



CONCEPTUAL STUDY ON APPLICATION OF fMRI TO OBSERVE THE PHARMACODYNAMIC EFFECT OF NASYA & BASTI ON BRAIN

¹*Dr. Bhairavi Suresh Shah and ²Dr. Neha Milind Sahare

¹Associate Professor, Department of Rognidan Avum Vikrutivigyan, B. R. Harne Ayurvedic Medical College and Hospital, Karav-Vangani, Thane, Maharashtra.

²Associate Professor, Department of Rog Nidan Vikriti Vigyan, Veena Vadini Ayurved College & Hosp. Bhopal, MP.

***Corresponding Author: Dr. Bhairavi Suresh Shah**

Associate Professor, Department of Rognidan Avum Vikrutivigyan, B. R. Harne Ayurvedic Medical College and Hospital, Karav-Vangani, Thane, Maharashtra.

Article Received on 16/06/2020

Article Revised on 06/07/2020

Article Accepted on 26/07/2020

ABSTRACT

Action and the clinical efficacy of each *Panchakarma* procedures are well explained in Ayurvedic literature and practiced thoroughly since long; but mechanism of action of *Panchakarma* procedures is still unexplored in modern perspective. *Nasya* and *Basti* treatment among the five, particularly have effect on the brain as can be understood by studying pharmacodynamics of these two procedures with the help of recent advancement in technology. Functional MRI (fMRI) is a new emerging interventional technique to study the metabolic functioning of brain. This non invasive technique studies the blood flow in brain (oxygenated haemoglobin molecule ratio to deoxygenated haemoglobin molecule) to detect the area of activity. fMRI also includes pharmacological functional MRI (phMRI) which is proved to be useful tool in monitoring changes in brain function resulting from drug administration / treatment. Although it is not technically a marker of target engagement, an fMRI signal can provide indirect evidence of target engagement if a biologically plausible link can be established between the fMRI response and the molecular target. Since pharmacodynamic mechanism of *Nasya* and *Basti* also includes Neural stimulation pathways, this can be well analyzed and understood in detail with the help of fMRI and thus can pave way for the globe to understand and accept the effectiveness of *Panchakarma*. In present study, the role of fMRI to evaluate the functional CNS effect of *Basti* & *Nasya* treatment will be discussed in detail.

KEYWORDS: *Basti*, *Nasya*, fMRI, Pharmacodynamics, CNS.

INTRODUCTION

Panchakarma is the most well known therapeutic concept of ayurveda. The *Panchakarma* (five treatment: *Vaman* (Medicated Emesis), *Virechan* (Medicated Purgation), *Basti* (Medicated Enema), *Raktamokshan* (Blood letting), *Nasya* (Nasal drops)) not only work on a particular organ or disease but on the body as whole. The *poorva karma* (Foremost action) (*Snehapan* (Internal oleation), *Snehan* (external oleation), *Swedan* (steaming)) converts this Detoxification process into process of Biopurification- acting not only on diseased part but body as whole. Along with this the *Paschat karma* (Follow up therapies) (*Sansarjan* (follow up), *Pathya* (diet)) followed for a particular time period gives long lasting effect of *Panchakarma*. *Nasya* and *Basti* treatment among the five, particularly have effect on the CNS as can be understood by studying the contemporary pharmacodynamic analysis of these two procedures.

Advances in Medical technology makes it possible for imaging scans to dissect the body into wafer-thin pictures and create three-dimensional models of organs and tissues to find abnormalities and diagnose disease.

Yet a relatively new type of scan called functional magnetic resonance imaging (fMRI) takes the technology one step farther. Being non invasive it measures brain activity by detecting changes associated with cerebral blood flow.

Pharmacodynamics of *nasya* and *basti*

Nasya treatment is a therapeutic procedure of instilling medicines in to the nose. It is completely different from ordinary intranasal medication with regards to mode of administration (*Purva* and *Pachat karma* included) and contents. Whereas *Basti* refers to enema therapy on the basis of its process of administration. But again it is different from enema as it expresses itself with its *veerya* (quality) and *prabhava* (Potency).

Mode of action of *nasya* Treatment^[1]

The pharmacodynamics of *nasya* can be explained better by taking into consideration both āyurvedic and contemporary references as follows:

A. Mucosal absorption of intranasal drug: It is the first step in mechanism for absorption through the nasal mucosa which includes para-cellular transport via movement between cell and trans-cellular or simple diffusion across the membrane. The medicines then gets absorbed into the superior olfactory veins and then move to the facial vein. Interestingly, both facial and ophthalmic veins have no venous valves in between. So, blood may drain on either side, that is the blood from facial vein can enter cavernous venous sinus of the brain in reverse direction. Thus, such a pooling of blood from nasal veins to cavernous sinus and then surpassing the blood brain barrier can reach the brain and cerebrospinal.

B. Neural pathway: Channels carrying the senses from the sense organs to the head are compared to sunrays and thus signify olfactory and trigeminal nerves. These nerves are chemoreceptor and connected to higher centres of brain. The delivery of drugs to the CNS from the nasal route may occur via olfactory neuroepithelium.

Mode of action of *basti karma*^[2]

1. By absorption mechanism
2. By system biology concept
3. By neural stimulation mechanism
4. By excretory mechanism

The Neural Stimulation Mechanism can be explained as follows- The gastrointestinal system has a network of nerve fibres, which is known as Enteric nervous system (ENS). Gut brain (ENS) is located in the sheaths of tissue lining the oesophagus to colon. ENS is loosely connected with central nervous system (CNS) through Vagus nerve but can mostly function alone. Internal viscera are again highly supplied with nerve fibers of Autonomic Nervous System which in turn has connection with CNS. There are many similarities between CNS -ENS regarding cellular structure, neuropeptide secretion and specific functions and recent studies has shown that there is great influence of CNS and ENS on each other.

Stimulation with *Basti* (either by chemo or mechano receptors) may lead to activation of concerned part of CNS which precipitates result accordingly. This action can again be explained in modern parlance by the direct action of active principles of drug on receptors in the gastrointestinal tract related to the enteric nervous system may act over the to stimulate the CNS causing secretion of required hormones or other chemicals.

Functional magnetic resonance imaging {fMRI}^[3]

fMRI is based on the same technology as magnetic resonance imaging (MRI) -- a non-invasive test that uses a strong magnetic field and radio waves to create detailed images of the body. But instead of creating images of organs and tissues like MRI, fMRI looks at blood flow in the brain to detect areas of activity. The technique relies on the fact that cerebral blood flow and neuronal

activation are coupled, thus help to understand more about how the brain functions. The oxygen-rich blood and oxygen-poor blood have a different magnetic resonance. As already known more active areas of the brain receive more oxygenated blood. The fMRI picks up this increased blood flow to pinpoint greater activity. The measurement of blood flow, blood volume and oxygen use is called the blood-oxygen-level-dependent (BOLD) signal.

Working of fMRI

MRI is based on a magnetic field and radiofrequency pulses and most of the MRI applications use the intrinsic tissue contrast relying on different features of ¹H protons in tissue water without the need of injecting contrast agents. In short, the technique provides excellent soft tissue contrast, rendering it very appropriate to investigate the brain.

The MRI machine, aims radio waves at protons -- electrically charged particles in the nuclei of hydrogen atoms -- in the area of body being studied. As the magnetic field hits the protons, they line up. Then the machine releases a short burst of radio waves, which knocks the protons out of alignment. After the radio-wave burst has ended, the protons fall back in line, and as they do, they release signals that the MRI picks up. The protons in areas of oxygenated blood produce the strongest signals. Functional magnetic resonance imaging (fMRI) is an excellent tool to study the effect of pharmacological modulations on brain function in a non-invasive and longitudinal manner. There are several blood oxygenation level dependent (BOLD) fMRI technique types, which include resting state (rsfMRI), stimulus-evoked (st-fMRI), and pharmacological MRI (phMRI). Respectively, these techniques permit the assessment of functional connectivity during rest as well as brain activation triggered by sensory stimulation and/or a pharmacological challenge.

A computer processes these signals into a three-dimensional image of the brain that can be examined from many different angles. Brain activity is mapped in squares called voxels. Each voxel represents thousands of nerve cells (neurons). It is necessary to statistically compare the relevant BOLD signal change image voxel-by-image voxel between the drug and placebo conditions. Note that drug and placebo conditions must be compared directly to deduce statistically significant drug effect. It is not sufficient to view brain activity separately in the drug and placebo conditions and observe that one appears larger than the other without performing a statistical test between the two. Color is added to the image to create a map of the most active areas in the brain.

Pharmacological fMRI^[4] specifically evaluates the neurovascular coupling which represent the relationship between a change in neuronal activity and the observable

hemodynamic response as measured by a BOLD signal change.

Challenges and way ahead

The results of fMRI can be a challenge to interpret as the psychometric nature of individual is to be recorded which is indeed difficult task. For instance, some individuals are very anxious which can elicit responses in areas of brain that are not normally engaged. Interpretation of data therefore depends on being able to collect large no of samples to be able to exclude false positive results. Despite its infancy, the use of phMRI has recently expanded in recent years having being used to examine the effects of CNS penetrating drugs both in humans and animals. Many studies have been done and ongoing in diseases specifically affecting CNS like schizophrenia, depression, Alzheimer's. Although it is not technically a marker of target engagement, an fMRI signal can provide indirect evidence of target engagement if a biologically plausible link can be established between the fMRI response and the molecular target.

Application of fmri in studying the pharmacodynamics of nasya and basti

As already discussed above, *panchakarma* procedures of biopurifications not only work on single organ but the body as whole. In particular the *Basti* and *Nasya karma* are known to act through Neural Stimulation pathways thus affecting the CNS. fMRI provides temporal and spatial resolution that makes it ideal for studying the acute effects of rapidly acting drugs. fMRI can be done to analyse effects of *Basti* and *Nasya* on CNS through different experimentations. For example Scan done before and immediately after the procedure or healthy and diseased person simultaneously after the procedures and even by using placebo and medicated drugs in the procedures. fMRI can help to identify the functional areas of brain which are involved/stimulated in the neural pathways of these procedures.

CONCLUSION

Panchakarma is the most effective and powerful unique identification of Ayurveda. But as the evidence based medicine/procedures are trending, a detailed study of dynamics of these procedures is required. Pharmacological fMRI has proven to be a useful tool in monitoring changes in brain function resulting from drug treatment and is likely to provide more sensitive markers of drug effect than the subjective behavioural reports which are commonly used in drug trials. With the help of collaborative team work of Ayurveda physicians, Radiologist and Neurophysiologist and modern tools/technology the efficacy of these procedures can be understood on the widely acceptable parameters. And thus can pave way for the world to understand and accept the effectiveness of this result oriented pathy.

REFERENCES

1. Vipin kumar, Conceptual Study on mode of action of Nasya, IJAPR, 2017; 5(7): 100-102
2. Gyanendra shukla et al., Pharmacodynamic understanding of basti: A contemporary approach, IJPBA, 2012; 3(4): 893-896.
3. Richard Wise, The role of fMRI in drug discover, JMRI, 2006; 28.
4. Elizabeth Jonckers et al The power of using fMRI on small rodents to study brain pharmacology and disease, Front.Pharmacol., 2015; 21.