

“Cart before the horse”

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“Cart before the horse” is an English idiom or phrase. It suggests something contrary to the conventional.[Whiting 1977] But, I use to get confused between ‘cart before the horse’ and ‘horse before the cart’. This may be due to my poor fund of knowledge in English language. Or, it may also be due to concretisation of thought in absence of abstract ability. Therefore, whatever may be the reason, I tried to find out a few examples of it. One of them, I found very interesting. It says that you are eating your dissert as starter.[The Free Dictionary 2016]

So, to start with let us ask ourselves some fundamental questions. First of them is what is disease? Following the ability to visualise organisms under the microscope as well as seeing the pathological changes under the same microscope after the inoculation of the organism into body, the ‘medico-pathological’ model, developed by Thomas Sydenham became the prototype of disease. That is, a definite aetiology causing specific pathological changes. Unfortunately, except in few infectious diseases, this model fails to explain many other diseases.[Semple & Smyth 2009]

Say for example, diabetes mellitus. Here, aetiology is varied. So also are the outcomes. The only commonality is the constellation of certain symptoms and signs that occur together in a particular fashion. Thus, comes into the picture the ‘syndrome’ model. There are several other models of disease. Like, ‘biological disadvantage’ model which says that because of the disease the sufferer is in a biologically disadvantageous position compared to the so-called ‘normal’. Then, ‘plan of action’ model says that disease justifies further investigations and treatment. Qualitative or quantitative deviation from the norm is assumed as disease by the ‘disease as imperfection’ model.[Semple & Smyth 2009]

In reality, disease seems to be a ‘concept’. It has a tendency to change over time. And in fact, may even have no real existence by itself.[Semple & Smyth 2009] One my student, now an eminent psychiatrist by himself, rather an academic psychiatrist who also uses to be the Executive Editor of the Open Journal of Psychiatry & Allied Sciences (OJPAS™)[Open Journal of Psychiatry & Allied Sciences 2015] wrote a beautiful, thought-provoking article on the subject.[Talukdar 2011] Now, if the definition of disease is not enough confusing, then let us ask ourselves the second fundamental question. That is why we need diagnosis then?

Let me share a story here. Pointing to the figure grazing grass in the field, once a MBBS student was asked “What is it?” The MBBS student promptly replied, “A cow”. Then, a postgraduate trainee was asked the same. After taking some time, the reply received was “A four-footed animal, probably a cow!” Finally, a consultant was asked who took a long time in replying. And finally the reply was “A four-footed animal, probably a cow but I will take help of genetic engineering.”[Das 2015]

After the story, now let us come to a real life event. A patient walks into your chamber and the story of his goes like this: he recently lost both his parents as well as his job. He is feeling low. He

has difficulty in sleeping. His appetite is reduced. There is pessimism about the future.[Semple & Smyth 2009]

What you as a psychiatrist do is ask for certain biochemistry tests from his blood in a laboratory. Also, a cerebrospinal fluid (CSF) analysis through the painful procedure of lumbar puncture. And even an imaging study of the brain, preferably a functional one.[Semple & Smyth 2009]

Since these facilities are not available in all the centres, at times patient needs to travel distance for doing the same with the costs of time, money, and effort. Finally after three months, he arrives to you with all the reports. Examining them, you declare to the patient that he is suffering from 'depression'. If I would have been that patient, then I seriously will doubt the credibility of the psychiatrist. Since without going through all these I could easily have said then only that yes, I am suffering from 'depression'. [Semple & Smyth 2009]

Common sense says that this patient could be diagnosed without going through the advised investigations. In practice also, we usually do so. But, does that mean that we psychiatrists do not look at the brain?[Semple & Smyth 2009]

In the popular Hindi movie, Munna Bhai M.B.B.S., [Hirani 2003] Munna bhai asks "Subject, subject, subject; subject ka naam nehi hein kya?" Don't the subjects have their names? Every individual likes to be identified as a person, not a label; while, we doctors are obsessed with 'labels'. Labels in medical science do have a purpose. They are basically characteristic signs and symptoms in combination. But, the same signs and symptoms have different meanings to patients and their doctors. It is as if both are moving away from each other. For patients, the symptoms are important for the individual nature. "These are happening to me!" "They are unique to me!" On the other hand, doctors try to look for similarity--similarity of the current patient's signs to an earlier patient whom we have seen or read about in 'case reports'--so that we can plan a diagnostic formulation.[Semple & Smyth 2009]

Ideally diagnosis needs to be based on aetiology. And naming is the first step in understanding something. We try to make a diagnosis in order to advocate treatment and thus predict the outcome. Ultimate goals are to know the pathology and the aetiology. This only will help us in developing means to prevent or tools to treat.[Semple & Smyth 2009]

Here, the idea is to put forward a 'cart before the horse' approach; thereby, pushing behind not only the aetiology but also the diagnosis. Instead, to start with the treatment first; many questions will rise for that- What? Why? When? Whom? How? And one needs to address them.

With "the 'double D' dilemma" about 'disease' and 'diagnosis' of medical science, let us now venture into our own speciality, i.e. psychiatry and the organ that we deal with, i.e. the brain. "Three pounds of matter, mostly fatty acid molecules, buzzing with such electro-chemical activity between 100 billion neurons that does not cease even for a second throughout the lifetime... consuming just enough energy to power a 20-watt light bulb, processing information at speeds that cannot yet be calculated-- that is an average human brain..."[Talukdar 2015]

If we go ahead some more, what we find is this. One third of the 25,000 human genes are expressed in the brain. Since most genes code for more than one protein, we have around 1,00,000 proteins in the brain. We know the functions of about 10,000 of them. And the currently available

therapeutic agents that we have with ourselves as of now target not more than 100 of these proteins.[Grebbe & Carlsson 2009]

In this regard, it is important to keep ourselves apprised of some interesting recent works in contemporary psychiatry. The Bipolar Schizophrenia Network on Intermediate Phenotypes (B-SNIP)[B-SNIP 2016] and the Neuroscience-based Nomenclature (NbN)[ECNP 2016] both try to classify disorders and their treatments according to biology of brain. This “common neurobiological underpinning to both the diagnosis and therapeutics of psychiatric disorders” led us to state the we are now entering the “fifth revolution of psychiatry”![Das et al 2015]

There are specific suggestions in order to make changes in our currently used diagnostic system. Inclusion of objectivity and flexibility are some of them. Response to treatment can be one of them.[Grebbe & Carlsson 2009]

First constructing a diagnosis, and then deconstructing it into symptoms so as to trace to the malfunctioning brain circuits is an approach. With knowledge of the neurotransmitters involved in the malfunctioning circuits on one hand and about the molecules having capacity to affect them on the other hand, we can derive a more effective ‘personalised or individualised medicine’ that can alleviate the sufferings of our patients in a much better way as exemplified in the ‘About the Cover’ of the volume 7 issue 1 of the Open Journal of Psychiatry & Allied Sciences (OJPAS™).[Stahl 2008, Talukdar 2016] Also, the Research Domain Criteria (RDoc) tells us about major domains and their respective units.[Kar 2015]

Coming to “The heart of the matter”,[Henley 1989] as sang by Don Henley, one of the Hotel California-famed Eagles, i.e. the conventional and the contrary, we have the tenth revision of the World Health Organization’s International Statistical Classification of Diseases and Related Health Problems (ICD-10)[World Health Organization 1992] and the fifth edition of the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders (DSM-5).[American Psychiatric Association 2013] They serve us menus from where we tick the items and thus come to a diagnosis. Moreover, the different treatment guidelines are hanging as swords around our neck and like The Ten Commandments asking us to do this and do that.

Under the circumstances, a traditional diagnostic formulation goes like this... “This years old of that sex hailing from this socioeconomic status of that background with symptoms of feeling worthless, appetite changes, and sleep disturbances for this many duration following stress factor in the forms of loss of parents and redundancy, and mental state finding of depressed mood and guilt as well as cognitive function revealing executive dysfunction is provisionally diagnosed to be suffering from major depressive disorder, and management is decided to be carried out as outpatient with pharmacotherapy of escitalopram, and psychotherapy of coping skills training.

But, “the times they are a-changin’.”[Dylan 1965] The System and Method of Medicine[2016] “does not detail *what* to think, but rather *how* to think”.

Dorsolateral prefrontal cortex (DLPFC) is the anatomical location for executive dysfunction. Amygdala is the anatomical location for depressed mood and guilt. In DLPFC, the physiological disturbance of histamine and dopamine are responsible for executive dysfunction. Likewise, physiological disturbances of serotonin and gamma-aminobutyric acid (GABA) in amygdala are responsible for depressed mood and guilt. Molecules like modafinil and bupropion can counter the effects of histamine and dopamine respectively in DLPFC. Similarly, either selective serotonin

reuptake inhibitor (SSRI) or serotonin norepinephrine reuptake inhibitor (SNRI) and GABA-ergic agent can counter the effects of serotonin and GABA respectively in amygdala.[Stahl 2008]

Therefore, the earlier diagnostic formulation of “This years old of that sex hailing from this socioeconomic status of that background with symptoms of feeling worthless, appetite changes, and sleep disturbances for this many duration following stress factor in the forms of loss of parents and redundancy, and mental state finding of depressed mood and guilt as well as cognitive function revealing executive dysfunction is ...” now takes the new look of “... having physiological abnormalities of histamine and dopamine in the anatomical location of dorsolateral prefrontal cortex as well as physiological abnormalities of serotonin and gamma-aminobutyric acid in the anatomical location of amygdala, and thus can be successfully managed by the combination of either modafinil or bupropion and either selective serotonin reuptake inhibitor or serotonin norepinephrine reuptake inhibitor along with addition of GABA-ergic agent.”[Keshavan & Mehta 2015]

Let us dare to imagine, as John Lennon did,[Lennon 1971] of having such a ‘diagnostic formulation’ since “understanding of the brain is now sufficient to make the conscious decision to build assessment and treatment of mental illnesses on this knowledge”.[Grebb & Carlsson 2009] At first glance this statement may seem contradictory to what is said already. After admitting that we know so less of the brain like the functions of only 10,000 out of possible 1,00,000 proteins and targeting no more than 100 only proteins, now the claim is to know sufficient. But, these statements go together hand in hand. Yes, we know sufficient, not all. Not only ‘we know what we know’ but also ‘we know what we do not know’,[Rumsfeld 2011] and that also is a tremendous advancement. So that, instead of living in utopia, we can pragmatically approach our patients in real life situations that helps them the most with our present knowledge base.

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