controls of corn or olive oil.

All but two studies added n-3 fatty acids to existing RA treatment regimens.

The minimal effective dose of n-3 fatty acids per day appears to be 3 to 5 g, or at least 10 capsules per day of most over-the-counter fish oil supplements. These contain about 300 mg of n-3, but “high-potency” capsules with 500 to 950 mg of n-3 are now available.

The finding that fish oil decreases CV risk is well established [Mozaffarian D. *Am J Clin Nutr* 2008; Albert CM et al. *N Engl J Med* 2002]. A protective effect seems evident at doses of long-chain n-3 fats >250 mg, much lower than those needed for symptomatic relief in RA [James M. *Proc Nutr Soc* 2010].

Fish oil may reduce CV events in RA via direct myocardial and, possibly, antithrombotic actions [Cleland LG et al. *J Rheumatol* 2006] and may also induce a favorable vascular response to ischemia [DiGiacomo RA et al. *Am J Med* 1989].

In a double-blind prospective study, 32 patients with primary or secondary Raynaud phenomenon were randomly assigned to olive oil placebo or fish oil groups. Data indicated that the ingestion of fish oil improved tolerance to cold exposure and delayed the onset of vasospasm in patients with primary ($p=0.05$), but not secondary, Raynaud phenomenon. The improvements were associated with significantly increased digital systolic blood pressures in cold temperatures [DiGiacomo RA et al. *Am J Med* 1989].

Dr. Kremer recommended three high-potency fish oil capsules (approximately 3 g n-3/day) in young patients with primary Raynaud, with at least 6 weeks of observation. He noted that the potential of n-3 fatty acids in the amelioration of CV comorbidity in inflammatory diseases, like RA, is worthy of further study.

Calcium, Bone Health, and CVD

Written by Rita Buckley

The benefits of calcium intake for bone health are very clear, but the risks—cardiovascular (CV), in particular—have become controversial. Richard Bockman, MD, PhD, Weill Cornell Medical College and Hospital for Special Surgery, New York, New York, USA, discussed calcium metabolism and the results of recent studies on calcium supplementation and CV health.