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#### Conclusions :

- 1. Urinary disorder is influenced by brain.
- 2. Brain is influenced by luteinizing hormone.
- 3. Pelvic floor muscles are influenced by brain.
- 4. Urological Chronic Pelvic Pain Syndrome(UCPPS) is influenced by brain.
- 5. Brain is influenced by the low intensity laser acupuncture stimulating thirteen ghost acupoints(includes CV1)

\* Keywords : brain, pelvis, review article, 골반, 뇌, 종설 논문

# I. INTRODUCTION

The safe performance of balance- and mobility-related activities during daily life, such as standing while performing manual tasks, rising from a chair and walking, requires adequate balance control mechanisms[1]. The disorders in balance control can be a consequence of pathologies, such as neurological disease, stroke, diabetes disease or a specific vestibular deficit, or can be due to age-related processes, such as a decline in muscle strength[2, 3], sensory functioning[4], or in generating appropriate sensorimotor responses[5]. Balance and mobility disorders can have serious consequences regarding physical functioning (e.g. reduced ability to perform activities of daily living) as well as psycho-social functioning (e.g. activity avoidance, social isolation, fear of falls) and may even lead to fall-related injuries. Advanced age alone carries an increased risk of perioperative morbidity and mortality[6, 7] Impaired cognition has also been correlated with adverse postoperative health outcomes, including an increased incidence of complications, delirium, a longer length of hospital

stay, and higher 6 month mortality[8]. Thus, more emphasis is being directed at cognition testing in the standard panel of preoperative risk assessment testing[6, 7]. ER Trowbridge et al.[9] say that screening for potential cognitive impairment in an ambulatory urogynecology population is feasible and useful in clinical practices.

For example, while walking, individuals with Huntington's disease(HD) demonstrated greater pelvic movement than controls in two conditions, peak anterior excursion and total anterior-posterior excursion. This indicates that during walking, individuals with HD tended to move farther into anterior pelvic tilt than the controls, while moving into an equivalent amount of posterior pelvic tilt. This finding is consistent with findings in elderly adults and individuals with traumatic brain injury[10, 11]. So pelvic condition is important for the quality of life.

Through the local reflex and central nervous system, acupuncture induces endocrine and autonomic responses to meet therapeutic effects[12, 13]. In East Asia, acupuncture has been used for a long time to treat many kinds of disorders especially including the neuropsychiatric illnesses[14, 15]. For decades, acupuncture was becoming increasingly popular in western countries and has aroused interests of scientists[16, 17]. Many studies[18–20] adopted fMRI or positron emission tomography (PET) to investigate the effects on human brain functions caused by acupuncture at the particular acupoint.

We researched about the relation of the brain and the pelvis by one principle of Korean medicine, 'shang bing xia qu, xia bing shang qu'(上病下取, 下病上取).

## $\Pi$ . METHOD OF RESEARCH

We searched the keywords, 'brain' and 'pelvic' in PubMed. We selected the papers from the

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results (2505 papers at 2018.9.28) which contained 'brain' and 'pelvic' at once. After reading their abstracts, we selected suitable some of them which were suitable with our objective. And of their reference, we selected suitable papers in same way. By reviewing them, we have come up with some conclusion.

## Ⅲ. REVIEW

#### 1. Research about Relation of the Brain and the Pelvic Floor.

#### 1) Urinary Disorder.

Camryn Harvie et al.[21] likelihood estimation map yielded six clusters of activation in the pons, cerebellum, insula, anterior cingulate cortex, thalamus, and the inferior frontal gyrus. Regions of the brain involved in executive control (frontal cortex), interoception (anterior cingulate cortex, insula), motor control (cerebellum, thalamus), and brainstem (pons) are involved in micturition. This analysis provides insight into the supraspinal control of voiding in healthy adults and a framework to understand dysfunctional voiding. Underactive bladder is a common voiding dysfunction in which the detrusor muscle is unable to generate an effective contraction sufficient to empty the bladder[22]. As many as 9–48% of men and 12 – 45% of women undergoing evaluation for lower urinary tract symptoms are diagnosed with underactive bladder[23, 24]. Leading theories suggested that the failure of the bladder to generate a sufficient bladder contraction during the voiding phase is likely due to an underlying neurological mechanism[25]. Evidence from animal experiments[26] suggests that during the voiding phase regions in the caudal brainstem coordinate the contraction of the detrusor muscle with the relaxation of the urethral sphincter but the initiation of micturition is determined in

regions of the forebrain. In humans, several neuroimaging studies have been performed to determine central mechanisms of micturition.

Using activation likelihood estimation method (ALE), Arya et al.[27] performed a meta-analysis of the regions of the brain activated during the storage phase of micturition. Afferent signals from the PAG are relayed via the thalamus to the insula, and likely the ACC which ultimately allows storage of urine in the bladder through increased sympathetic discharge, relaxation of the detrusor muscle relaxation of the bladder, and urethral sphincter contraction[28]. Using ALE meta-analysis, Arya et al.[29] reported on the regions of the brain that are activated during the filling or the storage phase of micturition.

C. Harvie et al.[30] provided the first voxel based meta-analysis to identify brain regions that are activated during the voiding phase of micturition. These regions include the brainstem, inferior frontal gyrus, insula, anterior cingulate cortex, thalamus, and cerebellum. Their finding that the anterior cingulate cortex (ACC) and the insula are activated in the voiding phase of micturition is clinically important. The ACC and the insula are also activated during bladder filling both in healthy controls as well as in subjects with overactive bladder, a condition of urinary urgency with or without incontinence[31, 32].

The insula, an area of the cerebral cortex that lies deep to the lateral sulcus receives afferent homeostatic information from the viscera, such as heart rate, respiration, digestive processes and micturition[33]. Also called the sensory cortex of the autonomic nervous system, activation of the insula during the storage phase represents afferent signaling from the bladder to the CNS. The ACC, located on the medial surface of the frontal lobe and surrounding the anterior genu of the corpus callosum, is called the motor cortex of the autonomic nervous system because it is responsible for

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emotional, behavioral, and motor responses to visceral stimuli[34]. Alternatively, activation of the ACC and the insula during voiding may represent tight coupling between afferent and efferent centers in the brain[30]. Activation of the PFC has been reported both in subjects who could void successfully as well as those who were unable to void in the scanner despite trying vigorously to do so[35-37]. Some findings suggested that the decision to void in likely generated in the PFC. Prefrontal cortex is part of the attention network and is also concerned with the highest level of brain function including executive decision making [38]. On the other hand, stimulation of the cell group situated more ventrally and laterally in the dorsal pontine tegmentum results in contraction of the pelvic floor including the urethral sphincter through the Onuf's nucleus in the sacral spinal cord and has been called the L-region or the continence center[26]. As part of the attention and awareness networks, thalamic activation during storage determines which afferent signals from the bladder should reach the cerebral cortex[39]. Animal studies have demonstrated extensive connections of the cerebellum to other parts of the central nervous system including those involved in micturition and lesions of the cerebellum in humans are associated with both storage and voiding symptoms[40].

BD Clarkson et al.[41] evaluated older women with Urgency urinary incontinence(UUI) receiving biofeedback-assisted pelvic floor muscle therapy (PFMT), which focuses on identifying the correct muscles via biofeedback, urge suppression strategies, and behavioral techniques to avoid panic reactions to urgency and compared them to a similar continent group ("controls") who did not receive treatment using three different approaches. Women who responded well to therapy had different baseline brain activation patterns associated with urgency[42] and these patterns tended to normalize among responders, but not among non-responders. Their results suggested that there

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may be at least two mechanisms contributing to UUI: one in which a breakdown in central control plays the greater role and is thus responsive to a behaviorally targeted therapy like PFMT and another in which central control is still largely intact and for which a brain/behavior-targeted approach is less useful.

#### 2) Luteinizing Hormone

Luteinizing hormone receptor(LHR) expression was also detected in nonpregnant human uterus (glandular and luminal epithelial cells, stromal cells, myometrial cells and vascular smooth muscle cells), syncytiotrophoblast of midterm but not term human placenta, fetal membranes and decidua[43], human and rat brain[44, 45], human trophoblast and syncytiotrophoblast from early pregnancies[46], porcine fallopian tubes and umbilical cord[47, 48], ovarian, decidual, endometrial and luteal macrophages[49, 50], and ovarian cancer cell cultures and tumor tissues[51]. Since the brain was reported to express functional LHR[44, 45], there is also a possibility that high LH levels in aging individuals may in some way participate in the development and progression of neurodegenerative process of several degenerative neurological diseases, including Alzheimer's disease.

Strong LHR expression in microglial cells in the brain cortex is of particular interest. Microglial cells are resident macrophages in the central nervous system, and LHR expression has been described in other types of human resident macrophages (ovary, decidua, endometrium and corpora lutea)[49, 50] Pathological activation of microglia has been reported in a wide range of conditions such as Alzheimer's disease, cerebral ischemia, prion diseases, multiple sclerosis, AIDS dementia, and other degenerative neurological diseases[52, 53]. Some of these degenerative diseases are associated with advanced age and high levels of circulating LH. High LH levels might pass the

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presumptive LH barrier of brain vessels expressing LHR, or vascular LHR expression might diminish with age, as in abnormal term placentae. Yet, elevated maternal midtrimester chorionic gonadotropin is associated with fetal cerebral blood flow redistribution and adverse perinatal outcome[54]. In addition, estrogens, which are known to cause a diminution of high LH levels in postmenopausal women, have been reported to be effective in the prevention and treatment of Alzheimer's disease[55–57]. Since CG increases secretion of a variety of cytokines by monocytes, and induces their inflammatory reaction and phagocytic activity[58–61], high LH levels in aging individuals may also activate resident macrophages in the central nervous system and contribute to the development of Alzheimer's disease and other inflammation-mediated neurodegenerative diseases. Outside of the area occupied by microglial cells in the grey matter of the cerebral cortex, weaker LHR expression was also detected in some nerve cells. A Bukovsky et al.[62] said that such nerve cells could be directly influenced by LH/CG proteohormones (with unknown consequences), while the nerve cells among microglial branching processes are protected from such an effect.

#### 3) Pelvic Floor Muscles Disorder

Pelvic floor muscles play a critical role in reproductive and excretory processes[63]. A link between stress urinary incontinence(SUI) and nerve injuries affecting the urethral viscerosomatic reflex has been reported[64]. Consequently, a number of therapies to manage SUI, ranging from Kegel exercises to electrical stimulation of sacral and pudendal nerves, have been proposed as potential therapies to improve the function of pelvic floor musculature and its innervation[65]

According to Williams G et al.[10] and Lee LW et al. [11], individuals with Huntington's disease(HD) demonstrated greater pelvic movement than controls in two

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conditions, peak anterior excursion and total anterior-posterior excursion while walking. This indicates that during walking, individuals with HD tended to move farther into anterior pelvic tilt than controls, while moving into an equivalent amount of posterior pelvic tilt. This finding is consistent with findings in elderly adults and individuals with traumatic brain injury.

#### 4) Urological Chronic Pelvic Pain Syndrome (UCPPS)

UCPPS represents a group of pain syndromes relating to male and female pelvic pain that are poorly understood and for which treatment is largely unsatisfactory[66-68]. Since 2007, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) [69] has combined Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS) and Interstitial Cystitis/Painful Bladder Syndrome (IC/PBS) into a single classification of UCPPS. The complex and largely unknown etiology, as well as the varied symptom presentation in UCPPS, presents tremendous difficulties in both diagnosis and classification [70-72]. This complexity inherent in UCPPS suggests that some potential combination of peripheral and central nervous system biomarkers may be the best approach to diagnosis and may lead to a better understanding of the condition itself. For example, a functional magnetic resonance imaging (fMRI) brain study has recently shown functional differences between CP/ CPPS patients and healthy controls (HCs) that seem unique to this specific pathophysiology [73]. Other noninvasive neuroimaging studies have also suggested structural and functional differences may exist between various pain conditions and HCs, including Irritable Bowel Syndrome (IBS)[74, 75], chronic back pain [76-78], chronic pancreatitis[79], and chronic complex regional pain syndrome (CRPS)[80]. The Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network (The MAPP Research Network

Study Group.) was developed to better understand the underlying pathophysiology of UCPPS and inform clinical management of patients[66, 81]. One important goal of the MAPP Network is to identify potential biological markers for UCPPS[82].

DE Harper et al. [83] interested in determining whether brain metabolite levels in several pain processing regions differ in UCPPS patients and controls. Additionally, they assessed whether regional metabolite levels related to functional connectivity of these regions. The results showed lower GABA and higher choline levels in the ACC of UCPPS patients, compared to age- and gender-matched control participants.

In patients, higher choline levels were related negative mood and higher ACC-tolimbic system connectivity. In addition, posterior insula Glx levels were related to higher pIC-to-ACC connectivity in patients compared to controls, in a region where significantly different metabolite levels were detected across groups. Their results add to the growing body of literature indicating central abnormalities in chronic pelvic pain and are the first to showing possible deficits in inhibitory neurotransmission in UCPPS.

The evidence for centralized components of chronic pelvic pain has been provided by brain neuroimaging studies, many from the MAPP Research Network, showing significant structural and functional anomalies in patients including white and gray matter differences, altered resting state functional connectivity[84–88] and heightened painevoked brain activity in and functional connectivity between painprocessing brain regions.

Furthermore, quantitative sensory testing has demonstrated widespread hyperalgesia, allodynia, and impaired endogenous analgesia in individuals with chronic pelvic pain, including UCPPS[89-97], which also strongly suggested involvement of the central nervous system.

Altered levels of brain metabolites have been observed in chronic pain patients with

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endometriosis[89] and in other non-pelvic pain conditions[76, 98-114].

However, mounting evidence from neuroimaging suggests that the pain in many UCPPS patients may be related to alterations in the function and morphology of the central nervous system (CNS)[82, 84–89, 115–117]. Similar abnormalities of the CNS occur in other chronic overlapping pain conditions that are frequently comorbid with UCPPS[118–121], including fibromyalgia (FM), irritable bowel syndrome, chronic fatigue syndrome, and temporomandibular disorders.

The evidence for centralized components of chronic pelvic pain has been provided by brain neuroimaging studies, many from the MAPP Research Network, showing significant structural and functional anomalies in patients including white and gray matter differences[82, 115, 116, 122, 123] altered resting state functional connectivity[84–88], and heightened painevoked brain activity in and functional connectivity between painprocessing brain regions[85, 124]. Furthermore, quantitative sensory testing has demonstrated widespread hyperalgesia, allodynia, and impaired endogenous analgesia in individuals with chronic pelvic pain, including UCPPS[89–97] which also strongly suggest involvement of the central nervous system. UCPPS patients presented with significantly higher choline and lower GABA in the ACC, compared to healthy controls.

### 2. Acupuncture about brain

In recent years, the low intensity laser acupuncture (LA) emerged as a new modality of acupuncture and became increasingly popular due to its painless and noninvasive advantages[125, 126] and its operations in a precise and controlled manner when performing acupuncture[125] since the stimulating depth and strength of LA are independent of the acupuncturist's experience. Some studies had demonstrated low intensity LA at particular acupoint could cause certain effect on brain activities[125,

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127-129]. For instance, in Siedentopf's study[125], laser acupuncture at an acupoint in foot (a target for visual disease treatment) caused the activation of the occipital cortex. Besides, Biella et al.[128], Hui et al.[129], Napadowet et al.[127] found activation of the hypothalamic-limbic system when stimulated the analgesic acupoints by using LA. Thus, the LA is appropriate to be introduced for stimulating thirteen ghost acupoints(TGA). Jian Lv et al.'s[130] understanding the effect of acupuncture on brain functions is mainly based on employing fMRI which allows us to investigate the activation of the brain by recording the blood oxy-genation level-dependent (BOLD) signals obtained from the time series collected when subjects are performing certain cognitive tasks[131] or at rest[132]. In their study, they employed rs-fMRI and evaluated the ReHo and ALFF values to investigate the alterations of brain spontaneous activation in healthy participants after laser acupuncture at TGA.

## IV. CONCLUSION

Treating the lower part of the body to heal the upper and treating the upper to heal the lower ('上病下取, 下病上取', 'shang bing xia qu, xia bing shang qu' - literally, 'upper disease, below treat, lower disease, upper treat') has been a widely applied treatment principle in Chinese medicine since ancient times. We explores and analyses the features of this treatment principle based on published clinical case studies and current research evidence.

We conclude that

- 1. Urinary disorder is influenced by brain.
- 2. Brain is influenced by luteinizing hormone.

3. Pelvic floor muscles is influenced by brain.

4. Urological Chronic Pelvic Pain Syndrome(UCPPS) is influenced by brain.

5. Brain is influenced by the low intensity laser acupuncture stimulating thirteen ghost acupoints(includes CV1).

The brain is mostly undiscovered part in the body. In Korean medicine, there are many principles about the brain. So we can discover them about the brain.

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