Mind-body medicine – concepts and controversies

Mind-body medicine looks at the psychophysiology of thought and belief.

ANIL RAMJEE, ***BSc, MB BCh, DFM (US), FCFP (SA)***
Family Physician, Welgelegen, Cape Town

Anil Ramjee graduated at the University of the Witwatersrand in 1993 and spent 2 years at Chris Hani Baragwanath Hospital before pursuing a career in family medicine. He previously held a part-time lecturer's post at the University of Cape Town, Family Medicine Division, and is now in full-time private practice. He has a special interest in psychosomatic and psychosocial medicine and its application and implementation in family practice

Mind-body medicine (MBM) explores the powerful ways in which emotional, mental, social and spiritual factors modulate disease and healing processes. As such MBM examines the physiological consequences of thoughts, feelings, emotions and behaviours. MBM acknowledges psychosocial and spiritual factors as fundamental prerequisites to understanding the illness-wellness dynamic. This article presents an overview of some of these concepts as well as particular areas of contention.

Mindless semantics

One of the greatest challenges of MBM and the most likely reason for its failed endeavours to secure a place in mainstream academic medicine is the intriguingly elusive definition of 'mind'. Many believe that the 'mind' is not limited to the brain or the body. On the other hand, the less enlightened declare 'psychosomatic' and 'placebo' to be unreal imagined peculiarities of the brain/mind. For practical purposes, this article will focus on the brain as an important organ of the mind.

Thoughts and emotions – the brain and beyond (Fig.1)

Thinking mind – emotional mind

Evolution has plotted a course for the evolving brain from instinctive reptilian to the emotional mammalian brain and more recently the addition of a neocortex for cognition. It is the thinking neocortex that allows us to feel our feelings and articulate our emotions. It is this thinking mind, capable of creating its own unique reality through memory and anticipation, that is the source of much modern-day stress. In contrast to the thinking mind, evolutionary preserved structures, which Jacobs[1] calls the 'ancestral mind', allow for abstract, non-verbal, emotional and intuitive senses below the level of consciousness. These structures include the thalamus, which filters sensory input from the environment, and the amygdala, which assigns emotional meaning to that stimulus and then determines the appropriate response. Responses are based on lifetimes of memories and experiences. The amygdala is tasked primarily with detecting danger and setting off the flight-fright alarm. It is also thought to regulate positive emotions. Interestingly, emotional stimuli relayed from the thalamus are sent simultaneously to the amygdala and the cortex.[2] Because input reaches the amygdala first, an immediate behavioural and autonomic response is possible before the stimulus reaches conscious awareness. In fact, some stimuli remain unconscious

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processes. This together with the fact that instinctive reactions of the amygdala take preference over slower processes of the thinking mind explains why when you're aroused emotionally, for example by fear or sexual attraction, your emotions dominate your thoughts. It also explains why changes in mood (e.g. anxious state), behaviour (e.g. agitation) and physiology (e.g. palpitations and muscle tension) sometimes occur without a conscious awareness. Unlike acute stress responses that are short-lived, chronic low-grade day-to-day stress is capable of maintaining abnormally higher states of arousal for prolonged periods, i.e. the subcortical structures remain switched 'on'. To add fuel to fire, the amygdala not only receives information from the external environment but also from the thinking mind so that anxiety-provoking thoughts and misperceptions aggravate these stress reactions.

Perceptions

A perception is the unique meaning we add to a sensory experience. Consider the following example of watching a movie like *The Passion of the Christ*. The extent to which your physiology responds is determined only by your ability to decide how real this experience is. And that depends through which lens you are viewing the movie. If you are a movie critic, you may be paying attention to the dialogue, the cinematography and the factual content. However, if you are a Catholic priest then the boundary between virtual and real becomes blurred. The sensory stimulus is no longer a passive brain process and your entire physiology is actively participating in the movie through an already primed cortex (thoughts), amygdala (emotions) and hippocampus (emotional memories). The physiological consequences can be fatal, as evident from documented cases of individuals having had fatal heart attacks while watching the climactic crucifixion scene in *The Passion of the Christ*.[3,4] This acutely stressful fatality is the result of autonomic reactions executed by the hypothalamus all because

of powerful perceptions. The hypothalamus which takes instructions from the amygdala also triggers neurohormonal reactions, so that the final consequences of thought and emotions could be anything from coronary artery plaque rupture (acute stress) to a change in natural killer cell activity (chronic stress). This is the basis for the mind-body link where thoughts and emotions modulate neuroendocrine and immune physiology.

Sensations

'The emotional brain is almost on more intimate terms with the body than it is with the cognitive brain, which is why it is easier to access emotions through the body than through language', according to David Servan-Schreiber, psychiatrist.[5] One way of modifying neuroendocrine processes below the level of consciousness is through physical touch. A 2001 Cochrane review refutes previous studies demonstrating benefits of touch on the growth and development of preterm or low-birthweight infants. More recent research conducted at the Touch Research Institute at the University of Miami Medical School shows that compared with preterm neonates receiving sham massage (light pressure), preterm neonates receiving massage therapy (moderate pressure) exhibited greater weight gain and increased vagal tone and gastric motility during and immediately after treatment.[6] They have also shown that stimulating the mother's feet, but not the hands or abdomen, can evoke fetal activity in mid-gestation.[7] Depressed pregnant women who were massaged showed higher dopamine and serotonin levels, lower levels of cortisol and norepinephrine and better neonatal outcomes (i.e. lesser incidence of prematurity and low birthweight) compared with their controls.[8]

Belief and placebo – the brain and beyond (Fig.2)

Placebo – powerful or powerless?

Placebo and the placebo effect has always been the subject of much controversy but it does allow us to examine psyche-soma processes and explore self-healing mechanisms through belief, faith and ritual. The effects of placebos have been known for centuries and placebos were used by priests, quacks and physicians alike. Strictly speaking, a placebo is inert and if it is inert then by definition it does not cause a placebo effect. Anthropologist Daniel Moerman points out that just because two things occur at the same time does not mean that one caused the other. He proposes and defines a 'meaning response' which is 'the psychological and physiological effects of meaning in the treatment of illness'.[9] Where such effects are positive then it is a 'placebo effect' and where such effects are negative they are 'nocebo effects'. Moerman also notes that what is positive in one situation can be negative in another, so this is not a fundamental distinction. Critics still question the authenticity of placebo, pointing out that many chronic conditions exhibit natural fluctuations, are self-limiting or regress to the mean, thus making it difficult to demonstrate cause and effect. A controversial meta-analysis by Hróbjartsson and Götzsche[10] and subsequent papers by the same authors looked at studies that compared placebo groups with groups that received no treatment at all in the same study. They concluded that the placebo effect does not have powerful clinical effects (objective effects). Counter-critics question whether 'no treatment' actually implies the absence of any therapeutic element, bearing in mind that merely participating in a clinical trial even without pills and procedures can produce clinical improvement if it includes a doctor-patient encounter. The balance of evidence supports placebo as a real and significant phenomenon.

- **All placebos are not equal**. Studies have demonstrated the differential effects of placebo. For example, a validated sham acupuncture device has a greater placebo effect on subjective outcomes than oral placebo pills[11] and subcutaneous injections of placebo are superior to oral placebos in the treatment of migraine.[12]
- **Placebos have side-effects – nocebo.** It is not uncommon for study subjects to withdraw from clinical trials because of side-effects related to placebos. Studies on asthma have also shown that placebo saline inhalers can cause bronchoconstriction or bronchodilation depending on the accompanying suggestion.[13]
- **Placebos involve definite neuro-physiological processes**. The physiological mechanisms of placebo are both conscious through conditioning and expectancy and unconscious through neurophysiological processes. Functional MRI scans show that the mere anticipation

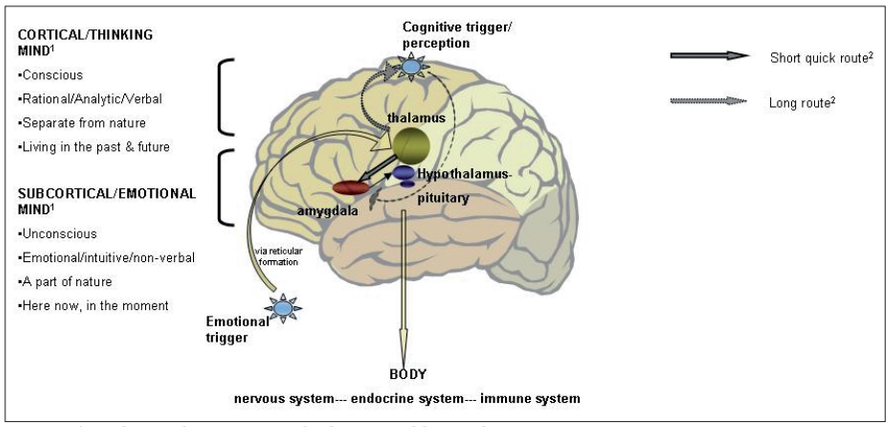

Fig. 1. Thoughts and emotions – the brain and beyond.

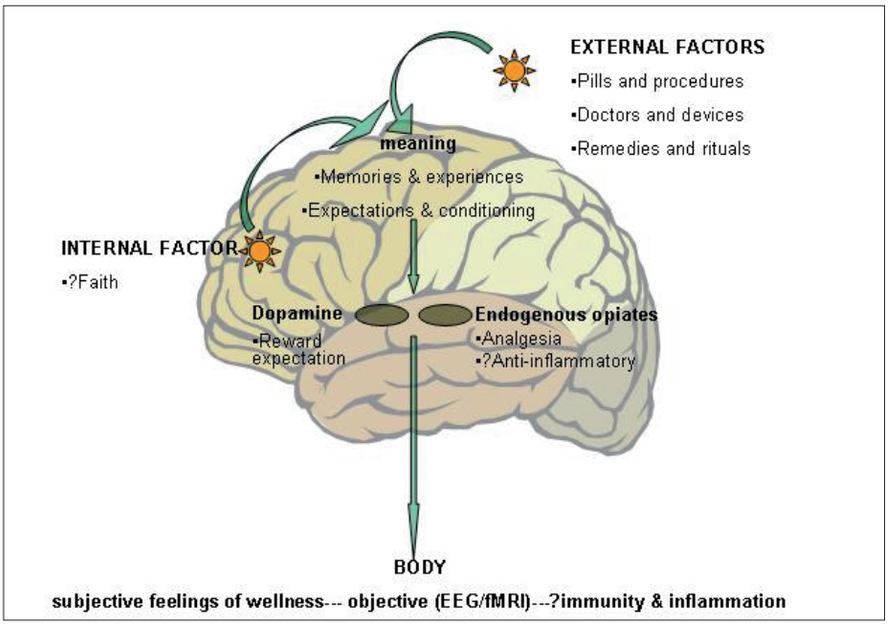

Fig. 2. Belief and placebo – the brain and beyond.

of pain even in the absence of a noxious stimulus activates cortical nociceptive networks.[14] Endogenous opioids and dopamine have now been shown to be significant mediators of placebo responses. Endorphins are released with placebo-induced analgesia[15] and it has been shown that a hidden injection of naloxone blocks this process. Dopamine is involved in the expectation of clinical improvement (reward) and placebo has been shown to release substantial amounts of endogenous dopamine in patients with Parkinson's disease.[16] Similarly nocebos (e.g. a physiological saline injection coupled with an expectation of pain) causes increased levels of blood cortisol,[17] and this effect can be also blocked with proglumide, a cholecystokinin antagonist.[18]

- **Placebos work best when the recipients are aware of it**. Hidden administrations of pharmacological and non-pharmacological therapies are less effective than the open ones.[19] A study testing the placebo effect on cancer pain found a greater effect with informed patients (those who knew details of the experiment) compared with patients who were not informed.[20]
- **Placebo adherence can improve survival.** A more provocative meta-analysis in 2006 showed that good adherence to placebo is associated with lower mortality.[21] An obvious confounder here would be that good adherers generally follow healthy protocols in all aspects of their lives. The question is should we be taking our placebos more regularly?

Placebo – beyond the brain

There is no doubt that a placebo can make one feel better but the question that often arises is whether a placebo can actually *make* you better. Evans hypothesises that the placebo effect may be mediated by alteration of one or more components of the acute-phase response and there is evidence that placebo-responsive conditions such as pain, swelling, stomach ulcers, depression, and anxiety all involve, to a greater or lesser extent, activation of the acute-phase response (the innate immune response).[22] There are consistent indications that skin and mucosal inflammatory diseases, in particular, are strongly modulated by placebo treatments. Morphine is known to suppress natural killer cell activity and this is thought to be mediated by central processes involving the sympathetic nervous system and dopaminergic systems.[23,24] Likewise, endorphins and dopamine may be the means by which the brain modulates peripheral immune reactivity through positive expectations and behavioural conditioning processes. These mechanisms link belief and the meaning response directly with the immune system.

A universal placebo

All medical and non-medical treatments involve some degree of placebo responsiveness. The effect of a placebo is determined by a number of factors, e.g. route of administration (oral versus injection), learned associations (green paracetamol may work better than the white), verbal instructions, logical reasoning and the clinical context. Moreover, the qualities of the therapist are very influential, as evident from the fact that the same placebo administered by one doctor may work consistently better than when administered by another. Placebo responses also vary within individuals and between cultures. There can never be a universal placebo and what is very effective for one person may have no effect on another.

Limits of placebo response

Evidence demonstrating the immediate analgesic and possible anti-inflammatory effects of a placebo supports the idea of a natural innate healing mechanism. Some argue that the placebo effect at best offers temporary symptomatic relief for pain and inflammation. Other studies show that the extent to which the placebo cures depression is short-lived.[25] Apart from anecdotal evidence, studies supporting a *curative* potential of a placebo in conditions other than pain and inflammation are rare. As mentioned earlier, placebos theoretically modulate natural killer cell activity (via endogenous opiates) in inflammatory conditions. Given that NK cells keep tumour activity in check, it is not unreasonable to speculate that placebos potentially support 'immune surveillance' or the *preventive* functions of the innate immune system on a daily basis. The mechanism, magnitude and extent of such an effect are uncertain. In reality though, once tumours are clinically detectable they have already eluded the primary immune defenses. Knowing that cancers themselves vary in their immune susceptibility and aggression and that not all aspects of the immune system are susceptible to psychological input, further challenges the placebo-immune-cancer postulate.[22] Lolette Kuby, author of *Faith and the Placebo Effect*,[26] argues that too much credit is given to the placebo (external factor) but that faith (internal factor) in a higher self is capable of mobilising the powers of self-healing sufficiently enough to effect a cure. Given that there are countless cases of non-medical cures and many patients who spontaneously heal without seeking medical attention, this theory does attract a certain curiosity. One has to also consider to what extent psychosocial elements capitalise from the self-healing mechanisms of placebo.

Psychosocial perplexities (Fig. 3)

Hemingway defines a psychosocial factor as 'a measurement that relates psychological phenomena to the social environment and to pathophysiological changes'.[27] Acutely stressful psychosocial events including emotional upset, physical exertion, earthquakes, wars and even Monday mornings have been linked to increased cardiac morbidity. Further evidence on cardiac morbidity and mortality supports a link with depression, poor social support, job stress and interpersonal conflict.[28-30] Chronic stress and negative emotions are also associated with poorer cardiac prognoses. A critical review of the literature by Garssen found that no single psychosocial factor has been implicated in cancer development but 'helplessness and repression seem to confer an unfavorable prognosis while evidence around depression and low social support were less convincing'. The review also notes that influences of life events (other than loss events), negative emotional states, fighting spirit, stoic acceptance/fatalism, active coping, personality factors, and locus of control were minor or absent.[31] In the SALSA study, where subjects were asked 'Are you hopeful about the future?', hopelessness predicted all-cause mortality in older and middle-aged adults.[32] However, the effect of positive attitude on physical health and immunity are mixed. Edward Creagan,[33] Mayo Clinic oncologist, draws a more realistic analogy: If you are run over by a bus or herd of buffalo, then it is highly unlikely that attitude and disposition have anything to do with survival because the assault on your body is completely overwhelming. If, however, you injure your knee in a sports accident or you are diagnosed with cancer and your psychological defences are firmly rooted, then it is possible to marshall enough resources to cope better with the illness or injury. Creagan also claims the only three common themes evident in long-term cancer survivors are not biological but psychosocial ones, namely a sense of religion (any belief system involving a higher power), a sense of spirituality (meaning and purpose in life) and a sense of social connectedness (meaningful relationships with others). New neurohormonal and immune mechanisms by which these psychosocial and behavioural factors impact health are being discovered every day.

More worrying are recent findings that maternal and environmental factors play a role in determining our autonomic tone and immune responsiveness. Early-life

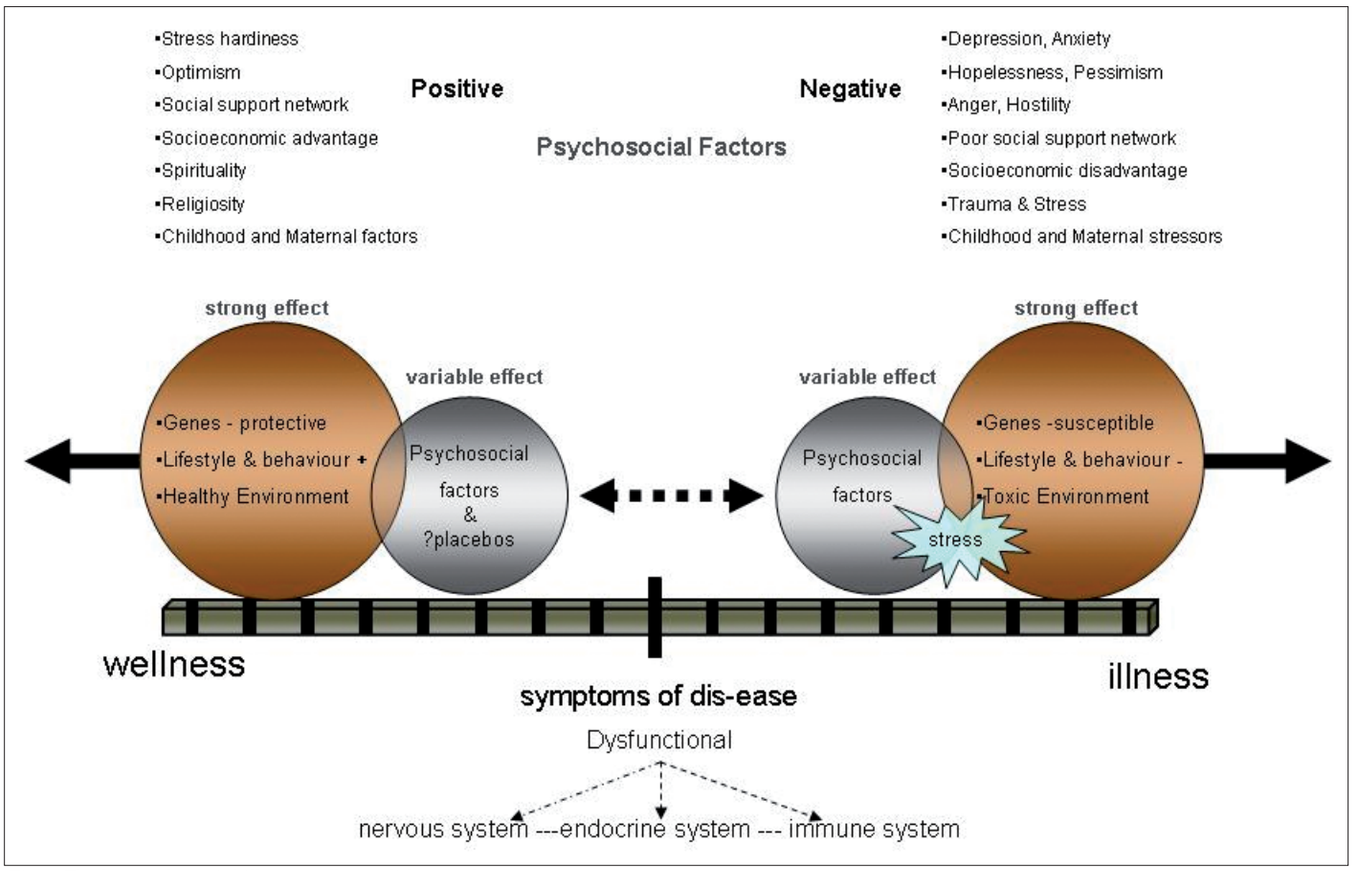

Fig.3. The biopsychosocial illness-wellness sliding scale.

traumatic events appear to permanently render the neuroendocrine stress response systems supersensitive[34] and unfavourable socioeconomic conditions early in life modulate genes that regulate inflammation to the extent that a heightened propensity to inflammation persists throughout one's lifespan. This is associated with an increased vulnerability to respiratory and cardiovascular diseases.[35] Psyche can also modulate soma at the most fundamental level of gene expression and 'many of the normal psychobiological states of everyday life such as waking, sleeping, dreaming, stress, emotional arousal, personal relationships, focused attention, physical exercise and responses to novelty and environmental enrichment are associated with different patterns of gene expression' – Ernest Lawrence Rossi.[36]

Almost all illnesses are multifactorial in aetiology, and psychosocial factors constantly interact with biological ones in a tug-of-war on a wellness-illness sliding scale (Fig. 3). The magnitude of their effect is determined by individual factors as well as the type, stage and aggression of the threatening condition.

Conclusions

There are a multitude of psychosocial factors that engage unlimited human variables to produce a range of effects that either support wellness or intensify illness. We will always know too little of that which we cannot easily control, measure or regulate in clinical trials. Scientific research on mind-body concepts is never absolute and should not renounce the intuitive evolutionary wisdom of nature. 'Miracles do not happen in contradiction to nature, but only in contradiction to what is known to us of nature' – St Augustine.

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In a nutshell

- Modern lifestyle and stress are distancing the thinking mind (verbal, rational, analytical) from the emotional mind (emotional, intuitive and non-verbal).
- Compared with the thinking mind, the emotional mind is closely linked to autonomic and immune physiology.
- Our bodies react to our perception of a stressful stimulus rather than the stimulus itself.
- Therapeutic touch can modulate neuroendocrine and immune processes.
- There is a physiological basis for belief (placebo), a phenomenon once thought to be 'all in the mind'.
- Our experiences, culture and meaning are closely linked to our biology.
- Placebos may modulate peripheral immune reactivity.
- Acutely stressful psychosocial factors are linked to cardiac morbidity and mortality.
- No single psychosocial factor has been implicated in cancer development.
- Everything we think, feel and do is mirrored in physiological processes.
- Genes and immunity are modulated by psychobiological states of everyday life.

Single Suture

Carotid plaque area a strong predictor of first myocardial infarction

A prospective, population-based study assessed the predictability of three factors related to a first ever myocardial infarct – carotid intima media thickness, total plaque area, and plaque echogenicity – and followed up more than 6 200 adults aged 25 - 84 for 6 years. It turns out that carotid plaque area is a stronger predictor of first-ever myocardial infarction than is intima media thickness and, overall, carotid atheroma is a stronger risk factor for myocardial infarction in women than in men.

Stroke 2007; 38: 2873.