Chapter 1: Principles of Neuropsychiatric Assessment

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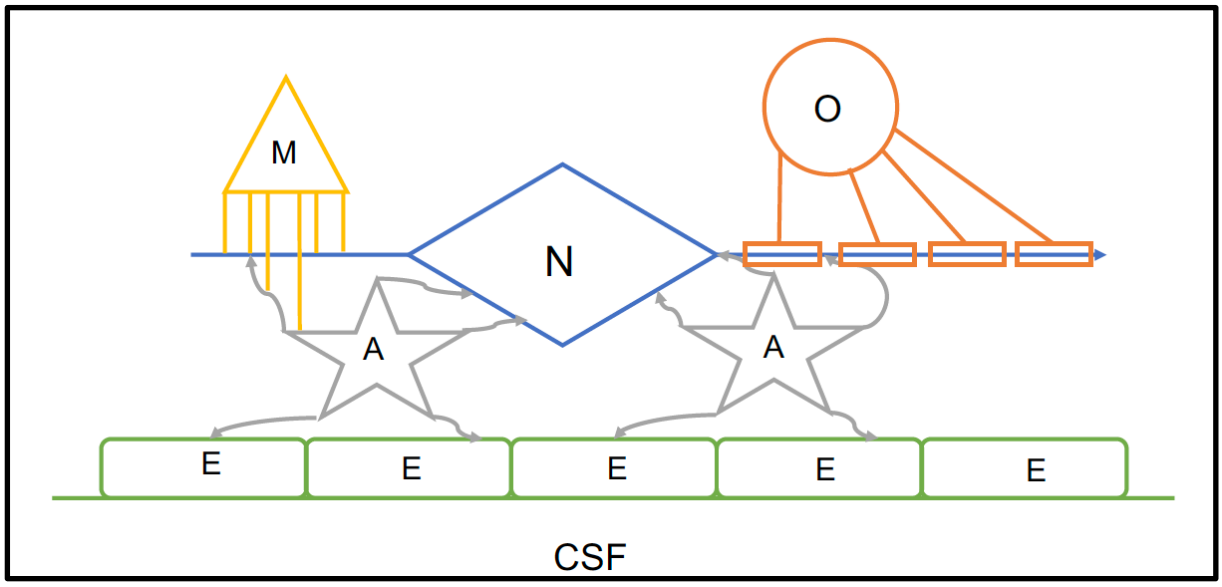
Introduction

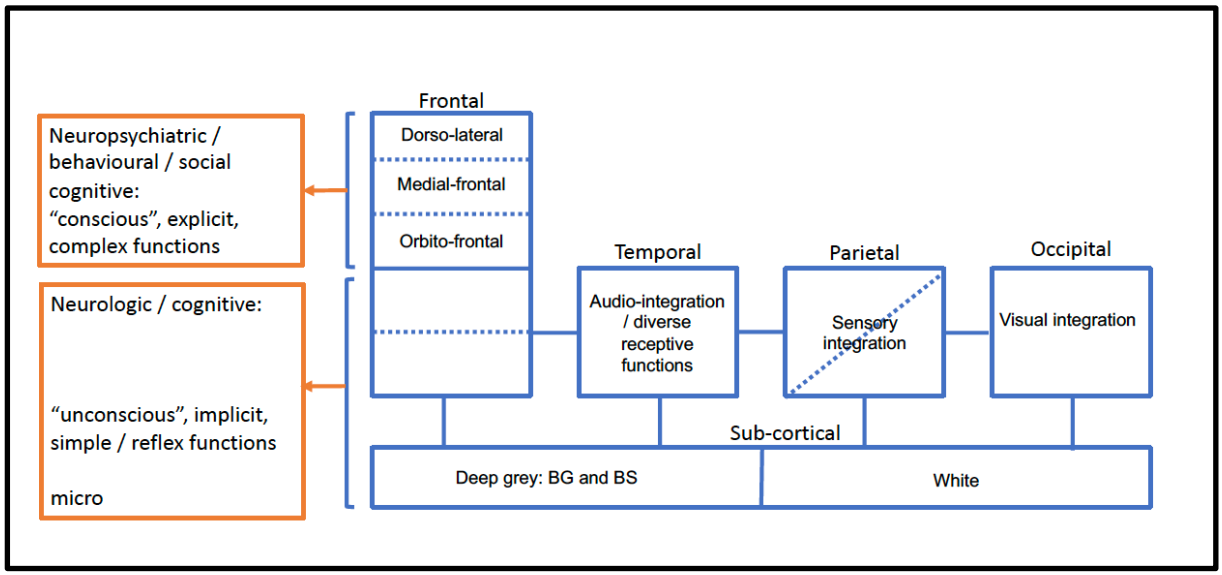
- ***Neuropsychiatry*** is concerned with the clinical assessment, investigation, treatment and medico-legal aspects of individuals with *behavioural, affective, psychotic and cognitive (so-called "psychiatric")* symptoms… as a result of neurologic disease.
- A neurologic disease is a condition of the human nervous system for which there is an identifiable pathology, by virtue of genetic, serologic, immunological, radiological or clinical evidence: a clear LESION
- Historically, these "neuropsychiatric disorders" (NPDs)were considered "organic mental disorders"; while general "psychiatric disorders" were considered "functional mental disorders". There has been a growing trend to call ALL psychiatric disorders "neuropsychiatric" possibly due to advances in neuroscience and description of "micro- and molecular- pathology" but for practical purposes, we separate "neuropsychiatric" as meaning, "a known pathology".
- In the DSM-5, NPDs would be Psychiatric Disorder due to Another (specify) medical condition. Also referred to as "secondary psychiatric disorders".
- We need to have a basic understanding of the ANATOMY (micro- and macro), as well as PHYSIOLOGY, and how they fit together into a FUNCTIONAL arrangement, in order to understand how NPDs present.

1.1. Micro-anatomic organization of the Human Nervous System



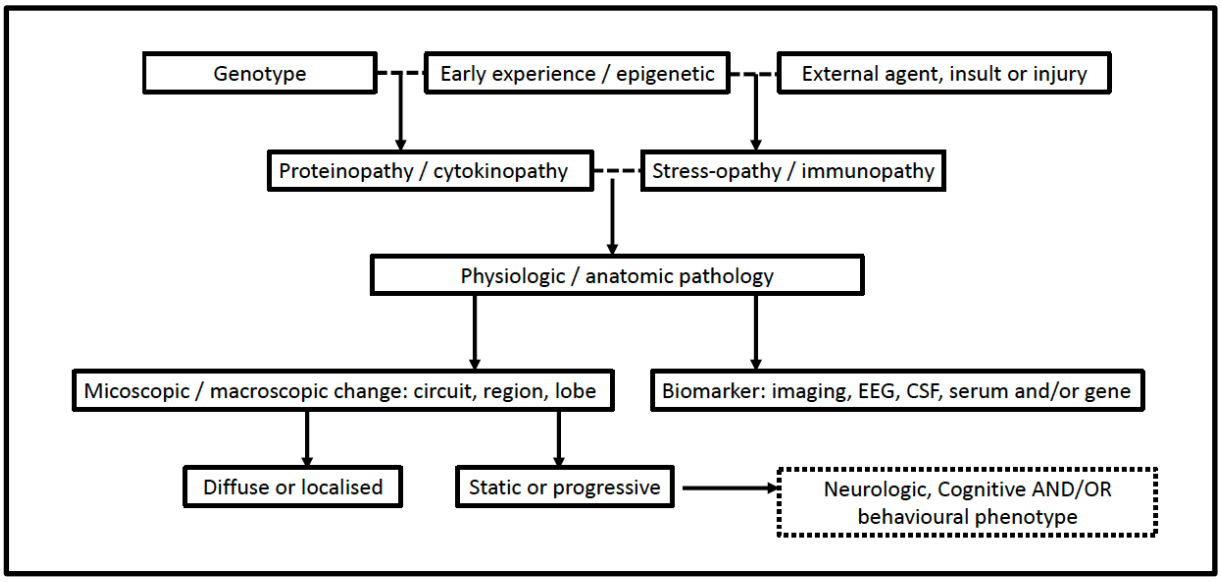
- The brain is a tightly regulated compartment, separated by vascular endothelium from the blood (BBB) and by the ependyma (E) from the CSF (Blood CSF Barrier). Transport of almost all ions, nutrients and drugs is regulated by the BBB/BCSFB via tight junctions and protein transporters. Disruption may occur through physical trauma, inflammation or radiation. This may lead to localized or extensive neuronal dysfunction in the region it occurs in.
- The Glia (astrocytes (A) and microglia (M)) form a significantly large component of the cellular CNS and are responsible for regulating the extra-cellular matrix of proteins and ions. This includes cytokines (both pro- and anti-inflammatory) as well as proteins. Glia may become activated or triggered by internal or external agents and form inflammatory nodes or giant cells. A pro-inflammatory cascade is then set up.
- Oligodendrocytes (O) are glial cells that extend processes around neuronal axons to form myelin sheaths. Damage to oligodendrocytes or myelin leads to slowed or disrupted neuro-transmission, and may occur with inflammation, micro-vascular disease or infection with demyelinating agents.
- Neurons (N) have cell bodies and axonal projections. The connections between neurons and glia through the synapto-dendritic network is a key feature of human cognition and its growth occurs throughout development. Density of the network is thought to underpin “cognitive reserve”, as the network may decay with age or disease, rendering the individual vulnerable to disorder.

1.2. Functional Arrangement of the Human Central Nervous System



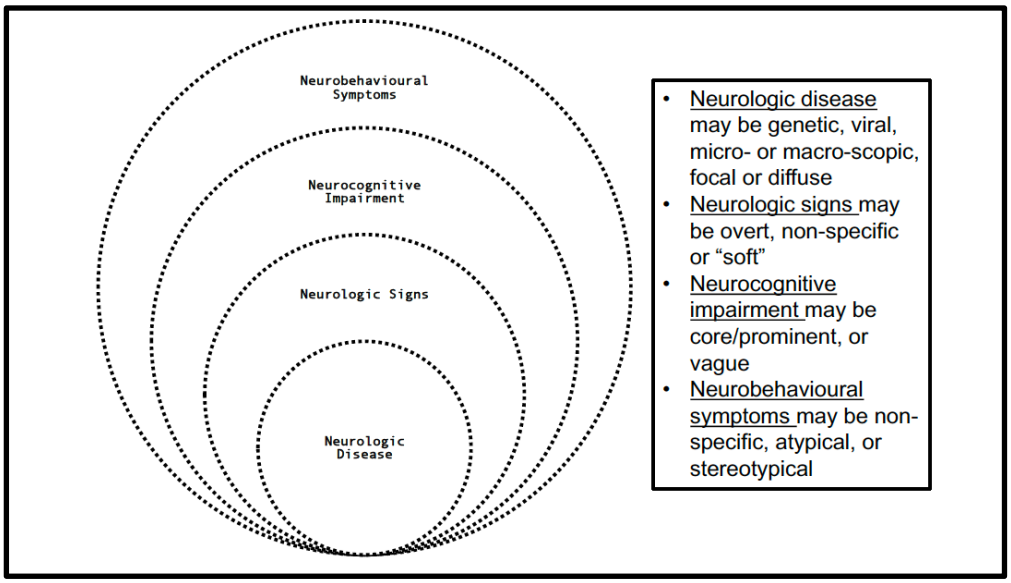
- There are several functional areas of the brain which inform the neuropsychiatric assessment process
- The brain is arranged into lobes, each with semi-discrete functions.
- The cortex (cortical grey) and sub-cortex (deep grey and white matter) are also functionally distinct. Cortical functions are often thought of as "conscious" or explicit, while sub-cortical are "unconscious" or implicit. Not all cortical diseases can be detected through conscious thought or are amenable to open enquiry (for example when patients are agnostic, or unaware). Similarly, some sub-cortical diseases are brought into conscious awareness through cortical awareness and observation.
- Another distinction is that cortical "processes" are often confined to premotor or executive functions, gnosis, praxis, visuo-spatial function and audio-visual memory; while sub-cortical functions are considered to be related to connectivity, so processing of thought, behaviour and motor function.
- There are multiple and varied connections throughout the CNS. These include connection via *proximity* (so a tumour or stroke will affect areas close together), connection via *vascularity* (so that areas fed by an artery will be affected by stroke, irrespective of functional region), or *circuitry* (so that cells that become electrically / chemically over-excited may discharge abnormally as with a seizure).

1.3. Aetiological Construct of Neuropsychiatric Disorders



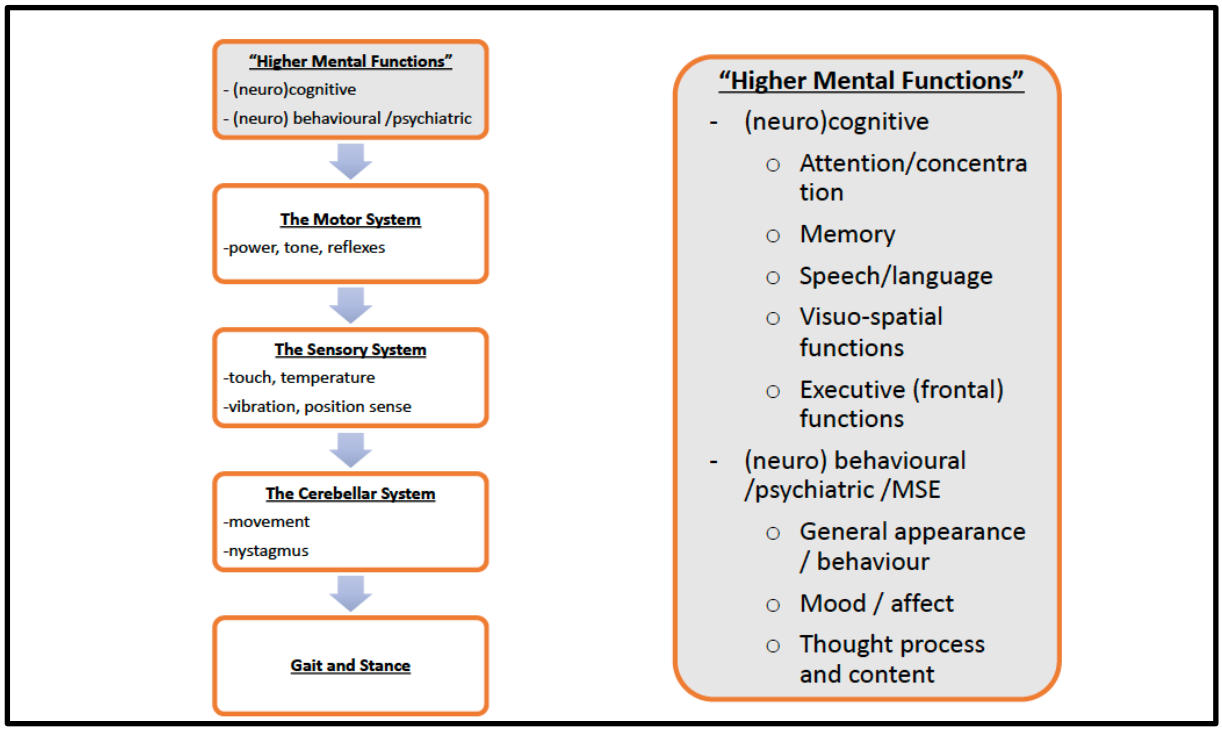
- Neuropsychiatric disorders arise as a result of single or multiple genetic defects or vulnerabilities, together with environmental changes or insults. Some conditions are purely genetic (eg Huntingtons disease), while others involve single “vulnerability genes” (eg APOE4 in Alzheimer’s disease), and still others are probably polygenetic and as yet poorly understood (eg epilepsy or sporadic Alzheimer’s disease). Disorders with clear external agents or insults, such as HIV or TBI, resulting in behavioural and cognitive disorders, probably also have underlying genetic and molecular factors.
- Once, triggered, pathological processes may start by affecting proteins (eg Amyloid or), they may be cell specific (such as HIV infecting glia but not neurons), they may affect white over grey matter (such as in multiple sclerosis), or they may be regional with regard to vascular supply (stroke) or external force (TBI).
- These conditions often, but not always, are diagnosed or tracked using one or more biomarkers: either the gene/protein assay, or a general investigation with a specific pattern (eg low vitamin B12, or a vascular pattern on MRI). Often a combination of biomarkers is needed to complete the diagnostic process (eg HIV test, CSF and MRI).
- Neurologic (nervous system) disease can affect any area: it can be discrete (localized) or diffuse (generalized), static (as in head injury) or progressive (as in infectious or degenerative conditions).
- As a general rule, neuropsychiatric diagnosis is made easier when: there is PROXIMITY in time to the cause or insult (genetic conditions may be distal to the phenotype, and post-ictal psychosis is close to it); there is a specific PATTERN of disease (often a syndrome of unique features eg motor and cognitive symptoms); and there is an anatomical or physiological PICTURE (neurologic hard signs are often easier to tie into the molecular cause, then less specific behavioural features).

1.4. Neurobiologic Construct of Neuropsychiatric Disorders



- At the heart of Neuropsychiatric Disorders is the underlying Neurologic Disease (or "brain disorder"). This is the genetic, molecular, chemical, circuit or regional condition referred to previously.
- Where the lesion(s) is "eloquent", discrete or clearly patterned, it may be detectable by clinical neurologic examination. Such disorders are of interest to neuropsychiatrists when they are associated with cognitive and behavioural features, as a major or minor component. Examples include multiple sclerosis, parkinsons disease, stroke or brain tumours.
- Where the lesion is less eloquent, perhaps not discrete, or not occurring in a region of the brain amenable to clinical neurologic examination, it may present with circuit or regional impairment, detectable by another pattern of brain dysfunction, namely cognitive impairment. Cognitive impairments are usually less specific than neurologic findings, but more so than behavioural changes. In this way, it is sometimes possible to distinguish cortical from sub-cortical neuronal damage, or between lesions that occur in different lobes of the brain (for example apraxia, agnosia or executive dysfunction). Strictly speaking, cognitive deficits ARE neurological (as are behavioural). Just for conceptual purposes we separate them out.
- Then in disorders that don't present to neurologists (there are no neurologic features), or those without overt cognitive symptoms (depending on how hard one looks), there is a behavioural phenotype, or "mantle". Behavioural symptoms and syndromes may be non-specific (such as agitation, aggression), but they may be more so (eg obsessive symptoms, or tics), or visual hallucinations. Sometimes behavioural symptoms occur together with cognitive ones, and the clinical picture is more apparent (such is with Lewy Body dementia, or HIV dementia).

1.5. Clinical Organisation of the Human Nervous System



- It is conventional to conduct the examination of the neurologic system in a step-wise manner, starting with Higher Mental Functions.
- In Neuropsychiatric assessment, these consume more time, and are a focus of attention. In addition to the *Bedside Cognitive Assessment* (see chapter 2), there is also a Bedside Behavioural Assessment. This will usually require a combination of key informant interviews ("collateral"); careful patient observation ("mental state"); and possibly the use of measures ("tools or instruments") which may guide change over time, and as a marker of severity.
- The rest of the neurologic examination remains critical, even to non-neurologists. The neuropsychiatrist must be able to make a basic assessment of the cranial nerves; motor function (focusing on power and tone, and its distribution); sensory signs (if they are in keeping with anatomical distribution); cerebellar and gait functions.

1.6. Neuropsychiatric Assessment: Disorder-specific vs Diagnostic Systems approaches

- Many neurologic and neuropsychiatric disorders are the remit of clinical and research groups, who develop and propose disease-specific criteria. These are available for many of the neurocognitive disorders, infections, head injuries and others. In this way, the research groups have defined what are usually “probable” and “possible” symptoms and signs and have attempted to describe and cluster them to allow for broad consensus and reproducibility across sites. In these systems, the CAUSE of the condition is usually known or suspected
- A different approach exists within general classification and diagnostic systems, such as the DSM5 or ICD10. These systems begin by defining clinical syndromes- for example “major neurocognitive disorders”, and then focus down on causation based on clinical and investigation findings.
- The DSM and ICD approaches usually demand a single best diagnosis, with allowance for a differential diagnosis. For example, MNCD due to Alzheimer’s disease; differential vascular dementia. The possibility of other specifiers exists, such as where severity may be noted, or functional impairment, or the presence of core features such as hallucinations.
- Where disorders are truly syndromic, or multi-causal, these systems often do not lend themselves to broader synthesis.

1.7. A syndromic approach to Neuropsychiatric Assessment

- Patients often present with clinical syndromes that do not lend themselves to one causative diagnosis
- An example is a person with a major neurocognitive disorder with agitation. They have a history of alcohol use, hypertension and poor nutrition. They achieved a grade 6 education, and have been variable employed. Psychotic symptoms are present. There is also motor slowing.
- The clinical assessment might elicit:
  - ❑ The presence of mild parkinsonism and slowing
  - ❑ A mixed cortical and sub-cortical cognitive impairment
  - ❑ Fixed persecutory delusions.

- The possibility of several explanations of the cognitive and motor syndromes exists: poor educational attainment, vascular brain disease, early Parkinsons disease, early Alzheimer's disease, vitamin B12 deficiency or chronic schizophrenia.
- It is only with careful attention to the weighting of possible contributors, removal of confounders, and a step-wise approach to investigation and treatment, that the diagnosis can become clearer.
- In this way, at least in the early stage of assessment, the use of a syndromic label as above, with a list of possible contributory causes, is not only correct but appropriate.

Key points

- An understanding of the anatomical layout, functional organisation, and clinical approach in neurology will guide neuropsychiatric assessment
- Causation in neuropsychiatry may vary from single genes or insults, to multiple genes, insults or unrelated causes
- The clinical syndrome in neuropsychiatry may present with symptoms and signs from discrete areas ("neurologic") and/or circuits or systems ("cognitive") and/or disseminated or non-eloquent areas ("behavioural").
- Patterns of impairment, such as in the Bedside Cognitive Assessment (see chapter 2) may provide clearer guidance
- These may constellate to guide as to cause, together with targeted special investigations.