



Wellbeing without pills

Dr. Barry Oken, of the Oregon Center for Complementary and Alternative Medicine in Neurological Disorders (ORCCAMIND), explains how complementary therapy is becoming a more widely-explored area in terms of medical research

What is the aim of the ORCCAMIND project?

We're trying to organise a centre that is focused on research and training in complementary therapies for neurological disorders and stress. The centre has broader interests in general, but my specific lab is interested in mind/body therapies.

How did you move out of conventional medicine into this field?

I guess I saw the opportunity as a very unexplored area with benefits. Some of the complementary therapies do have very valid benefits and it seemed as if it was a very open area of research. From a personal point of view, I had an interest in yoga and the scientific opportunity was a major part of it.

It is estimated that almost 50 per cent of Americans use complementary therapies. Why do you think this is so?

I think that there are a couple of things here. One is that they want to take care of their own health and wellbeing without taking a pill; it's a case of taking charge – what we call self efficacy. The other thing is that these therapies are good for disorders that conventional therapy does not have a very good track record with, for example chronic lower back pain. Historically, it's been poorly treated with conventional therapy. The inclusion of chiropractic and acupuncture has been a useful adjunct. Many conventional medical centres now offer these therapies.

What do you think of the labels such as 'alternative' and 'complementary' – are they useful?

Initially the title was *alternative*, but that was frowned upon. The idea was to have

both working together – complementarily. *Complementary* became the major term and it was accepted. I was OK with that, but there is a push now for *integrated medicine*, merging the two systems if you like. Some organisations such as NIH are now wondering if Complementary and Alternative Medicine (CAM) are the best terms.

How do you measure your success rate?

I think it helps with a sense of wellbeing – especially in non-specific symptoms such as fatigue. As far as specific symptoms are concerned, I've not done formal evaluations but some of the studies have resulted in changes to conventional clinical care. For example, physical therapists have incorporated chunks of yoga into their treatments.

What can you tell us about mindfulness training?

Most of the clinically used mindfulness training have two components: bringing your attention to your current moment; and not attaching an emotional tag to your observations. So, for example, if your spouse starts yelling at you because they have dementia, the idea is to almost shrug your shoulders and not attaching an emotional tag to your observations. It's very useful to situations where you have stress. We have one study on post-traumatic stress disorder and I think it will be helpful there.

How has your work been received among the more conventional medical sectors?

The better studies are received well among clinicians. I think that some academics look down upon it, and also some within the complementary medicine field do that too. We're kind of stuck between the two camps. Sometimes we take hits from both sides – I guess that's a good sign!

Can you tell us a little about your partners in this project and what they contribute?

ORCCAMIND has been developed in part because of its linkage to the complementary medicine institutions. Portland is fortunate in that we have three other doctorate granting complementary medicine institutions in town (oriental, chiropractic and natural medicine) and I think that linkage has been helpful us to guide us in terms of our herbs and botanical studies, for example. Sometimes in conventional medicine, they are not quite in tune to the finer points of botanical therapy – even some NIH funded trials have not had the correct attention to detail for the dietary supplements. Having that linkage between the institutions provides us access to carry out that sort of research.

Have you faced any obstacles?

One of the issues we face is that, with complementary work, it's almost on the edge of funding – who funds it and who doesn't? I should explain that sometimes the research falls under the remit of health promotion and it's unclear who funds that kind of stuff. NIH becomes a moving target for funding complementary medicine – which organisation will fund what you're trying to achieve?

What's the broader impact of your work?

Well, for example, I performed one study using yoga in Multiple Sclerosis sufferers, and at the time it was thought that those with Multiple Sclerosis shouldn't exercise as it would worsen their symptoms. It became clear from my study that physical exercise was in fact beneficial and it has now become a standard aspect of clinical care.

The goal of the Oregon Center for Complementary and Alternative Medicine in Neurological Disorders (ORCCAMIND) is to advance the understanding and application of complementary medicine treatments for neurological disorders

Complementary centre without walls

THE CENTRE BEGAN in 1999 under the leadership of Barry Oken, MD, with its first grant from the National Center for Complementary and Alternative Medicine at NIH focused around complementary medicine interventions that might reduce stress. The term *stress* was broadly used to include chronic psychological stress as well as metabolic oxidative stress and interventions were implemented in humans as well as animal models. The term *complementary medicine* is used similarly to the term integrative medicine.

The centre initiated formal collaborations between Oregon Health & Science University (OHSU) and neighbouring institutions: three CAM institutions – the National College of Natural Medicine, Western States Chiropractic College, and the Oregon College of Oriental Medicine; the Linus Pauling Institute at Oregon State University; and the Portland Veteran Affairs Medical Center. One set of animal studies led by Dennis Bourdette, MD, explored natural antioxidants in a mouse model of multiple sclerosis and found alpha lipoic acid significantly attenuated clinical signs and central nervous system inflammation in this model. Studies have teased apart the mechanism of this benefit of alpha lipoic acid (Maracci *et al*, 2002, Salinthonne *et al*, 2008) and human trials have begun.

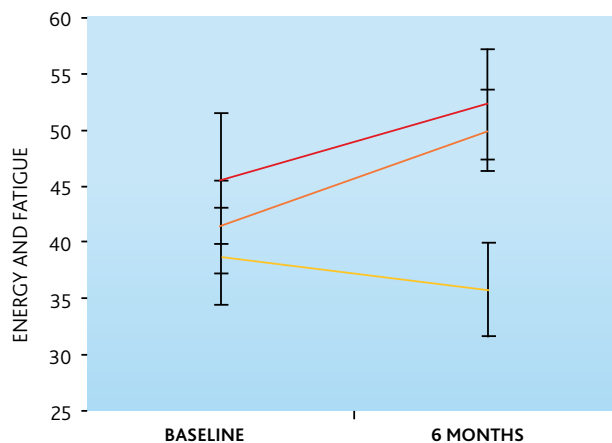
Joseph Quinn, MD, and Balz Frei, PhD led another project investigating mouse models of age-related cerebral degeneration, focusing on amyloid mouse models of Alzheimer's disease. Initial results observed that ginkgo biloba extract and lipoic acid both improved the behavioural function of amyloid transgenic mice but that both produced no effect on the amyloid deposits in the brain (Stackman *et al*, 2003, Quinn *et al*, 2007). Follow-up studies extended the work to many other dietary supplements including coenzyme Q, fish oil, and docosahexaenoic acid. Jeffrey Kaye, MD, led the first moderate-sized (133 subjects) primary prevention of dementia study in healthy over-84 year olds. Subjects who took ginkgo biloba extract for four years had a lower incidence of cognitive decline but the common intention to treat statistical analysis of all subjects fell just short of the common cut-off for significance, with a p value of 0.06. (Dodge *et al*, 2008).

Barry Oken, MD, led a project that included one of the earliest reasonably-sized, well-controlled trials of yoga in a clinical population. One study focused on those with Multiple Sclerosis and found that those randomised to six months of a yoga class or to an exercise class had significantly less fatigue than those randomized to a wait-list control group (Oken *et al*, 2004, see figure to right). Fatigue is a significant problem for those with multiple sclerosis and this important finding has been incorporated into standard clinical care. Another study with similar interventions in a group of healthy 65-85 year olds, also found that those randomized to yoga had significantly less fatigue (Oken *et al*, 2006). Both studies found no clear effects on cognitive function.

The follow-up NIH-funded centre grant to the original ORCCAMIND grant focused on mind-body medicine with an emphasis on expectancy and placebo effects, again with both animal and human projects. One project developed an animal model of a conditioned therapeutic response

that had many features of a placebo effect (Jones *et al*, 2008). One project demonstrated the cognitive improvement in healthy seniors from simply the expectancy effect of taking a cognitive-enhancing agent (Oken *et al*, 2008). The two other projects examined the expectancy effect in humans with Parkinson's disease and with metabolic syndrome. The expectancy or placebo effect, which is mediated through the brain and its connections, needs to be better understood in order to improve clinical research design and also to develop methods to clinically utilise the benefit of this mind-body effect (Oken, 2008).

Current ORCCAMIND research has kept a focus on mind-body medicine (Wahbeh *et al*, Neurology 2008), using intervention techniques based on meditation and mindfulness training. Current projects have focused on clinical populations experiencing high psychological stress levels (e.g., caregivers and those with post-traumatic stress disorder). In addition to defining the clinical benefits of these therapies, there is a significant effort to develop biomarkers of stress and of well-being. This is being done utilising serum markers (e.g., cytokines) and electrophysiologic measures (e.g., EEG and autonomic nervous system function) in addition to the more commonly used self-rated instruments. These physiologic markers utilise conventional methods (Wahbeh *et al*, Alz Disease and Related Disorders 2008) as well more innovative methods (Ellingson *et al*, 2008; Fonareva *et al*, 2009). In addition to ORCCAMIND's mind-body focus, there continues to be a focus on diet and dietary supplements for age-related cognitive decline (Bowman *et al*, 2009; Shinto *et al*, 2008; Wadsworth *et al*, 2008; Calabrese *et al*, 2008).



THE EFFECT OF 6 MONTHS OF EXERCISE (RED), YOGA (ORANGE), OR ROUTINE STANDARD OF CARE WAIT-LIST (YELLOW) - HIGHER NUMBERS ARE GREATER SELF-RATED ENERGY

AT A GLANCE

PROJECT TITLE

OREGON CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE IN NEUROLOGICAL DISORDERS

CONTACT

Andy Fish

CR-120
Oregon Health & Science Univ. CR-120
3181 SW Sam Jackson Park Road
Portland, OR 97239

T 503 494 9519

F 503 494 9520

E fisha@ohsu.edu

www.ohsu.edu/orccamind.edu

DR. BARRY OKEN received a B.A. degree in mathematics from the University of Rochester and an M.D. degree from the Medical College of Wisconsin. He completed a residency in Neurology at Boston University Medical Center and a fellowship at Massachusetts General Hospital and Harvard Medical School. Since 1985, he has been a member of the faculty at Oregon Health & Science University, where he is Professor in the Departments of Neurology and Behavioral Neuroscience. His research has been continuously funded by the U.S. National Institutes of Health for 20 years and he has over 150 publications.

ORCCAMIND has a major interest in collaboration with the Portland area CAM institutions mentioned above. This collaboration has been highlighted by the two NIH-funded centre grants that included project leaders and pilot grants at each of the three CAM institutions and has been extended to facilitation of faculty appointments and research interactions with OHSU faculty. ORCCAMIND supported research has extended to acupuncture and oriental medicine, naturopathy (Shinto *et al*, 2008a), and chiropractic (Haas *et al*, 2004). This collaboration with the CAM institutions extends to an annual invited CAM Distinguished Lectureship (sponsored by the Oregon Collaboration for Integrative Medicine), an annual Symposium for Portland-Area Research on Complementary and Alternative Medicine (SPARC), and the NIH research education grants awarded to the three Portland CAM institutions.

ORCCAMIND has always had a major emphasis on training academicians. The original ORCCAMIND centre grant provided four career development awards. Two

awardees with clinical doctorates went on to obtain their own five-year NIH career development grants as a result. One of these clinicians, Lynne Shinto, ND, MPH, also began a Wellness Clinic within the Department of Neurology. Dr. Oken is principal investigator of an NIH-funded institutional training grant, "CAM Research Training in Neuroscience and Stress" that has been funded since 2005. There have been twelve post-doctoral fellows and one pre-doctoral fellow based at either OHSU (Departments of Neurology, Behavioral Neuroscience, or Psychiatry) or the Linus Pauling Institute at Oregon State University. Research by these fellows has extended from basic science to health services research. ORCCAMIND works closely with the OHSU Human Investigation Program, a certificate or masters degree program to educate clinical researchers beginning their post-doctoral careers. Dr Oken has just received funding for his own five-year NIH career development award that will further enhance his mentorship of junior academicians as well as advance his ability to utilise advanced signal analysis to improve mind-body medicine research.

References

Bowman GL, Frei B, Calabrese C, Dodge HH, Oken BS, Kaye JA, Quinn JF. Ascorbic acid and rates of cognitive decline in Alzheimer's disease. *Journal of Alzheimer's Disease* 2009, 16:93-98.

Calabrese C, Gregory WL, Leo M, Kraemer D, Groves M, Bone K, Oken B. Effects of a Standardized Bacopa monnieri Extract on Cognitive Performance, Anxiety and Depression in the Elderly: A Randomized Double-blind Placebo Controlled Trial. *Journal of Alternative and Complementary Medicine* 2008, 14:707-713.

Dodge HH, Zitzelberger T, Oken BS, Howieson D, Kaye J. A randomized placebo-controlled trial of ginkgo biloba for the prevention of cognitive decline. *Neurology* 2008, 70:1809-1817.

Ellingson RM, Eriksen KJ, Schaller JJ, Zajdel D, Kudura A, Oken B. Second generation complementary and alternative medicine physiologic data collection and monitoring research platform. *Conference Proceedings IEEE Engineering in Medicine and Biology Society* 2008, paper ThDPo071.

Fonareva I, Zajdel D, Herting M, McGee W, Oken B. Cognitive processes in older adults: potential impact of stress and physiologic function. *Cognitive Neuroscience Society annual meeting*, San Francisco 2009.

Haas M, Group E, Kraemer DF. Dose-response for chiropractic care of chronic low back pain. *The Spine Journal* 2004, 4:574-583.

Jones RE, Moes N, Zwickey H, Cunningham CL, Gregory WL, Oken B. Treatment of experimental autoimmune encephalomyelitis with alpha lipoic acid and associative conditioning. *Brain, Behavior and Immunity* 2008, 22:538-43.

Kaye JA, Dodge H, Zitzelberger T, Moore M, Oken B. MRI evidence for a disease modifying effect of Ginkgo Biloba extract in a dementia prevention trial. *International Conference on Alzheimer's disease*. 2008. Presentation number IC-02-01.

Lovera J, Bagert B, Smoot K, Morris CD, Frank R, Bogardus K, Wild K, Oken B, Whitham R, Bourdette D. Ginkgo for improvement of cognitive performance in multiple sclerosis: a randomized, placebo-controlled trial. *Multiple Sclerosis* 2007, 13:376-385.

Marracci GH, Jones RE, McKeon GP, Bourdette DN. Alpha lipoic acid inhibits T cell migration into the spinal cord and suppresses and treats experimental autoimmune encephalomyelitis. *Journal of Neuroimmunology* 2002, 131:104-14.

Oken BS, Kishiyama S, Zajdel D, Bourdette D, Carlsen J, Haas M, Hugos C, Kraemer DF, Lawrence J, Mass M. Randomized controlled trial of yoga and exercise in multiple sclerosis. *Neurology* 2004; 62:2058-2064

Oken, BS, Zajdel D, Kishiyama S, Flegal K, Dehen C, Haas M, Kraemer DF, Lawrence J, Leyva J. Randomized controlled 6-month trial of yoga in healthy seniors: effects on cognition and quality of life. *Alternative Therapies in Health and Medicine* 2006, 12:40-49.

Oken BS, Flegal K, Zajdel D, Kishiyama S, Haas M, Peters D. Expectancy effect: impact of pill administration on cognitive performance in healthy seniors. *Journal of Clinical and Experimental Neuropsychology* 2008, 30:7-17.

Oken BS. Placebo effects: Clinical aspects and neurobiology, *Brain* 2008, 131:2812-2823

