Acupuncture – self-appraisal and the reward system

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Abstract

Acupuncture is an ancient therapy with a variety of different explanatory models. A cascade of physiological effects has been reported, both in the peripheral and the central nervous system, following the insertion of a needle or light tapping of the skin. Clinical trials testing the specific claims of acupuncture have generally tried to focus on testing the efficacy of applying specific techniques and/or specified points. However, different conditions may respond differently to different modes of stimulation.

Recently, it was demonstrated that both superficial and deep needling (with *de qi/Hibiki*) resulted in amelioration of patellofemoral pain and unpleasantness. The pleasurable aspect of the acupuncture experience has largely been ignored as it has been considered secondary to its pain alleviating effects. This aspect of acupuncture treatment is likely to be related to activation of self-appraisal and the reward system.

When a patient seeks a therapist there are expectations of a specific effect. These expectations are partly based on self-relevant phenomena and self-referentia introspection and constitute the preference. Also, when asked about the effect of the treatment, processes that orientate pre-attentive anticipatory or mnemonic information and processes that mediate self-reflection and recollection are integrated together with sensory detection to enable a decision about the patient's perception of the effect of acupuncture treatment. These 'self-appraisal' processes are dependent on two integrated networks: a ventral medial prefrontal cortex–paralimbic–limbic 'affective' pathway and a dorsal medial prefrontal cortex–cortical–hippocampal 'cognitive' pathway.

The limbic structures are implicated in the reward system and play a key role in most diseases and illness responses including chronic pain and depression, regulating mood and neuromodulatory responses (eg sensory, autonomic, and endocrine). The pleasurable and neuromodulatory aspects of acupuncture as well as 'placebo needling' may partly be explained by the activation or deactivation of limbic structures including the hippocampus, amygdala, and their connections with the hypothalamus.

In patients with patellofemoral pain, the effects of superficial and deep needling remained for six months. These long term pain-alleviating effects have been attributed to activation of pain inhibiting systems in cortical and subcortical pathways. When considering long term effects the cortical–cerebellar system needs to be taken into account. The cortical–cerebellar system is probably central to the development of neural models that learn and eventually stimulate routinely executed (eg motor skills) and long term (eg pain alleviation) cognitive processes. These higher order cognitive processes are initially mediated in prefrontal cortical loci but later shift control iteratively to internal cerebellar representations of these processes. Possibly part of the long term healing effects of acupuncture may be attributed to changes in the cerebellar system thereby sparing processing load in cortical and subcortical areas.

As cortical and subcortical structures are activated and/or de-activated following stimulation of receptors in the skin, disregarding site, 'placebo or sham needling' does not exist and conclusions drawn on the basis that it is an inert control are invalid.

'Self' may be seen as a shifting illusion, ceaselessly constructed and deconstructed, and the effect of acupuncture may reflect its status (as well as that of the therapist).

Keywords

Acupuncture, cerebellum, depression, limbic structures, medial prefrontal cortex, pain, placebo control, reward system, self-appraisal.

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Introduction

Acupuncture is an ancient therapy with different explanatory models.[1] A number of physiological effects have been reported, both in the peripheral and the central nervous systems, following the insertion and stimulation of a needle. Trials testing the specific claims of acupuncture have generally tried to focus on testing the efficacy of varying stimulation techniques and/or specified points. However, insertion of needles into the body can stimulate specific effects though these are not dependent on the locations of stimulation.[2] Therefore, factors that are simultaneously site specific and unrelated to the site of needling might play a role in the outcome of acupuncture therapy for pain. It is also important to note that different pain conditions might respond differently to different modes of stimulation.[3]

Patellofemoral pain syndrome (PFPS) is one of the most common musculoskeletal disorders, especially in young adults.[4] It has been suggested that patients suffering from PFPS are more prone to develop knee osteoarthritis. However, there is no consensus on the definition of PFPS, its classification, assessment, diagnosis, or management. Symptoms and clinical findings in subgroups of individuals with PFPS, classified on the basis of the findings in radiological examinations and compared with subjects with healthy knees, have recently been reported.[4] An orthopaedic surgeon and a physical therapist consecutively examined 75 patients clinically diagnosed as having PFPS. Radiography revealed pathology in 15 patients, and scintigraphic examination revealed focal uptake of technetium in two patients indicating local pathology. Diffusely increased uptake (sign of sympathetic hyperactivity) was present in 29 patients. In the remaining 29 patients, radiographic and scintigraphic examinations were normal. Subjects with healthy knees differed significantly from the three patient groups in all clinical tests measuring pain in response to provocation: ie compression test, medial and lateral tenderness and passive gliding of the patella. Differences in clinical tests between the patient groups were not significant. The main finding and conclusion of the study was that, in patients with PFPS, it was not possible to detect peripheral pathology with the tests used and that the pain might be due to sympathetic hyperactivity.

A randomised controlled study was conducted to evaluate the effect of acupuncture treatment of patients with PFPS.[5] Fifty eight patients, clinically and radiologically examined, were randomly assigned to either deep acupuncture treatment with low frequency electrical stimulation or minimal superficial acupuncture with attached electrodes but without electrical stimulation. The patients were treated twice weekly for a total of 15 treatments. The main outcome measurements were one leg vertical jump, functional score, daily visual analogue scale (VAS) recordings of perceived pain intensity, and skin temperature. Fifty-seven patients completed the study. After the treatment period, pain intensity was rated significantly decreased within both groups but with no significant difference between the groups. The decline in pain recordings remained significant even after three and six months in both groups. Even though the pain was rated as decreased after sensory stimulation, the ability to jump on one leg, the functional score, and the skin temperature remained unchanged. This study showed that patients with PFPS appear to benefit from both electroacupuncture treatment and subcutaneous needling. The pain relieving effect of acupuncture remained for six months. The effects are likely to be attributable to activation of pain inhibitory mechanisms or deactivation of pain processes in the central nervous system. Also, it is generally observed following acupuncture that many patients experience reduction of unpleasantness, restoration of wellbeing (health) and their sense of self.

Recently, Hui using accumulative neuroimaging results, thereby achieving larger sample sizes than previously obtained from a single trial, reported that superficial tactile stimulation results in changes in a subset of deep brain structures, although of weaker magnitude and more limited in extent than real acupuncture (matched for acupuncture points and subjects).[6] The difference between real acupuncture and tactile stimulation varied with the acupuncture points, which may be attributed to differences in innervation of the stimulated tissue. This is supported by Wu and collaborators who found that superficial needling produces many of the sensations elicited with 'real' acupuncture needling, but at a lower frequency and with a different pattern of distribution.[7] It has been reported that superficial needling results in the activation of A-beta and A-delta nerve fibres

inducing analgesia.[8] One reason why previous studies on acupuncture neuroimaging have not reported on the effects of superficial acupuncture is possibly related to the fact that these studies have been underpowered to reveal the more subtle actions of superficial needling. Moreover, many of the limbic structures located at the base of the brain such as the amygdala are vulnerable to susceptibility artefacts and suffer signal loss in studies that use thicker sections in the axial orientation (Hui KKS, personal communication).

Acupuncture and self-appraisal

In many patients, reduction of unpleasantness, restoration of wellbeing (health) and the patient's sense of self may be of greater importance than the actual reduction in pain intensity. Neuroimaging studies have shown that there are dedicated brain systems central to appraising the self-relevant content of one's environment and one's conscious mental events.[9] These systems are adjusted to the detection of environmental phenomena (exteroceptive and interoceptive information: sensory, somatic, autonomic) that convey significance to a patient. Also, the systems are able to install self-relevant information (introspective information: thoughts, memories) from past experience to create abstract associations with stimuli, or, to initiate such information independent of external stimuli altogether (for example expectancy). In this way, one may consider salience simply as propagation of sensory information (like acute pain) sufficient for attention, whereas wellbeing and self-relevance are central processes generated by at least two integrative sub-systems: one that orientates pre-attentive information to self-relevant phenomena and one that engages pensive processes like self-reflection.[9-15]

The task domains that orient preventative or mnemonic information (pre-attentive biasing information) to salient or openly self-relevant phenomena fall into the broad cognitive–affective domains of reward, fear, pain, and affection. The neural substrata include the ventral medial prefrontal cortex (vMPFC), anterior cingulate (ACC), nucleus accumbens (Nacc, also denoted ventral striatum), amygdala (Amg), and insula. The vMPFC is central for detection of self-relevant information (prepotent, biasing or self-relevant) whereas the primary function of Amg and Nacc (limbic structures) is discrimination of a neuromodulatory response (sensory, autonomic, and endocrine) to specific biasing features of the tasks to facilitate heightened watchfulness of immediately or potentially self-relevant environmental cues.[16-50]

When patients are asked how an acupuncture treatment (stimulus) makes them feel (self-relevant tasks) there is a shift to one's self as the referent which results in activity in distinct neural structures including the ventral and dorsal medial prefrontal cortex (dMPFC), dorsorostral (rACC), and posterior cingulate (PCC). These findings have implications for acupuncture research, suggesting that so called 'placebo acupuncture' is not inert as the patients are continuously asked how the stimulation makes them feel. Also, treatments (stimuli) that convey general information for survival or wellbeing are related to activation in the vMPFC and ACC, Amg, Nacc and insula. Taken together, detection of self-relevance from exteroceptive or interoceptive inputs (needle manipulation and being asked about the treatment effect) triggers a cascade of subcortical processing that orientates the subject or patient on to an increased response potential. Re-integration of this information at vACC and MPFC loci prevent or diminish re-direction of attention based on prior experience through integration with contextually appropriate memory traces, of one's past experiences. This would suggest that when given a treatment (drug or acupuncture), the specific meaning of the treatment results in activation of associated self-relevant processes ie an intervention for pain alleviation results in pain alleviation and a drug for insomnia results in induction of sleep.[51-77]

The neural substratum that engages introspective processes includes the dorsal–ventral MPFC, dorsorostral ACC and PCC.[9] Specifically, this response pattern has been observed during self-appraisal of one's own personality traits, as well as one's opinions, personal morals, attitudes, and during appraisal of one's own preference (eg food, colour). PCC is involved in retrieval of personally significant memories (episodic information) and the dorsorostral ACC function in executive control processes such as selective attention. In contrast to the attention allocating mechanism of the dorsorostral ACC, the dorsal anterior MPFC is involved in evaluative processing of self-relevant mental content. This distinction between anterior MPFC and dorsorostral

ACC function is in line with conclusions drawn from a recent meta-analysis on social cognition, wherein the prior structure was implicated in self-knowledge, and evaluative processes in selective attention.

When a patient seeks a therapist there are expectations of a specific effect. These expectations are partly based on self-relevant phenomena and self-referential introspection and constitute the preference. Also, when asked about the effect of the treatment, processes that orientate pre-attentive anticipatory or mnemonic information and processes that mediate self-reflection and recollection are integrated together with sensory detection to enable a decision about the patient's perception of the effect of acupuncture treatment. These 'self-appraisal' processes are dependent on two integrated networks: a ventral medial prefrontal cortex–paralimbic–limbic 'affective' pathway and a dorsal medial prefrontal cortex–cortical–hippocampal 'cognitive' pathway.[9;68]

Pariente and collaborators explored the cerebral consequences of needling and expectation with 'real' acupuncture, 'placebo control' acupuncture (Streitberger needle – non-penetrating, blunt telescopic needle) and skin prick (blunt needle), using a single blind, randomised crossover design with 14 patients suffering from painful osteoarthritis, who were scanned with positron emission tomography (PET).[78] The results of the PET scans showed that insula ipsilateral to the site of stimulus was activated to a greater extent during real acupuncture than during the 'placebo control' intervention. Both 'real' and 'placebo control' acupuncture with the same expectation of effect caused greater activation than skin prick (which had no expectation of a therapeutic effect) in the right dorsolateral prefrontal cortex, anterior cingulate cortex, and midbrain. These results suggest that 'real' acupuncture and 'placebo control' acupuncture have specific physiological effects and that patients' expectation and belief regarding a potentially beneficial treatment modulate activity in cortical and subcortical areas. That 'placebo control' acupuncture may have a physiological effect is also supported by recent studies showing that stimulation of skin mechanoreceptors coupled to unmyelinated afferent C nerve fibres result in activity in the insular region.[2] Activity in these C tactile afferents has been implicated in a limbic reward response. It is likely that control procedures used in many acupuncture studies (superficial or minimal needling) aimed at being inert are in fact activating these C tactile afferents and consequently are not inert. Furthermore, these 'control procedures' probably activate the reward system and as such induce feelings of wellbeing.[2]

Default mode

It has been suggested that PCC, rostral ACC, and MPFC compose a network characterised by a default mode of high level baseline activity, and further, that this baseline is similar to the brain's continuous resting oxygen extraction level. Possibly the default mode encompasses processes similar to introspection and the time relaxing between and after an acupuncture treatment.[57;79-82] This is presently under investigation by Kathleen Hui and collaborators.

Acupuncture, reward and neuromodulation

Limbic structures play a key role in most diseases and illness responses including chronic pain and depression, regulating mood and neuromodulatory responses (eg sensory, autonomic, and endocrine). The pleasurable and neuromodulatory aspects of acupuncture as well as 'placebo needling' may partly be explained by the activation or deactivation of limbic structures including the hippocampus, amygdala, and their connections with the hypothalamus, septal area, and portions of the tegmentum.[83] As the limbic structures are activated or deactivated following stimulation of receptors in the skin, disregarding site, 'placebo-needling' does not exist and conclusions drawn on the basis that it is an inert control are false and truly misleading.

The hippocampus and frontal regions of the cerebral cortex have received much attention since reductions in hippocampal (and cortical) volumes were reported in patients with chronic pain, depression and post-traumatic stress disorder in whom memory and cognitive dysfunctions are commonly reported. Also, a decline in hippocampal function, which exerts inhibitory control over the hypothalamic-pituitary-adrenal (HPA) axis, could contribute to the hypercortisolemia found in a subset of depressed individuals. Bucinskaite and co-workers previously reported on the effects of repeated electroacupuncture treatments on open-field behaviour and on hippocampus concentrations of neuropeptide Y (NPY), neurokinin A (NKA), substance P (SP), galanin (GAL) and vasoactive intestinal peptide (VIP)-like immunoreactivities (-LI)

in the two rat strains Wistar-Kyoto (WKY) and spontaneously hypertensive rats (SHR).[84] Significantly higher concentrations of SP-LI, NKA-LI and NPY-LI were found in the hippocampus immediately after three weeks of electroacupuncture treatment compared to untreated animals with similar changes in neuropeptide concentrations in the two rat strains. Open-field behaviour was significantly reduced during the treatment period in both strains. Also, rats receiving treatment had higher thresholds to nociceptive stimuli and were calmer than control rats. There were significant negative correlations between behaviour and neuropeptide concentrations in spontaneously hypertensive rats, suggesting interdependency with sympathetic activity. It was proposed that some of the effects of electro-acupuncture in rats are related to increases in NPY-LI, NKA-LI and SP-LI in the hippocampus. Interestingly, it has been reported that basal NPY-LI is lower in the hippocampus of 'depressed' rats (Flinders Sensitive Line) compared with controls, and that electroconvulsive stimuli (ECS) raise NPY-LI in the hippocampus.[85] These findings suggest that NPY is involved in depressive disorder and that antidepressant effects of ECS may in part be mediated through NPY. Furthermore, the hippocampus has been implicated in the regulation of anxiety and memory processes and low concentrations of SP-LI and NKA-LI has been seen in rats with chronic 'pain'. Possibly, this disturbance could be compensated for by repeated electro-acupuncture treatments. Another, modality of stimulation that may prove to be effective in depression is laser-acupuncture (Quah-Smith, personal communication).

While the hippocampus and frontal cortex are involved in aspects of chronic pain and mood disorders, these regions do not account for all symptoms.[86-101] In recent years a role for other parts of the brain including the brain's reward regions have been demonstrated. Studies have identified the nucleus accumbens (NAcc) and its dopaminergic inputs from the ventral tegmental area (VTA) of the midbrain, as one of the most important anatomical substrates for rewards, such as food, sex, and social interactions. The amygdala, traditionally viewed as being critical for learned associations between negative emotional stimuli and environmental cues, serves a similar function for rewarding stimuli. Interestingly, many patients with chronic pain and depression show reduced ability to experience pleasure (anhedonia) and loss of motivation, as well as abnormalities in several neurovegetative functions such as appetite, sleep, energy level, and circadian rhythms. All of these processes are part of highly overlapping and interacting circuits in which the dopaminergic VTA-NAcc pathway plays a critical role.[102-135] A role for acupuncture and moxibustion in these conditions is supported by studies showing that they result in the activation of the reward system.[78]

Probably, the transcription factor CREB (cAMP response element binding protein) is a key regulator of the reactivity of brain reward circuits and thereby regulates individual sensitivity to emotional stimuli.[135-148] Short term increases in CREB activity in NAcc, induced by normal rewarding or aversive stimuli, could serve to dampen responses to subsequent stimuli and facilitate the ability to deal actively with the situation at hand (eg consumption of reward, escape from danger) ie increased resilience. Under more pathological conditions, however, larger and more sustained increases in CREB activity, induced by drug abuse or excessive stress, would lead to an excessive dampening of emotional reactivity. Conversely, sustained reductions in CREB activity, which are seen under conditions of social isolation, would heighten emotional reactivity and in the extreme be associated with a state of anxiety. The regulation of depression-like behaviour by changes in CREB activity within the NAcc is partly mediated by dynorphin.[149-152] Possibly, excessive activation of CREB by chronic stress increases dynorphin expression in the NAcc, which feed back to decrease VTA dopamine function and trigger certain features of chronic pain and depression. Recent findings indicate that acupuncture as well as moxibustion like stimulation modulates CREB (unpublished observations).

Brain derived nerve growth factor (BDNF) and other neurotrophins like nerve growth factor (NGF) play an important role in the reward system.[153-162] Under normal conditions, this BDNF signalling is critical for the appropriate memories of potentially rewarding or dangerous settings. Under pathological conditions, however, this signalling may establish abnormal associations, which would lead to certain symptoms of pain and depression even in the absence

of true external threats. Probably, BDNF signalling in the VTA-NAcc is required for the establishment of important associations with negative emotional stimuli. This could possibly explain why some patients who have tried acupuncture and experienced it as being unpleasant are less inclined to try it again as the mere thought could evoke unpleasant associations.

The hypothalamus plays an important role in reward mechanisms and in the neuromodulatory responses (sensory, autonomic and endocrine) to illness.[163-172] This has been explained in part by the fact that dopaminergic fibres from the VTA project to the NAcc through the lateral hypothalamus. Studies of feeding behaviour have especially provided new insights into the interaction between hypothalamus and VTA-NAcc. Recent work has begun to draw connections between hypothalamic feeding peptides and depression. Of particular interest in this respect is melanin-concentrating hormone (MCH), which is a major orexigenic (pro-appetite) peptide expressed in a subset of lateral hypothalamic neurons. Administration of MCH into the NAcc stimulates feeding behaviour, whereas blockade of its receptor (MCH1 receptor) decreases feeding. Moreover, several MCH1 receptor antagonists administered systemically or directly into the NAcc, exert antidepressant-like effects. Another transmitter in the lateral hypothalamus that also plays a role is orexin (hypocretin). Orexin increases feeding by promoting a state of wakefulness and alertness via orexin OX1 receptors. Further, orexin is also involved in regulating sleep-wake cycles. Abnormalities in orexin signalling have been implicated in disparate types of sleep abnormalities reported in chronic pain and depression. Taken together, two types of patients emerge: one whose chronic pain and depression is characterised by reduced activity and weight gain and one who exhibits increased activity, anxiety, and weight loss. An anti-depressant acting on one subset of receptors may therefore be effective or ineffective whereas acupuncture may work differently 're-establishing the balance' between the regulating centres disregarding the 'subtype'.

Many patients report their most serious symptoms in the morning with some improvement as the day progresses. This may represent an imbalance in their circadian rhythms causing fluctuations in mood, motivation, energy level, and responses to rewarding stimuli.[173-176] The suprachiasmatic nucleus (SCN) of the hypothalamus is considered the master circadian pacemaker of the brain. Here, circadian rhythms are generated at the molecular level by different transcription factors like Clock, Bmal, Per and Cry genes. Clock dimerises with Bmal and that dimer induces the expression of Per and Cry genes, which in turn feedback to repress Clock-Bmal activity. This Clock-Per cycle in the SCN is essential for matching circadian rhythms with the light-dark cycle. These circadian genes are also found in the VTA and NAcc indicating that they play a role in the regulation of mood. Furthermore, there has been interest in NPAS2 (neuronal Pas domain protein-2) in mood regulation.[177-179] NPAS2 is homologous to Clock and, like Clock, dimerises with Bmal to regulate the expression of Per and Cry in a circadian fashion. NPAS2 is not expressed in SCN but in several limbic structures and especially within the NAcc.[20] Interestingly, NPAS2 knockout mice show increased anxiety-like behaviour and deficits in fear conditioning. It has been suggested that NPAS2 is a critical mediator of circadian rhythms in emotional responses via actions in limbic regions of the brain such as the NAcc. Preliminary findings suggest that acupuncture regulates NPAS2 activity.

Further studies are needed to explore the basis of acupuncture treatment in reward and reinforcement (delayed or uncertain), in implicit or procedural (stimulus-response) representational systems and in explicit or declarative representational systems. Individual differences in sensitivity to delays and uncertainty may contribute to the variable responses to acupuncture. Learning (attributing a meaning) and choice (preference) with delayed and uncertain reinforcement are related but in some cases dissociable processes. The contributions to 'delay discounting' and 'uncertainty discounting' of neuromodulators including serotonin and dopamine, and of specific neural structures have recently been reviewed.[180] Activation of the reward system by acupuncture stimulation is strongly supported by recent studies investigating the effects of electroacupuncture on serotonin and dopamine contents in the brain rewarding system in restrained conscious rats.[181] The results showed that electroacupuncture increased the serotonin and dopamine contents of the nuclei accumbens, caudate, putamen and lateral hypothalamus, whereas

decreased content of these monoamines were seen in the dorsal raphe nucleus and amygdala. Differences in frequency effects (1Hz or 100Hz) on dopamine and serotonin were also reported. It was indicated that the effects of electroacupuncture compensated for the changes elicited by the restraint stress.

Acupuncture and long term effects

Napadow, Hui and collaborators recently used functional magnetic resonance imaging (fMRI) to evaluate the short and long term effects of acupuncture and 'sham' stimulation at acupoint LI4 in patients with carpal tunnel syndrome and in healthy controls.[186] Carpal tunnel syndrome patients responded to acupuncture with greater activation in the hypothalamus and deactivation in the amygdala as compared with healthy controls. A similar difference was found between carpal tunnel syndrome patients at baseline and after acupuncture treatments. For baseline carpal tunnel syndrome patients responding to acupuncture, functional connectivity was found between the hypothalamus and amygdala – the less the deactivation in the amygdala, the greater the activation in the hypothalamus, and vice versa. Furthermore, hypothalamic response correlated positively with the degree of maladaptive cortical plasticity in patients with carpal tunnel syndrome. This study provides evidence that chronic pain patients have a different response to acupuncture than healthy controls, through a coordinated network including the hypothalamus and amygdala. One reason that some previous studies on acupuncture imaging have not reported on the deactivation effects of acupuncture is possibly related to the fact that some authors, who use Statistical Parametric Mapping (SPM) for data analysis, have refrained from reporting deactivation, even if present, because of the dispute in the interpretation of blood oxygen level-dependant (BOLD) signal decreases.

In addition to the mentioned networks above, the cortical-cerebellar system needs to be taken into account. Ramnani and collaborators argue that a cortical-cerebellar system is central to the development of neural models that learn and eventually stimulate routinely-executed cognitive processes.[184;185] Initially, higher order cognitive processes, mediated in prefrontal cortical loci, shift control iteratively to internal cerebellar representations of these processes, resulting in sparing processing load on less efficient executive pre-frontal resources. Evidence exists for this cortical–cerebellar system in the acquisition of motor skills, which enables rapid 'effortless' execution and sequencing of bodily movements.[43;186-192] Furthermore, a growing body of results indicate that internal cerebellar models may extend across a much broader range of contributory cognitive processing, inclusive of attention to anticipated informational cues, processing prediction errors for monetary reward, and autobiographical memory. As with highly efficient cerebellar models of motor actions, which simulate complex bodily actions from simple motor commands, so too these models may facilitate detection processes inherent to appraising self-relevant content from task features, or, attentional shifting between one's external environment and introspective mental content.[43;186-192] The influences of task relevance to the self may determine the effects of acupuncture suggesting that not only the pain system should be taken into account when assessing the effects of acupuncture. Also, part of the long term healing effects of acupuncture may be ascribed to changes in the cerebellar system thereby sparing processing load in cortical and subcortical areas.

Conclusion

In conclusion, the results of current research suggest that acupuncture techniques as well as non-penetrating 'placebo controls' activate the patients' expectation and belief regarding a potentially beneficial treatment thereby modulating activity in the reward system.[193;194] Acupuncture may be viewed as an intervention that triggers and enhances expectancy but not equivalent with expectancy itself. These mechanisms are activated in addition to the well known analgesic effects of acupuncture.[195;196]

'Self' may be seen as a shifting illusion, ceaselessly constructed and deconstructed, and the effect of acupuncture may reflect its status (as well as that of the therapist).

Further studies on acupuncture and the default mode are essential when assessing the effects of acupuncture using the neuroimaging paradigm in general.

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