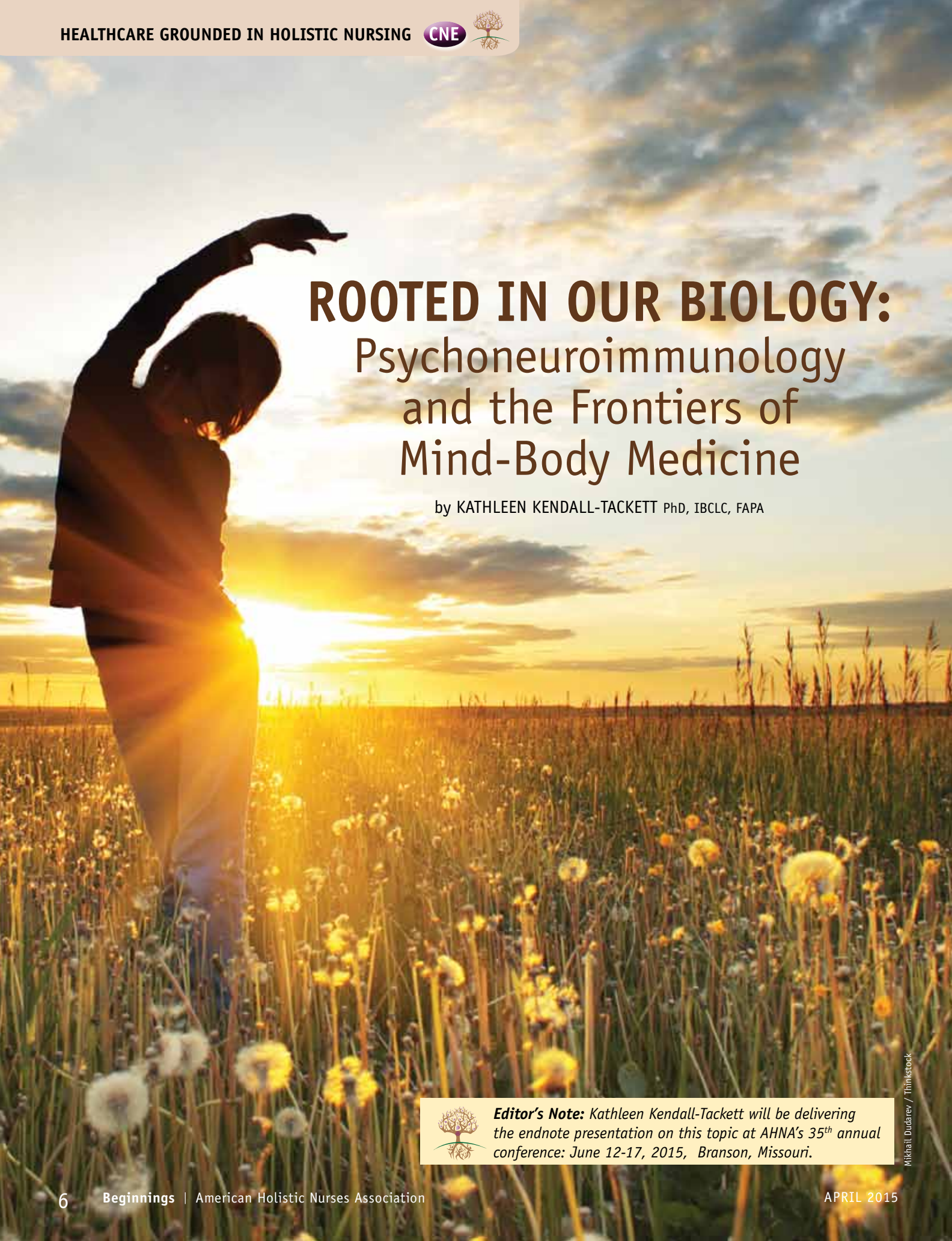

ROOTED IN OUR BIOLOGY:
Psychoneuroimmunology and the Frontiers of Mind-Body Medicine

by KATHLEEN KENDALL-TACKETT PhD, IBCLC, FAPA

Editor's Note: *Kathleen Kendall-Tackett will be delivering the endnote presentation on this topic at AHNA's 35th annual conference: June 12-17, 2015, Branson, Missouri.*

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In recent years, researchers have discovered that inflammation is an important underlying cause of a number of serious diseases including heart disease, diabetes, cancer, and Alzheimer's. Where does inflammation come from? A number of possible environmental causes have been identified, including diet and environmental toxins. Clearly these factors do have an influence, but the impact of mental health is often missing in the discussion. This is where research in the field of psychoneuroimmunology (PNI) offers valuable insight.

The Stress Response

The stress response is key to understanding PNI. The human stress response can be described with three main components. Two of these will be familiar. The third may be less so. The first part of the stress response is the catecholamine response, also known as fight-or-flight. It has been well-documented since the 1950s and is designed to either help you fight your way out of a situation or run away from it.

The second part of the stress response is the hypothalamic-pituitary-adrenal (HPA) axis. The HPA axis is where you get the stress hormone cortisol. Researchers became very interested in the HPA axis in the 1990s. They were particularly interested in the interaction between cortisol and norepinephrine, part of the catecholamine response (Kendall-Tackett, 2000).

The third part of the stress response is actually the key to understanding PNI: the inflammation response. In response to threat, our bodies increase inflammation by increasing the number of proinflammatory cytokines we have in our plasma. Two key purposes of these molecules are fighting infection and healing wounds. If our bodies perceive that we are under threat, it makes sense for us to "rally the troops." The problem is when this response is chronically activated. When there is chronic inflammation, there is increased risk of disease (Kendall-Tackett, 2010c). This has been demonstrated by studies on depression, trauma, and racial/ethnic health disparities, which are briefly described below.

Depression & Inflammation

Depression was one of the key outcomes that PNI researchers studied. In the perinatal field, Michael Maes, a researcher in the Netherlands, was the first to identify that women who had postpartum depression and anxiety had high levels of proinflammatory cytokines in their plasma (Maes & Smith, 1998). Through a number of studies, researchers found that proinflammatory cytokines were high in people who were depressed, and they appeared to have a causal role (Berk et al., 2013). Depression causes inflammation, and inflammation causes depression. Inflammation and depression become a mutually maintaining system that perpetuates depression.

PNI research helps connect a person's mental state with physical disease by providing an understanding of underlying mechanisms. For example, consider the link between depression and heart disease. Why might depression increase the risk of heart disease? PNI research can tell us: Depressed people often have high levels of inflammation. Chronically high levels of proinflammatory cytokines damage the vasculature, leading to clots, which can lead to cardiovascular events (Kop & Gottdiener, 2005).

There have been similar findings regarding preterm birth. Depression during pregnancy increases the risk for preterm birth. Again, the question is, why? Two of the inflammatory molecules involved in depression, IL-6 and TNF-alpha, also ripen the cervix (Coussons-Read, Okun, Schmitt, & Giese, 2005), but countering inflammation can help. In a randomized controlled trial in which a group of pregnant women ate eggs enriched with the anti-inflammatory omega-3 DHA during the last trimester, there was an increase in gestation length of six days (Smuts et al., 2003).

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Psychoneuroimmunology (**PNI**) is the study of interactions between the nervous and immune systems and the relationships between mental processes and health. PNI is multi-disciplinary, drawing from fields such as psychology, neuroscience, immunology, nursing, psychiatry, and behavioral medicine. PNI studies the physiological functioning of the neuroimmune system in health and disease and disorders of the immune system, such as autoimmune diseases, hypersensitivities, and immune deficiency.

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Inflammation is also relevant for how we treat depression. In the past 10 years, researchers have discovered that the entire range of treatments for depression are all, in some way, anti-inflammatory. This is true for omega-3 fatty acids, social support, exercise, cognitive therapy, St. John's wort – even the selective serotonin reuptake inhibitors, such as fluoxetine, paroxetine, and sertraline (Kendall-Tackett, 2010a). Treatments for depression will be more effective if we understand the role of inflammation. As Maes et al. (2009) notes, when we focus only on the monoamine neurotransmitters, such as serotonin and norepinephrine, treatment for depression will only be partially effective. If we deal with inflammation in addition to serotonin and norepinephrine, we can increase the effectiveness of our treatments. Anti-inflammatory omega-3 fatty acids boost the effectiveness of medication. Actually, adding any anti-inflammatory agent should do that – and it does (Kendall-Tackett, 2008; Maes et al., 2009).

PNI research is also relevant to depression in new mothers and helps us understand breastfeeding's protective role (Kendall-Tackett, 2007). Maureen Groer's research documented that breastfeeding specifically downregulates the stress and inflammatory response systems (Groer & Kendall-Tackett, 2011). It is one of the reasons why mothers who exclusively breastfeed their children have lower rates of depression (Dennis & McQueen, 2009; Kendall-Tackett, 2007). A study of 6,410 new mothers found that exclusively breastfeeding mothers get more sleep than their mixed- or formula-feeding counterparts (Kendall-Tackett, Cong, & Hale, 2011). There was no significant difference between mothers who were mixed feeding versus exclusively formula feeding; the benefit comes from exclusively breastfeeding. This is concerning because the first thing new mothers are often told is to supplement. Kendall-Tackett et al. (2011) and several other researchers have found that mothers who supplement actually get less sleep, not more, which increases mothers' risk of depression (Doan, Gardiner, Gay, & Lee, 2007; Dørheim, Bondevik, Eberhard-Gran, & Bjorvatn, 2009; Goyal, Gay, & Lee, 2007).

Trauma & Inflammation

Childhood abuse often leads to health problems in adults. Anda et al. (2009) amply demonstrated this connection in their Adverse Childhood Experiences study, which was conducted as

Depression and Breastfeeding: A Mother's Story

PNI research has helped us understand breastfeeding's protective role for new mothers. This is a story that one mother shared with me about the benefits of exclusively breastfeeding and how it helped her during the postpartum months:

When my first was born, I was completely overwhelmed with the feeling of being her primary caregiver. I had no family or friends in the area, and my husband had to go back to work when she was five or six days old. I had panic attacks, and felt like there was no way I was up to being the kind of parent she deserved. Breastfeeding was going well, though, and it was often the only thing that I felt like I was doing right …

Well-meaning family and friends often tried to suggest that I let my husband give her a bottle, to reduce the "burden" on me of caring for her. They also suggested that if we moved her out of our bed, I could get more and better sleep, and recover more easily. I knew that keeping her close at night helped to make it more OK that I wasn't holding her all the time during the day, and also that I was able to get more sleep and rest by nursing her in bed. As things started to improve for me hormonally, I was able to look back at the fact that I met her most basic needs, even as I was struggling. It helped me feel better about myself, which helped my emotional healing. I know the advice I received came with good intentions, but I was so vulnerable then, and I wanted a magic cure to all of my problems. I seriously considered sleep training, and letting my husband give her an occasional bottle of formula, even though it didn't feel right. I am so glad that my husband was strong to help me through that horrible time in other ways, and he always reminded me of our daughter's needs in a kind and loving way. (Kendall-Tackett, 2010d, p. 63)

Source: Excerpt from "Breastfeeding Beats the Blues" by Kathleen Kendall-Tackett published in *Mothering* magazine (Sept/Oct 2010).

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a collaboration between Kaiser Permanente's Health Appraisal Clinic and the CDC. The first large-scale study of adults in an HMO with more than 17,000 patients, this study showed that adverse childhood experiences, such as abuse, household dysfunction, and neglect, are related to serious and life-threatening health problems in adults. So again the question arises, what is the underlying mechanism? PNI research can tell us this too. Just like depression, post-traumatic stress disorder (PTSD) increases inflammation in trauma survivors (Kendall-Tackett, 2009; Kendall-Tackett & Klest, 2009). But what is often overlooked is the health impact of a person's beliefs. If people experience trauma, especially as children, they are likely to develop a hostile worldview (Kendall-Tackett, 2009). In other words, they think others are out to get them, which is a reasonably accurate belief – people have harmed them. However, a hostile worldview is extremely detrimental to health (Suarez, 2006). Hostility has been linked to heart disease, diabetes, and metabolic syndrome – because it increases inflammation! The good news is that beliefs can be changed; they are a modifiable risk factor for trauma survivors.

Another modifiable risk factor is sleep. Trauma has a profound impact on sleep: shorter sleep duration, more time needed to fall asleep, and more daytime fatigue (Kendall-Tackett, 2009). Poor sleep is related to increased symptoms of metabolic syndrome, which magnifies the risk for heart disease and diabetes (Haffner & Taegtmeyer, 2003; Hall et al., 2008). Even short periods of sleep disturbances increase insulin resistance (McEwen, 2003). Sleep problems are linked to serious health consequences and chronic disease because poor sleep quality increases inflammation (Suarez & Goforth, 2010).

Another related issue for trauma survivors is hypervigilance. Prior traumatic events "prime" the stress response, so that it is more reactive to subsequent stress (Kiecolt-Glaser et al., 2007; Kiecolt-Glaser et al., 2005). From the body's standpoint, that makes sense. It becomes hypervigilant to anything that is potentially harmful. However, hypervigilance can be a very difficult symptom for trauma survivors to live with. In essence, trauma survivors become more vulnerable to stress.

Trauma survivors can protect their health by learning to downregulate their stress response (Ruglass & Kendall-Tackett, 2015). Exercise helps with this (Emery, Kiecolt-Glaser, Glaser, Malarkey, & Frid, 2005; Kiecolt-Glaser et al., 2010), as well as omega-3 fatty acids, particularly EPA (Ferrucci et al., 2006; Kendall-Tackett, 2010b). Surprisingly, breastfeeding can also help trauma survivors downregulate their stress response. In an analysis of our 2011 study, 994 of the 6,410 new mothers had a history of sexual assault (Kendall-Tackett, Cong, & Hale, 2013). Not surprisingly, there was a pervasive negative effect of sexual assault on all the measures of sleep, anxiety, depression, and anger/irritability. When we added feeding method into the analyses, however, we saw a specific downregulation of those negative effects. Although the sexually assaulted/exclusively breastfeeding women still showed signs of trauma, they were significantly

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Holistic Nursing and Psychoneuroimmunology

Holistic nurses aim to treat the whole person and are in an ideal position to use PNI research in their clinical practices. Conventional care treats the body and may ask the patient to modify behavior. The mind is completely separate from the heart and spirit. Holistic care acknowledges the importance of patients' thoughts and beliefs that may drive harmful behavior, their social connections, and their emotional health. Holistic practitioners can combine conventional and CAM treatments to ensure patient health.

Recent studies have demonstrated that many diseases, such as heart disease, diabetes, cancer, and Alzheimer's, have an inflammatory base. The key to good health is figuring out how to lower inflammation. The holistic nurse understands that behavior is not the only thing that impairs health. PNI research identifies the many ways the inflammatory response system is upregulated. Our cognitions about self and others, and our connections to other people can literally mean the difference between life and death. With a holistic approach to lowering inflammation, patients can expect the best possible outcomes – and they'll have their nurses to thank for that.

attenuated compared to the sexually assaulted mothers who were mixed or formula feeding (Kendall-Tackett, et al., 2013).

Racial/Ethnic Disparities & Inflammation

PNI research can also inform us about health disparities among racial/ethnic minorities (Kendall-Tackett, 2014). Health psychologists study a variable called "perceived discrimination." It refers to people's beliefs that others are looking down on them. It's not to say that discrimination is not real. It is. Yet when it comes to activating the inflammatory response system, it is the belief or perception that is key (Lewis, Aiello, Leurgans, Kelly, & Barnes, 2010). Microaggressions are a threat to self – our bodies treat them as a threat to our survival (Panksepp, 2011). When human beings are faced with a threat, our inflammatory response system activates. Inflammation is the underlying cause of many of the diseases where health disparities exist: heart disease, diabetes, and metabolic syndrome.

Preterm birth is another interesting case. The World Health Organization (2014) has identified preterm birth as the number one cause of infant mortality worldwide. In the United States, infant mortality due to preterm birth varies greatly by race and ethnicity, and the rates are more than double for non-Hispanic black women compared to non-Hispanic white women (MacDorman & Mathews, 2011). This too is related to inflammation. The mechanism is similar to what is seen in depression. In groups who face chronic discrimination, researchers might expect that preterm birth rates would be high. And they are. If clinicians can target inflammation directly, it should help. In the Smuts et al. (2003) study cited above, the sample was a WIC population in Kansas City that was 70% African American. A small dose anti-inflammatory DHA in eggs consumed by pregnant women increased gestation length by six days. Imagine what a larger dose could do. Understanding the inflammation connection provides some ideas about how we can specifically intervene.

Understanding the link between inflammation, mental health, and disease is key to improving the health of our clients and patients. Psychoneuroimmunology research tells us why this is important, and more importantly, what we can do. It is really the frontiers of mind-body medicine, and once we understand it, it will change the way we practice.

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