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Feature Article

Developments of NMR - From Molecules to Human Behaviour and Beyond

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Abstract. NMR has made rapid progress in the last more than seven decades after its discovery. This article reviews the development of this field over the years with emphasis on some of the recent developments with interesting consequences for the study of mental health and human behaviour.

Keywords. NMR, MRI, fMRI, Molecular structure, Brain imaging

INTRODUCTION

Nuclear Magnetic Resonance (NMR) is perhaps the only field which has produced seven Nobel Laureates till date in all the disciplines of science in which the prize is given, in a short span of about seventy years from the discovery of the phenomenon. Over this period, it has thus established itself as a full-fledged interdisciplinary science rather than being just an analytical technique. Its utility has been fully exploited by physicists, chemists, biologists, clinicians, agriculturists, industrialists, computer scientists, psychologists and social scientists. The developments of the field up to 1996 are described in the eight-volume Encyclopaedia of NMR[1] published in the year 1996 to commemorate 50 years of the discovery of the phenomenon. The growth of the field has been so voluminous that a supplementary 9th volume of the encyclopaedia had to be published within 5 years of the initial publication.[2] This presentation gives a brief description of the field over these years from the perspective of the authors. The articles published by the authors earlier have been liberally used. Developments of the field 'at a glance' are presented in Fig.1.

NMR IN BULK MATERIAL

Purcell in MIT/Harvard and Bloch in Stanford became interested in experiments leading to accurate measurements of magnetic fields/magnetic

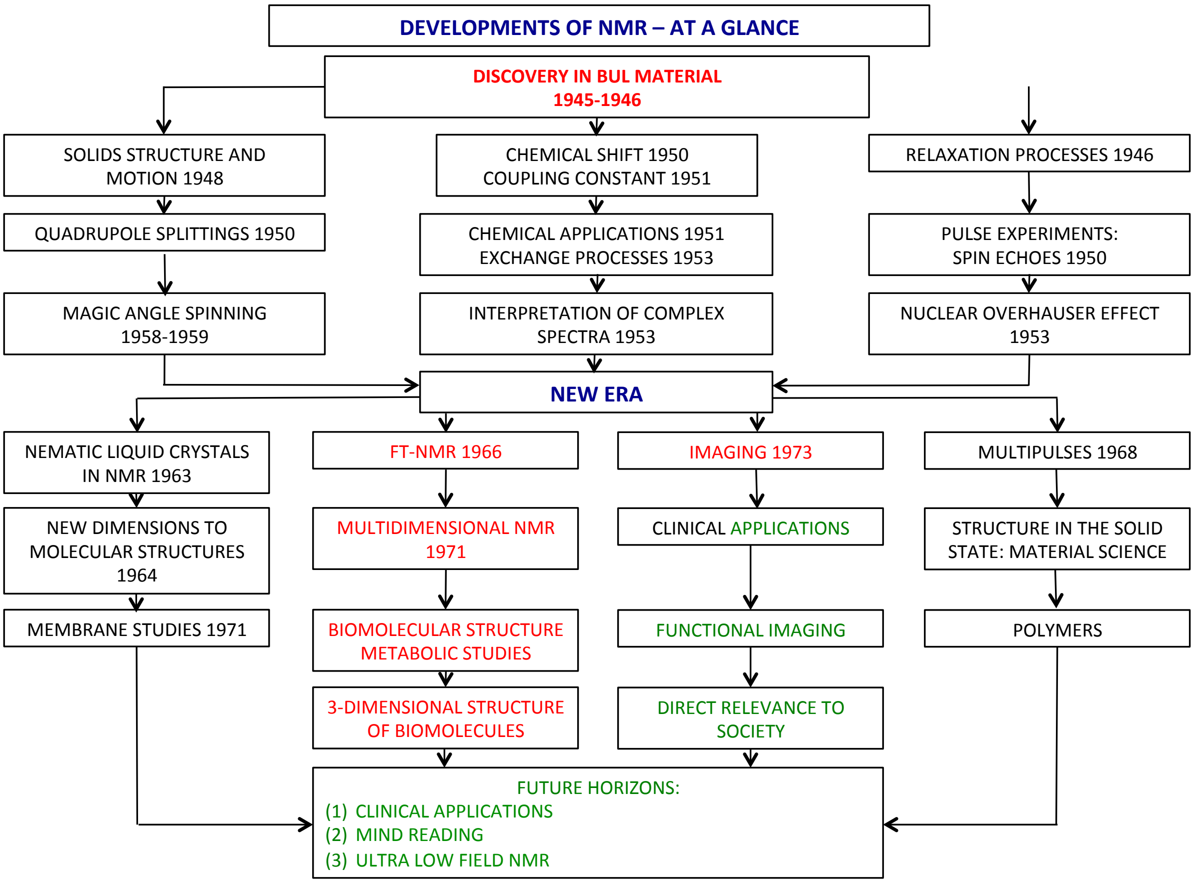

Figure 1. Developments of NMR at a glance.

moments. Both the groups succeeded and NMR in Bulk materials was born in 1945 and the results published in the same issue of the Physical Review.[3,4] Both the scientists got the Nobel Prize in Physics in 1952. NMR in India started in 1951 with the first report of NMR experiments carried out in flowing liquids by Suryan[5] who demonstrated that the arrival of fresh polarized sample at the RF coil decreases saturation and results in a more intense NMR signal. He was able to estimate Spin – lattice relaxation time (T_1) from the flow rate and the geometrical parameters of the system.

NMR IN CHEMISTRY

Proton Chemical Shifts: Dramatic observation[6] of separate lines for non-equivalent protons in the same molecule, by Arnold, Dharmatti and Packard in 1951 set the stage for most of the applications of NMR in various branches of sciences dealing with structural studies. The first molecule to be studied was acetic acid and then ethyl alcohol (Fig. 2). This led to the discovery of 'Chemical Shifts' in protons and it formed the basis of most of the applications of NMR.

Indirect Spin-Spin Couplings: This is another parameter which is of great significance in structural studies.

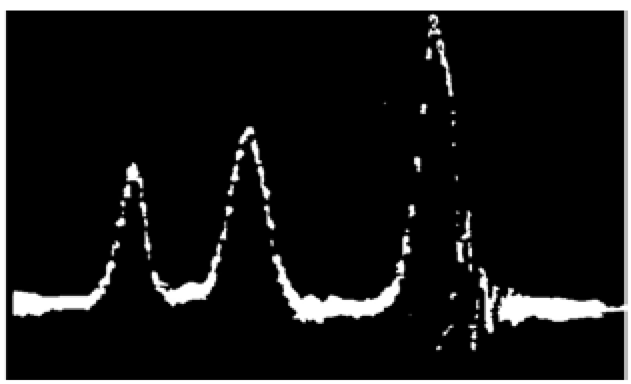

Figure 2. First reported proton NMR spectrum 1 spectrum of ethyl alcohol. Reprinted from Ref. 6, with the permission of AIP Publishing.

Unlike Chemical Shifts, it is field-independent. It is difficult to establish unequivocally the real discoverer of Spin-spin Couplings; at least the following three groups can be considered independently responsible for its observation.

1. Arnold, Dharmatti and Packard did get the indication of some fine structure as line-distortion particularly in the methyl peak in their original spectrum of ethyl alcohol (Fig. 2) but this distortion went unnoticed.
2. Gutowsky and Hoffman observed 2 lines of comparable intensity in the ^{19}F spectrum of PF_3.[7]
3. Hahn and Maxwell observed the same effect in entirely different manner – as 'slow-beats' in the spin-echo envelope for non-equivalent protons[8].

In structural studies, the spin-spin couplings have been extensively employed to estimate the dihedral angles using Karplus equations.[9] The couplings for protons on adjacent saturated carbons ($J_{Vicinal}$) can be employed to estimate the dihedral angles within a precision of a few degrees using the following empirical equations:

($J_{Vicinal}$) = 8.5 cos2 j-0.28 Hz (for 0°<j<90°)
($J_{Vicinal}$) = 9.5 cos2 j-0.28 Hz (for 90°<j<180°)

NEW ERA IN NMR

The following discoveries changed the destiny of NMR and the field entered a new era.

1. Fourier Transform NMR (1965-66)
2. Two-dimensional NMR (1971-72)
3. Magnetic Resonance Imaging (1973-74)

Fourier Transform NMR: The development of Fourier transform methods[10] represents a turning point in the history of NMR. In an NMR experiment at a particular magnetic field strength (B_o), the angular frequency of precession (ω_o) of the nuclei is given by the Larmor equation $\omega_o = \gamma B_o$ where the proportionality constant γ is the magnetogyric ratio (ratio of the magnetic moment to the angular momentum). In a conventional continuous wave NMR experiment, the resonance condition is arrived at either by keeping the frequency of irradiation fixed while varying the magnetic field fixed or vice versa. Such slow scan experiments were of limited utility especially for studies of solutions with low concentrations of the nuclei of interest, nuclei with low natural abundance, larger molecules, fast dynamic processes and so on. Even as efforts to improve the sensitivity of the NMR experiment were in progress, to speed up the experiment Ernst and Anderson[10] suggested the use of the Fourier transform method. Herein, a short burst of radiofrequency (r.f.) excitation, called a pulse of r.f., excites nuclear spin resonances over a broad band of frequencies. The precession of nuclear spins having resonance frequencies falling in this band-width generates the NMR signal in the time domain. Subsequent Fourier transform of the signal provides the frequency domain NMR spectrum. This innovation changed NMR signal acquisition from frequency-domain to time-domain and thus on the one-hand made the NMR experiment faster by several-folds. On the other-hand, it opened up the flood-gates for innovation in NMR and the possibility of carrying out a whole lot of new experiments. Thus a new era of research and applications of NMR was born. Though difficult to publish the results at the time, the experiment formed the basis of the 1991 Nobel Prize in Chemistry to Richard Ernst.

Two –dimensional NMR: The concept of two-dimensional (2D) Fourier transform NMR was given by the Belgian Physicist J. Jeener who presented his results at Ampere International Summer School, in 1971.[11] He proposed a simple sequence of two 90° pulses separated by a time period $t_1$which is incremented between the experiments. This is followed by double Fourier transformation of the signal acquired after the second pulse. A spectrum is thus obtained which has spread in two frequency dimensions and for homonuclear experiments has diagonal as well as cross peaks. The cross peaks carry important information as they result due to magnetization transferred from one nuclear spin species to another that has an indirect spin-spin coupling to it. The results were never published formally. The school was attended by Thomas Bauman of Richard Ernst's group. When briefed by Baumann, Ernst was very excited but still did not pursue the idea for quite some time since firstly he considered it as "Jeener's Property" and secondly he did not have a computer adequate to handle the two-dimensional data storage and processing. Eventually, he applied the concept to a different area namely magnetic resonance imaging (vide below) initially and later on published a series of papers that formed the foundation of two-dimensional NMR as a methodology.[12]

Magnetic Resonance Imaging (MRI): Paul Lauterbur conceived the idea of using magnetic field gradients to obtain 2 and 3 dimensional spatial information about the distribution of magnetic nuclei in a sample placed inside NMR coil. He thus created the picture of the object by NMR and called the technique as Zeugmatography. He published the work in Nature[13] in 1973 and also submitted it as a poster presentation at the triennial conference of the International Society of Magnetic Resonance held in Bombay in 1974. The presentation was however, converted into an invited plenary talk by the organizers.

MRI is based on the principles of NMR but instead of revealing structures of molecules, MRI reveals the structure of an object, by mapping the distribution of a molecule (usually water) in the object. MRI's most successful and well known application is in the field of medicine where it is used to image organs of a human body in microscopic details. In human MRI, a person lies inside a large hollow magnet. With a combination of magnetic field gradients and radio waves, signals are produced. A computer converts these signals into a series of 2-D images. The images can then be combined to create high-resolution 3-D pictures of the subject. Advancements in the area such as Fourier imaging (by Kumar et al.[14]) and Echo Planar Imaging (EPI) introduced by Mansfield[15] contributed to a rapid expansion of the use of the technique in a number of contexts.

Nuclear Magnetic Resonance and Magnetic Resonance Imaging and Spectroscopy have developed into valuable diagnostic tools during the past three decades. The Radiologists and the Clinicians have literally captured the technique during this period like what the chemists did about a half a century back. Reasons for such a widespread growth are built into the origin of the phenomenon, which involves the use of low energy electromagnetic radiation. The effects produced are, however, large and easily detectable with the present day technology, leading to details of molecular structures obtained at the atomic level.

APPLICATIONS OF NMR AND MRI

NMR is being used in a variety of areas. The range of application of NMR is illustrated in Fig.3. Leaving out some of the well known applications of NMR in Chemistry, in Bio-molecular structure determination and in Material Science, we highlight here applications in some of the other areas.

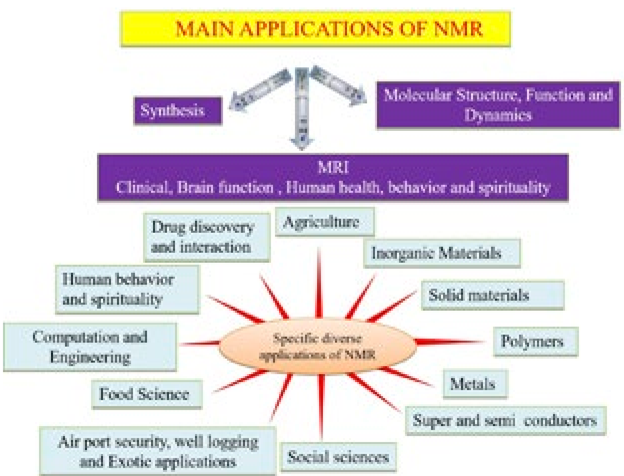

Figure 3. Major applications of NMR in different areas.

NMR APPLICATION IN AGRICULTURE

Hydration in food stuffs: It is based on the fact that water molecules in many such products are more mobile than the protons in the host matrix. The proton spectra thus consist of sharp signals superimposed on broad background.[16]

The state of absorbed water: It has been investigated in meat, seeds, dairy products, and vegetables.[17]

The effect of storage: Significant differences in the free and bound water on storage have been reported on potatoes, garlic and apples.[18]

Rapid distinction between oil and water in agricultural products: NMR has been employed in rapid distinction of oil and water and dedicated instruments manufactured for such purposes. The instrument manufacturers with publicity such as "…. Accurate moisture contents in SECONDS…. Not in hours" became multi-billionaires.[19]

Oil build-up as a function of time after flowering of the seeds: NMR has been used to examine the quality of the oil as a function of maturity of the seeds as well as the determination of percentages of individual saturated and unsaturated fatty acids in intact seeds .[20]

Total oil content in individual seeds: NMR has found extensive utility for selecting the best seeds for plant breeding. Such a fast and non-destructive method provides a means to increase the average oil content of corn 2.25 times when compared with traditional selection methods resulting in gains over five generations that would have otherwise taken 20-30 generations.[21]

Spatial distribution of water and oil in intact seeds: The spatial distribution of oil and water in intact groundnut and sunflower seeds have been obtained.[22] In the immature commercial groundnut seeds complementary oil and water distributions have been observed (Fig.4). The two images exhibit distinctly different features indicative of different intracellular environments in the two cotyledons – oils is present predominantly in one the cotyledons and water in the other. In this immature groundnut seed, it has been interpreted as the incomplete oil-build up with the result that the oil and water within the seed are preferentially localized in complementary manner. The water soluble sugars yet to be converted to storage lipids are confined in one of the cotyledons. A physiological disorder may be responsible for this differential micro environment in the two cotyledons.

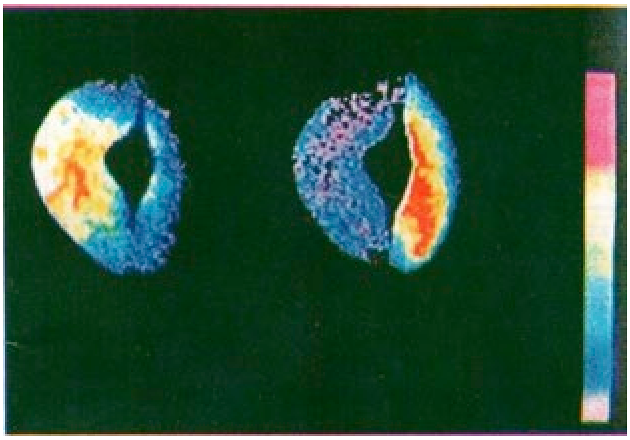

Figure 4. [1]H NMR images of transverse section of a commercial variety of ground nut seed. Left: Water image and right: Oil image. The extreme right shows the scale with the concentration increasing from top to bottom. PERMISSION IN ATTESA

SOME CLINICAL PROBLEMS INVESTIGATED USING NMR

The objective has been to identify specific markers for the quick and non-invasive diagnosis of the diseases and to monitor the treatment. Several problems related to human bile, liver graft dysfunction, Fulminant Hepatic Failure, bacterial urinary tract infection, mal-absorption syndrome, obstructive jaundice, breast disorders, congenital heart disorders, benign and malignant gallbladders, alkaptonuria, and mitochondrial diseases have been reported.[23-33] Results on three typical studies are briefly mentioned below. For details, one may refer to the cited literature.

Human Bile: Human bile being a complex mixture of numerous metabolites provides highly overlapping and complex spectra requiring the need for the highest field NMR especially for quantification of the individual components. A typical 800 MHz is reproduced in Fig.5. The

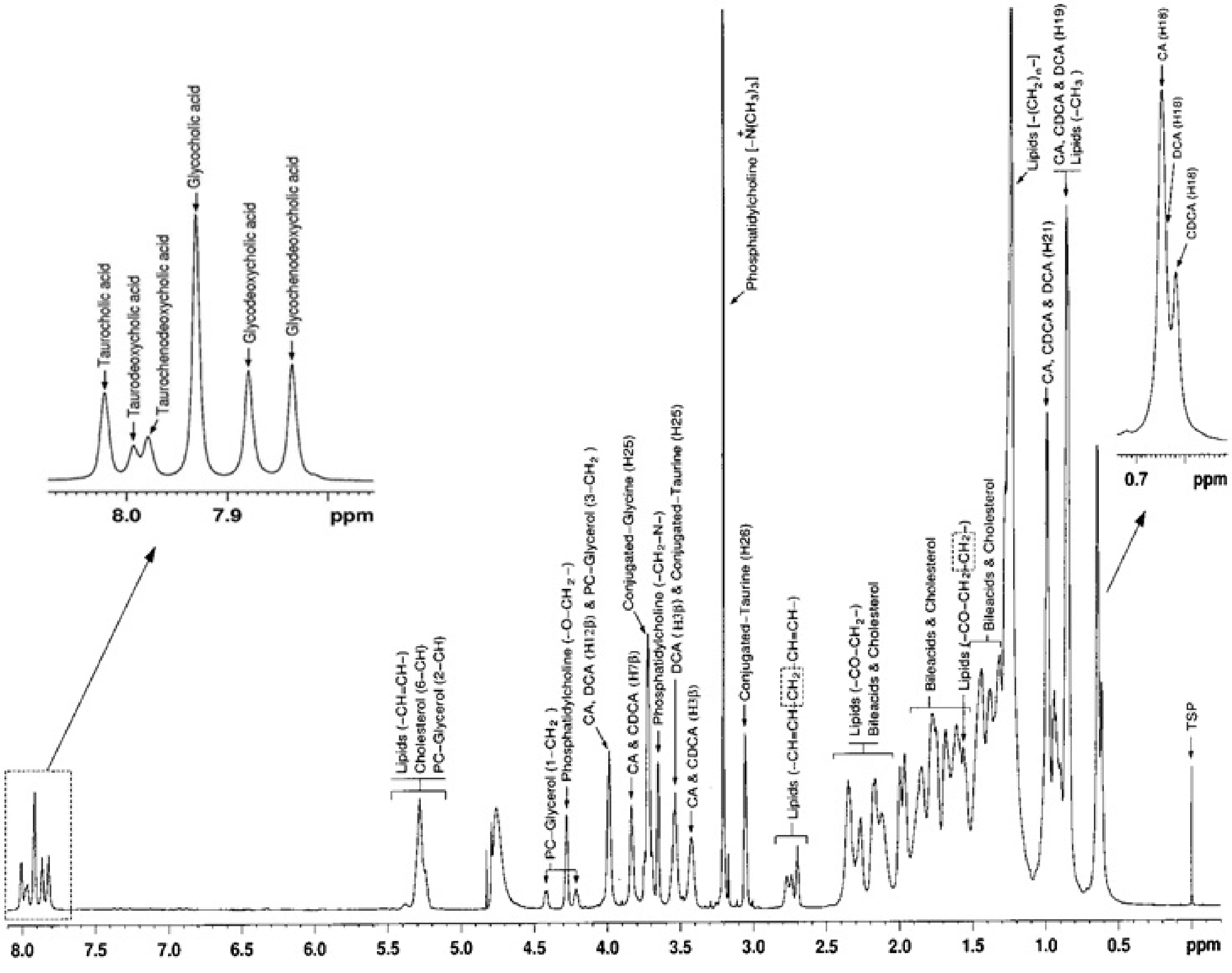

Figure 5. [1]H NMR spectrum of human bile at 800 MHz. Reproduced from Ref. 26 with permission of Springer.

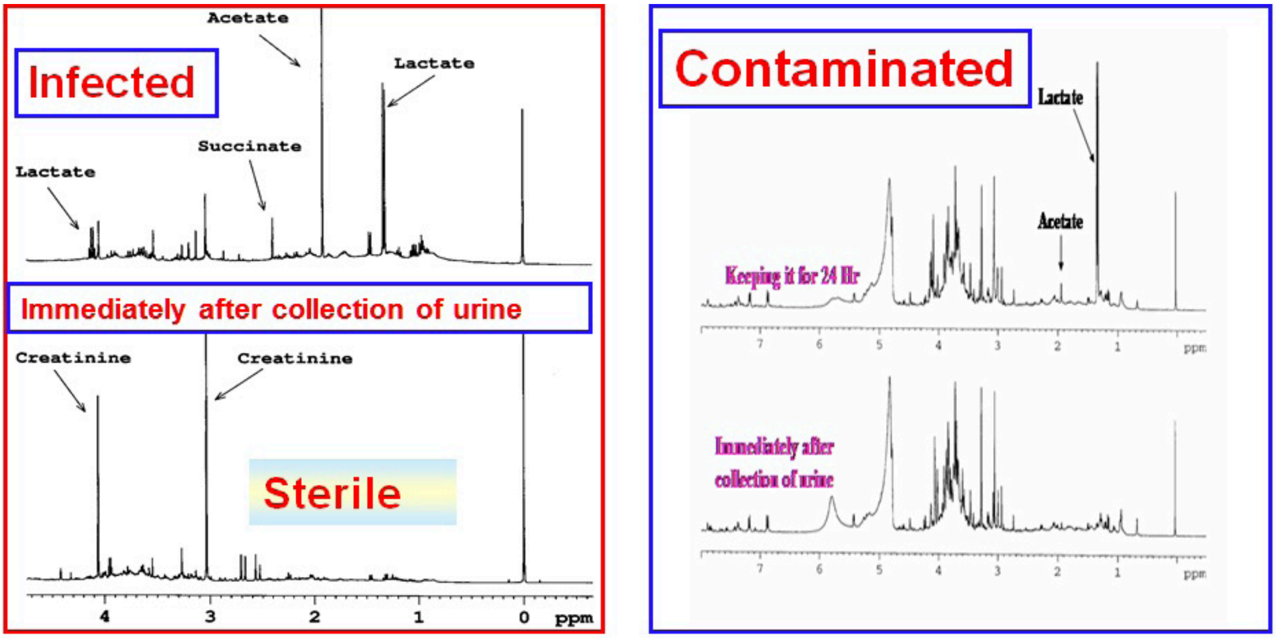

Figure 6. Distinction between real bacterial infection and contamination. Reproduced from Ref. 31 with permission from John Wiley & Sons, Inc.

assignments of the resonances due to various metabolites are shown in the Figure. NMR in fact, provides a novel, unique single step method to identify and quantify such a large number of metabolites present in a mixture. Once this was achieved several problems related to Human Bile have been investigated.[23-27]

Assessment of liver graft dysfunction: A study of patients who underwent liver transplant was carried out. It was noted that some of the patients died before they were discharged from the hospital though surgically all operations appeared satisfactory. In this study, the use of NMR has been made to find out the reason for the death. Studies on serum and urine samples of patients before liver transplantation and every 24 hours after the liver transplantation, till the time they were discharged/alive, were taken. High levels of glutamine in both serum and urine and concomitant reduced urea levels in urine were found to be evidence of impairment in urea cycles and compatible with abnormal graft function. Increased glutamine levels lead to brain death, if untreated. This is medically useful information since it gives prior information on what is going to happen and one may take corrective measures in advance.[28]

Prediction of therapeutic outcome in patients with Fulminant Hepatic Failure: Fulminant Hepatic Failures (FHF) are associated with severe liver injuries leading to impairment of hepatic function followed by hepatic encephalopathy within eight weeks of the onset of the illness. The mortality rate is as high as 80%. Liver transplant for FHF patient appears to be the only effective answer to this. Since the survival rates are low, rapid diagnosis is necessary to identify patients for transplantation. Until today, there is no means to predict the spontaneous recovery or non-recovery for such patients. ^{1}H NMR to quickly identify molecular markers such as glutamine in serum and urine and urea in urine promise a potential in quickly deciding on liver transplantation. NMR spectroscopy has been used to determine the molecular markers in serum and urine to distinguish between those recovered patients and those who did not. Glutamine in serum and urine glutamine/Creatinine ratios were higher in non-surviving patients compared with surviving patients. On the other hand, no significant differences were found in conventionally employed clinical parameters such as serum alanyl-amino transferase, aspartyl-aminotransferase and bilirubin.[29]

Bacterial urinary tract infection: Qualitative and quantitative estimations of metabolites produced as a result of bacterial infection in the urinary tract have been reported. Absolute concentrations of the metabolites provide the severity of the infection and, are likely to be very valuable in patients on antibiotic therapy with negative urine cultures.Major bacteria in UTI are E.coli, K. penumoniae, P. aeruginods and P. mirabilis. They uniquely metabolize lactose to lactate, glycerol to 1, 3- propanediol, nicotinic acid to 6 hydroxy nicotinic and methionine to 4-methyl-oxobutyric acid, respectively.[30-33] These properties have been exploited to identify and quantify specific bacteria responsible for the infections. The NMR technique has also been employed to distinguish between the real infection and contamination as shown in Fig.6. This is in fact one of the major problems in the precise diagnosis of UTI and NMR provides a solution.

EXAMPLES OF APPLICATIONS OF MRI

MRI is especially valuable for detailed imaging of the brain and the spinal cord. Nearly all brain disorders lead to alterations in water content, which is reflected in the MRI picture. A difference in water content of less than a percent is enough to detect a pathological change. In multiple sclerosis, examination with MRI is superior for diagnosis and follow-up of the disease.[34] The symptoms associated with multiple sclerosis are caused by local inflammation in the brain and the spinal cord. With MRI, it is possible to see the of the inflammation in the nervous system and how intense it is, and also how it is influenced by treatment. MRI is an important preoperative, improved diagnostic and reduced suffering tool for patients.

MRI has been used to reveal the effects of YOGA on brain. The results show that concentration of Gamma Amino Butyric Acid (GABA), increases by performing certain YOGA exercises.[35] It implies that YOGA, and perhaps some other forms of exercise should be utilized as a complementary treatment for depression and anxiety disorders. The results have clear public health utility. Yoga should be compared with other forms of exercise to determine whether or not it is the nature of YOGA postures that results in raised GABA levels, or it is an effect of any exercise.

FUNCTIONAL MRI (fMRI)

Functional MRI is based on the fact that oxyhemoglobin is diamagnetic but when oxygen is consumed in metabolism, the haemoglobin becomes paramagnetic. This permits visualization of the regions of the brain in which metabolic activity occurs in response to an external stimulus.[36] It can characterize functions while brain processes thoughts, sensations, memories, and motor commands. Functional MRI makes it possible for neurologists to detect early signs of Alzheimer's disease and other disorders, to evaluate drug treatments, and pinpoint tissue housing critical abilities like speech before venturing into a patient's brain with a scalpel. Such results provide a basis for designing new intervention techniques.

ILLUSTRATIVE APPLICATIONS OF fMRI

Considering the importance of the subject and its direct societal relevance, numerous interdisciplinary groups and institutions in this field have been established all over the world during the past few years. Basic and social scientists, psychologists and medical doctors are now joining hands to exploit the interdisciplinary nature of the field in order to diagnose and understand not only the molecular structure and the diseases in human beings but also to understand the metabolic and structural changes in them. Some illustrative applications are briefly described below:

The dyslexics and non-dyslexics: Numerous groups all over the world are involved in investigating biological bases of learning and learning disorders essentially because of great societal need. It has been reported that the deficiencies in functional brain organization underlying dyslexia can be reversed after sufficiently intense intervention lasting as little as 2 months. The reading difficulties in many children represent a variation of normal development that can be altered by intensive intervention.[37] Such investigations are of great importance.Immediate creation of an interdisciplinary school on child psychiatry, social science and fMRI is the need of the hour in societal interest.

Alcoholism in young adult, female alcoholics: Specific areas of the brain impaired by years of heavy drinking have been identified in young adult women. Previously, investigators have relied on thinking and memory tests to gauge brain dysfunction in alcoholics, but no one had identified the actual brain sites where impairment occurs in young adults. Even young and physically healthy individuals risk damaging their brains through chronic, heavy use of alcohol.[38]

Pretty female faces: They trigger activity in men's brains. A beautiful woman's face is like chocolate, cash or cocaine to a young man's brain.[39] When men in the study were shown pictures of various faces, only the female faces deemed beautiful triggered activity in brain regions previously associated with food, drugs and money.

Sex differences in mental rotation and spatial working memory: Behavioural and neural sex differences in sex-specific spatial abilities have been investigated.[40] Males typically surpass females on tasks dealing with mental rotation and spatial navigation, while females tend to excel males on tasks dealing with object location, relational object location memory or spatial working memory.

Crime and lie detection: During the past few years, the data on crime detection by NMR has become voluminous. Several hundred thousand entries are found in 'Google search' under this category. Pathological liars have been found to have brain abnormalities. Brain deformities have been observed in people who habitually lie, cheat and manipulate. The brain area just behind the forehead exhibits structural difference among pathological liars[41] and their white matter content is more. The finding could be used in making clinical diagnosis and may find applications in daily life, criminal justice system and the business world. The fMRI is bound to transform the societal values system, the security and the judicial processes. By mapping the neural circuit behind deception, fMRI will provide a new kind of 'lie detector' that is more probing and accurate than the polygraph – the standard lie-detection tool being employed for nearly a century. fMRI may change the entire judicial system. It will be useful in high-profile crimes like terrorism. It may appear that fMRI is expensive, bulky, noisy and time consuming for such routine applications. However, if one thinks of the cost of judicial process taking years to discover the truth or the price of missing a terrorist, nations can certainly afford it as far as the present costs are concerned. With more advances in technology, many of the limitations may be overcome as discussed in the subsequent sections.

Enhancement of trust among humans: Intranasal administration of oxytocin, a neuropeptide causes a substantial increase in trust among humans.[42] Oxytocin specifically affects an individual's willingness to accept social risks arising through interpersonal interactions. An fMRI study may throw light on Biological basis and provide scientific evidence on the role of oxytocin or human behaviour.Most charitable people show enhanced activity in the top and back of the brain – an area normally linked to processing incoming information, sorting out social relationships and controlling movements! Understanding the function of this region may give clues on the origin of social behavior.[43]

*Science behind health benefits of YOGA and meditation***:** Though it is well known that YOGA and MEDITATION can reduce stress and cure many diseases, recent times have seen the emergence of scientific evidence to demonstrate these beneficial effects using modern scientific technologies such as fMRI. These results are drawing worldwide attention. Neuro-imaging and genomics technology have been employed to measure physiological changes in greater detail. Some typical studies are outlined below:

fMRI study of neuro-cognitive effect of sound "OM" on human Brain: The sound "OM" is of paramount importance and is supposed to relax human beings physically, mentally and emotionally. The fMRI results delineate the exact brain area involved in response to OM sound and reveal that listening OM recruits areas of both left and right hemispheres including left prefrontal cortex. This corresponds to "OM" as a pleasant melodic sound which increases attention and emotional quotient and creates intuitive feeling towards spirituality (Fig. 7). Such studies provide a unique idea to employ modern scientific technologies to demonstrate whether YOGA pertains to a

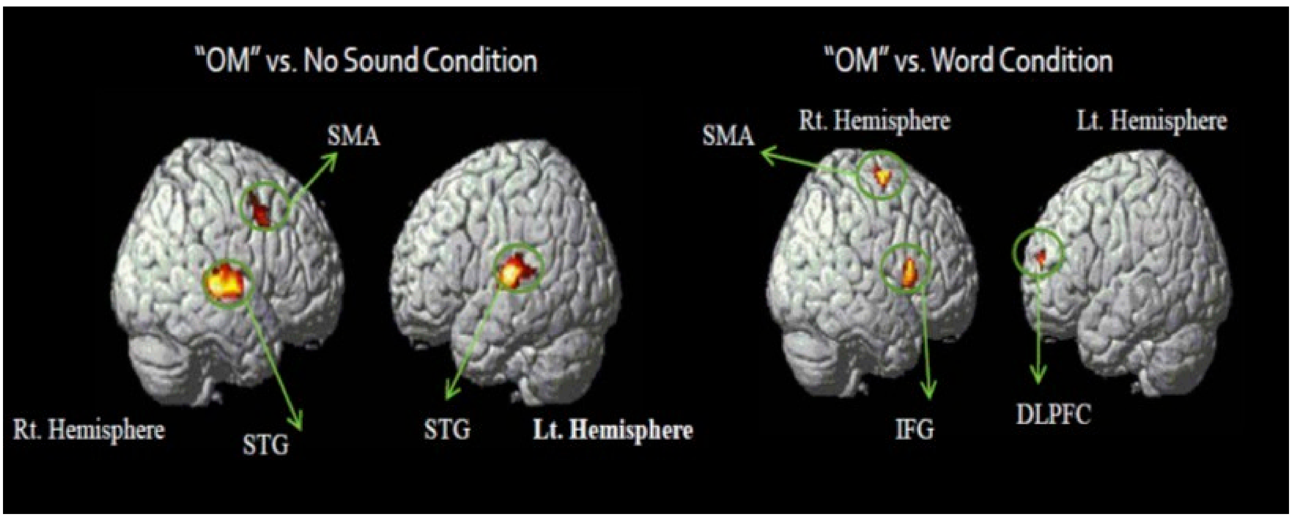

Figure 7. Neuro-cognitive effect of "OM" sound. (Supplementary Motor Area (SMA):Involved in MotorcoordinationSuperior temporal gyrus (STG): Auditory perceptionInferior frontal gyrus (IFG): Perception of pleasant soundDorso-lateral pre-frontal cortex (DLPC): involved in monitoring of attention process.)

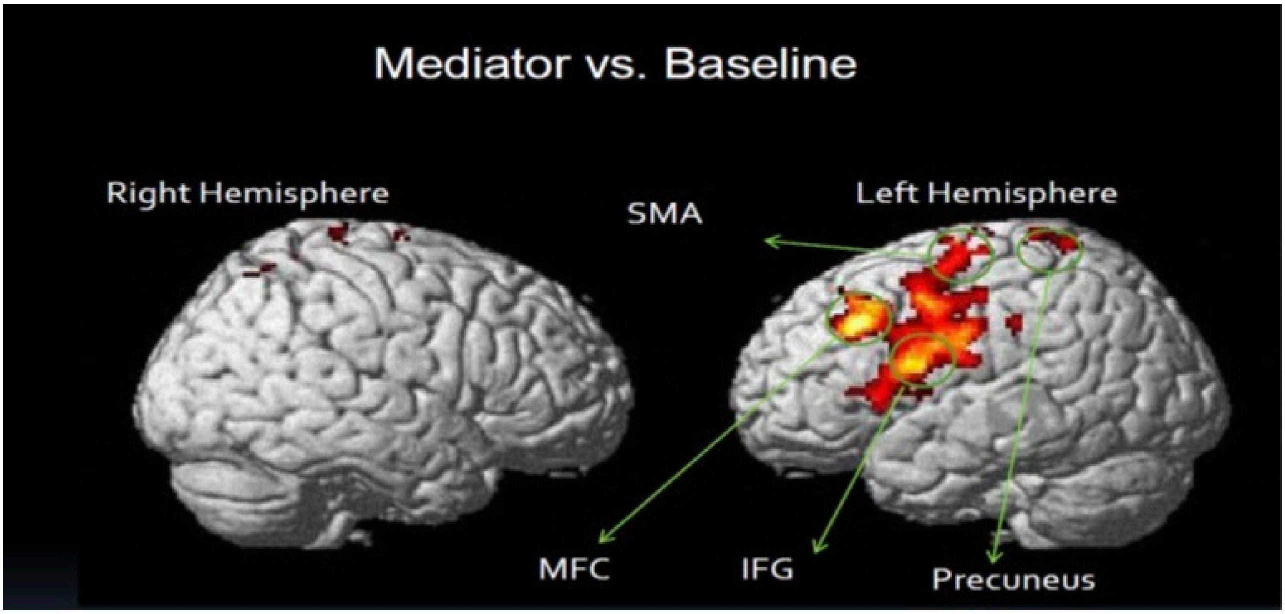

Figure 8. Effect of SOHAM Meditation on the brain. Middle frontal cortex (MFC): This implies regulation of attention, which in the case of meditation is directed at the subjects own mental and bodily state.Left Inferior frontal gyrus (IFG): involved in the cognitive aspects of emotional processing , such as paying attention to emotion or the identification of emotion.Precuneus: involved in the execution or preparation of spatially guided behaviors. Reprinted from Ref. 45, Copyright 2013, with permission from Elsevier.

particular faith or religion or it is universal. It may go a long way to establish religious harmony and world peace if such an idea is pursued. The observation of the international YOGA day has generated hot debates particularly in India on whether YOGA pertains to a particular religion or faith. The use of modern scientific technologies such as functional MRI and other technologies can throw light on the issue in an unbiased manner and will go a long way to establish world peace and happiness and religious harmony. The functional MRI studies reported above delineate the exact brain areas involved in response to OM sound and reveal that listening to OM sound recruits areas in the brain involved in increasing attention and emotional quotient and creates intuitive feelings of happiness.[44-47] A question arises whether such studies can result in providing a scientific approach to achieve religious harmony and world peace? It would be interesting to see whether 'OM' is faith specific or it affects similarly to all irrespective of the religion or faith. One could even study the effects of "Mantras" preached by different religions. If all have similar effects, it will establish scientifically for the first time that all religions preach the same thing and if the effects are specific only to OM, then it will establish that this sound is universal and is independent of the religion. If studies of the Mantras preached by different religions demonstrate changes in different areas of the brain but they too have positive health benefits it will throw a challenge to scientists to discover a "universal Mantra" which takes into accounts positive aspects of all faiths. The results will establish a correlation between spirituality and science.

"SOHAM" Meditation: The parts of the brain that show activity during meditation in general in fMRI is illustrated in Fig. 8. In "SOHAM" meditation one merely observes the breathing process even as one repeats the word "SOHAM" in mind, synchronising it with breath. Therefore the process is when one inhales, one mentally repeats the sound "SO" and while exhaling the sound "HAM" is repeated. As one breathes in and out the sound "SOHAM" is repeated. Grey Matter in the brain fills about 40 percent of the whole brain in humans and consumes 94 percent of oxygen. The senses of the body (speech, hearing, feelings, seeing and memory) and control of the muscles, are part of the grey matter's functions.

Differences in Grey Matter are observed between "SOHAM" meditators and non-meditators (Fig. 9). Three distinct regions show higher grey matter concentration in meditators .

*Positive attitude insures happiness***:** The power of positive attitude or perception, meditation, reciting and listening *mantras* etc in coping up of the various stresses and strains in human daily life is well known and is widely practiced. However, it may have better impact on common man's daily life if one can demonstrate this by a sci-

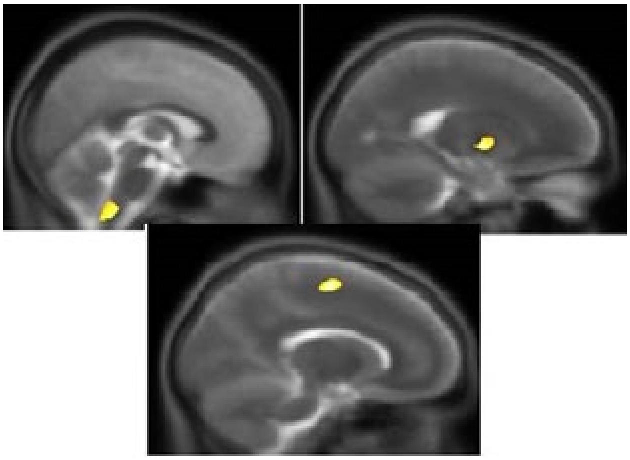

Figure 9. Grey Matter differences in "SOHAM" meditators and non-meditators: Three distinct regions show higher grey matter concentration in meditators. Left Image: Brain stem - Regulates breathing and anxiety level. Right Image:Ventral palladium- Regulates positive mood and motivation. Bottom Bottom:Motor area - Regulates motor aspects.

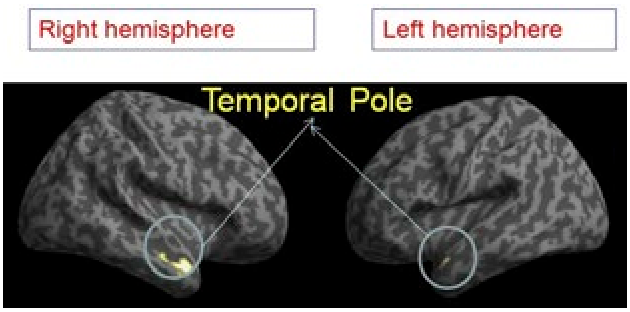

Figure 10. Influence of negation on Human Brain. Distinct neural regions for negative sentences: Temporal Pole: This region is associated with anxiety and depression.

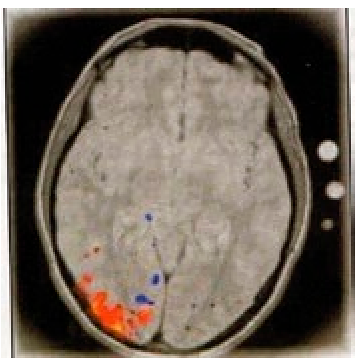

Figure 11. Brain activation (bright color) characterizing the functioning of anxious and depressed persons as they Process emotional information and respond to various types of positive and negative stimuli. Reproduced with permission of the Stanford Mood and Anxiety Disorder Laboratory.

entific evidence. A preliminary fMRI study *(Brain imaging and behavior, August 2012)* demonstrates that negativity is perceived by different brain regions compared to positive perception. The experiments decode specific regions in human brain involved in positive and negative perceptions. A crucial finding was the activation of the bilateral temporal pole for negative sentences (indicating sadness, anxiety and stress). No such effects were observed in affirmative sentences (Fig. 10). A study[48] on mentally depressed and anxious individuals also shows activation pattern similar to that in subjects with negative thoughts (Fig. 11).

RECENT ADVANCES IN NMR, MRI AND FMRI TECHNOLOGY

Nano particles and fMRI: The new generation of nanoscale calcium contrast agents being developed will have applications in understanding learning, memory, and behaviour and will allow functional fMRI to make transition from imaging gross properties of brain to a fine-tunes analysis based on information flow involving cells and circuits .[49]

A new low-cost, portable MRI technology: A novel laser-based MRI technique is being developed by the Alex Pines and his colleagues in Berkeley. It provides a viable alternative for MRI detection with substantially enhanced sensitivity and time resolution. It will result in the development of a low cost, compact, portable and battery-powered portable MRI technology and an on-line analytical instrument for monitoring chemical reactions and biological processes.[50]

NMR: *From K gm to Pico gm*: The quantity of the paraffin sample initially used by Purcell when he discovered NMR in bulk material was 1 K gm in weight and with developments or organic molecules possessing electronic properties analogous to those of Gallium Arsenide, it seems likely that NMR spectra of Pico gm quantities of Proteins and Nucleic acids could be recorded.[51]

NMR nanometer-scale device: NMR has received considerable attention in the context of quantum computation and information processing which require controlled coherent qubit operations. Towards achieving this goal, a self-contained NMR semiconductor device has been implemented that can control nuclear spins in a nanometre-scale region. High sensitivity at the microscopic level has been demonstrated for probing materials whose nuclei contain multiple spin levels and thus form the basis of a versatile multiple qubit device.[52]

NMR on a chip: If a Nanoscale gallium Arsenide structure is excited with an oscillating Magnetic Field, superposition of nuclear spin states can be created and detected electrically. Quantum computing could be the beneficiary.[51]

CONCLUSIONS

To the question "Is there an end in sight for the new exciting developments in NMR?", the answer is a simple "NO". If one just looks at the advances in technology and the possible applications outlined above, one may predict that the best is yet to come. If a young man wants to remain "young", here is an opportunity to enter the "young" field and get assured enjoyment and excitement for the rest of the life.

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