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UCLouvain Institute of NeuroScience

Neurology and psychiatry: was it really necessary to divorce?

Professeur Adrian Ivanoiu

NEURO-PSYCHATRIE, iCANN, 24/06/2023
Bruxelles

Homo Duplex : mind / body

Neurology and Psychiatry : the first appearance of the terms

Neurology : neuron, Gr & nervus, Lat. = tendon, cord

- *Anatome corporis humani*, *Jean Riolan le Jeune* (1580–1657)
- Thomas Willis (1621-1675) : νευρολογια (*Cerebri Anatome*, 1664)

'Neurologia pensum, difficile licet, utile ac iucundum est'

('The task of Neurology, though difficult, is useful and pleasing')

Psychiatry *:* ("soul healing") :

- about 1640
  - *psykhē (Gr.), psyche (Lat.) :* the invisible animating entity that occupies and directs the physical body; seat of thought and the faculty of reason
  - ≠ *pneuma* (as representing the divine breath breathed into man)

Janssen. BRAIN 2021: 144; 1–2

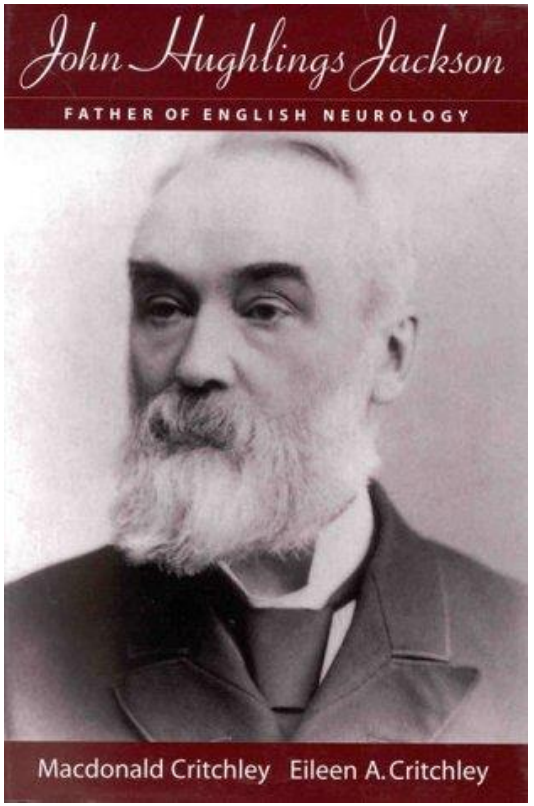
https://www.sciencedirect.com/topics/medicine-and-dentistry/history-of-psychiatry

The founding fathers of neurology

The founding fathers of neurology were all... neuro-psychiatrists!

Moritz Heinrich Romberg
(1795-1873)

Jean-Martin Charcot
(1825-1893)



John Hughlings Jackson
(1835-1911

The great split of the 20th century

Towards an institutionalized mind/brain dichotomy !

Neurology

Anatomo-clinical method

= Post-mortem study of the brain (Bichat 1771-1802)

- organic diseases (with detectable tissue damage)
- "nerve" diseases (without observable lesions)

Psychiatry

Psychoanalysis

- lack of interest in studying the brain
- dissociation from the medical model

Neurology and Psychiatry : separate disciplines

Progressively from the ’50 :

- Separate curriculum
- STOP common savant societies
- STOP common journals

The final cut :

- In the USA : RCC* for Neurology separated from the RCC for Psychiatry in 1983
- In Belgium : Neurology separated from Psychiatry in 1989

“To get neurologists and psychiatrists of that period (the 1950ies) in time to sit down together without police present was in itself an accomplishment. . . .” Price et al. Neurology 2000;54:8–14

* Residency Review Committee for Psychiatry and Neurology (RCC),

Views & Reviews

Neurology 2000;54:8–14

Neurology and psychiatry

Closing the great divide

Bruce H. Price, MD; Raymond D. Adams, MA, MD; and Joseph T. Coyle, MD

"We call for the introduction of new training curricula and accreditation criteria for both neurology and psychiatry and recommend more effective collaborations with neuropsychology, cognitive neuroscience, and neurosurgery."

The 21th century : lumping again ?

Towards a new reconciliation ?

Neurology

- Anatomo-clinical method have limits : Migraine, Tourette sdr., Restless legs, Post-commotional syndrome etc.
- Cognitive & behavioral symptoms in neurology : dementia, Parkinson, epilepsy, MS etc.

Psychiatry

- Psychopharmacology (depression, anxiety, psychosis)
- Genetics (ex. twin studies in schizophrenia)
- Neuroscience (functional brain imaging, neurophysiology, MEG etc.)
- Decline of psychoanalysis

Case 1 : 47 years old, masculin

- Hospitalized in psychiatry for a year for major depression (first episode). *“The troubles seem to have started quite abruptly with feelings of cold sweats, palpitations, weight loss, feeling "completely drained" and one fine day, not being able to go to work.”*
- No familial history, except for a father described as “very stressed”
- R/ Temesta 2 x 2 mg, Cymbalta 60 mg 1x, Risperdal 2 x 1 mg, Seroquel 100 2 x.

Case 1 : 47 years old, masculin

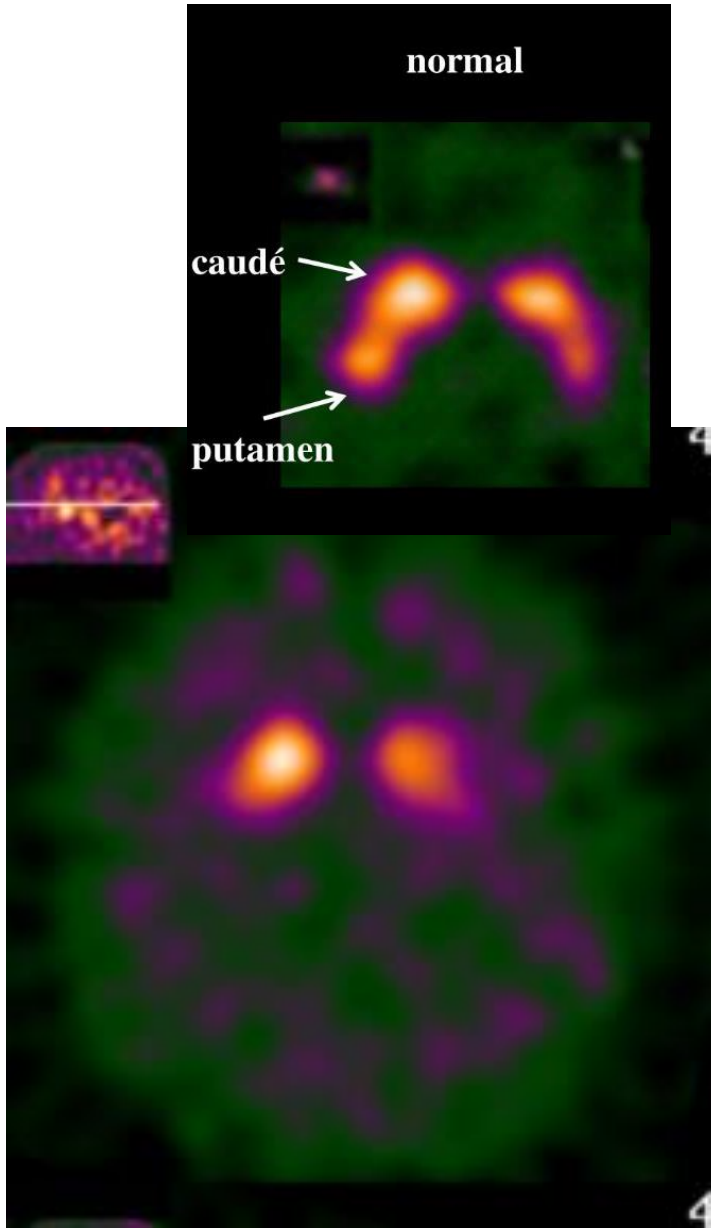
- Adressed by a colleague psychiatrist who worked with us at the Memory Clinic. He suspects a neurological disorder
- **Examination** : hunched posture, hypomimia, generalized hypokinesia. There are no abnormal movements, no dyskinesias, no tremor at rest. He is obviously bradypsychic.

⇒ **A parkinsonian syndrome is suspected (R/ neuroleptic ?)**

Case 1 : 47 years old, masculin

Complementary exams :

- MRI brain : normal
- DAT scan : significant degeneration of the bilateral nigrostriatal (L>R)
- PET scan FDG : uptake abnormalities in the upper frontal region > the posterior associative regions
- Neuropsychological exam : cognitive impairment, mainly dysexecutive (frontal type)
- HTT gene : negative



Ccl : parkinsonian syndrome & dementia ?

Case 1 : 47 years old, masculin

Follow-up : 6 years

For a year: refractory depression, with major apathy and apragmatism (psychotic-like)

R/ Levodopa, Pregabaline

Then, rapid improvement (over 3 months) : return home and work, resumed driving

Stable for 4 years.

Ccl : Idiopathic akineto-rigid Parkinson's disease, right lateralized, levodopa sensitive, with normal cognition

Prodromal depression in PD

- A sizable number of those with PD first display co-morbid depression early in the prodromal stage
- The early depressive symptoms are correlated with alterations in neurotransmission that are not necessarily directly associated with the midbrain dopaminergic neurodegeneration that occurs in PD
- Depressive symptoms are not normally alleviated by l-DOPA or other dopamine-based therapies. It is thought that diffuse pathology involving not only dopamine, but also glutamatergic, noradrenergic, and serotonergic systems are likely involved in depressive and other non-motor features of PD
- Pathological α-synuclein aggregation in brain stem nuclei : locus coeruleus, raphe nuclei => responsible for early occurring monoaminergic brainstem dysfunction that gives rise to depressive symptoms before any frank neurodegeneration is evident

Hayley et al., Neurobiology of Disease 181 (2023) 106115

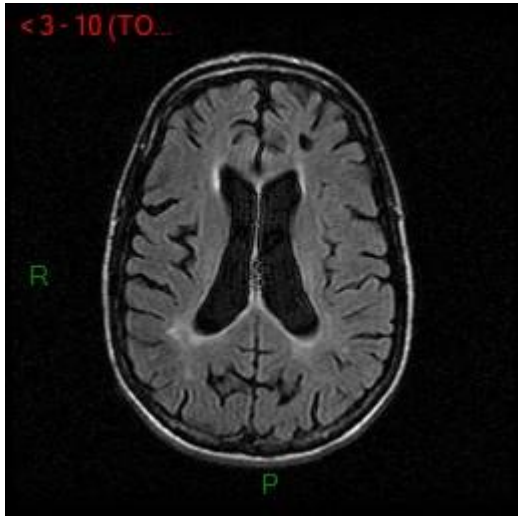
Case 2 : 31 years old, masculin

- Hospitalized in neurology for migraine-like headaches, sudden confusion, spatial-temporal disorientation, ataxia, frontal lobe syndrome (disinhibition, urination behavior)
- MRI brain scan : a myriad of inflammatory lesions
- LCR : hyperproteinorachia
- Brain biopsy : multifocal necrosis lesions associated with atypical vasculitis.

Ccl : brain vasculitis

Case 2 : 31 years old, masculin

- Sequellar cognitive impairment (dysexecutive) : unable to work, lives alone under the supervision of relatives
- A year and a half later, a sudden deterioration in behavior: *while on vacation with his family, he began to have delusions, mostly on mystical themes, significant insomnia, then he became increasingly bradypsychic and apathetic, refusing to eat and take his medication.*
- Complementary exams : rule out relapse



MRI brain scan (+ 2 yrs)
Brain atrophy
Sequelar white matter lesions

Dg. manic crisis

Case 2 : 31 years old, masculin

Follow-up :

- ❑ No more relapse
- ❑ Persistance of cognitive impairment
- ❑ Persistance of a trend toward hypomanic behavior (R/ neuroleptic, followed by psychiatrist)

Dg. bipolar type 1 disorder ? (but no atcds.)

Relationship with brain vasculitis ?

- ➢ Independent ?
- ➢ Common ground ?

Review Article

Mania secondary to focal brain lesions: implications for understanding the functional neuroanatomy of bipolar disorder

David Satzer & David J Bond. Bipolar Disorders 2016: 18: 205–220

- The prevalence of mania in patients with brain lesions varies widely by condition, from <2% in stroke to 31% in basal ganglia calcification.
- Mania occurs most commonly with lesions affecting frontal, temporal, and subcortical limbic brain areas.
- Right-sided lesions causing hypo-functionality or disconnection (e.g., stroke; neoplasms) and left-sided excitatory lesions (e.g., epileptogenic foci) are frequently observed.

Review Article

Mania secondary to focal brain lesions: implications for understanding the functional neuroanatomy of bipolar disorder

David Satzer & David J Bond. Bipolar Disorders 2016: 18: 205–220

- Secondary mania should be suspected in patients with neurological deficits, histories atypical for classic bipolar disorder, and first manic episodes after the age of 40 years.
- Treatment with antimanic medications is typically required.
- Typical lesion locations fit with current models of bipolar disorder, which implicate hyperactivity of left hemisphere reward-processing brain areas and hypoactivity of bilateral prefrontal emotion-modulating regions.
- Lesion studies complement these models by suggesting that right-hemisphere limbic-brain hypoactivity, or a left/right imbalance, may be relevant to the, pathophysiology of mania.

Table 1. Causes of secondary mania

Category	Subcategory	Examples
Neurologic	Neoplasm	Frontal lobe meningioma (63)
		Temporal lobe glioma (57)
	Trauma	Traumatic brain injury (34)
	Vascular	Ischemic stroke (9)
		Intracerebral hemorrhage (12)
	Infection	AIDS (175)
		Prion disease (176)
		Viral encephalitis (177)
	Neurodegenerative	Frontotemporal dementia (78)
		Huntington's disease (84)
	Other	Epilepsy (97)
		Multiple sclerosis (67)
		Neurosurgery (99)

Case 3 : 52 years old, masculin

University level, full time demanding work, no medical history, athletic

- The patient consults the neurologist for "mental confusion" and involuntary movements (for 6 months)
- His wife : inatentive and off topic in conversation, at some moments pulling from the mouth to the left and a stiffness of the index finger, which is of short duration.
- Significant sleep disturbances (insomnia on falling asleep, fragmented sleep)

Another neurologist : functional disorder

Case 3 : 52 years old, masculin

EEG-video :

- A sporadic bitemporal slow focus sometimes better visible on the left, especially in the transition period to the sleep or in sleep, absence of obvious abnormal epileptiform activity
- Twenty episodes - corresponding to the usual episodes - are reported by the patient. No electrical anomaly is not visible on the EEG and there is no true clinical stereotypy.

Ccl : functional neurological disorder

Case 3 : 52 years old, masculin

Three months later

Psychiatric emergency ward

The same movement disorders,

Spatiotemporal disorientation, memory problems on recent events,

Episodes of nocturnal restlessness & agressivity (he said *"I have to kill you with a knife"* to his wife)

The psychiatrist refutes a psy pathology

Case 3 : 52 years old, masculin

Rehospitalized in neurology

- EEG : no epileptiform element
- LP : hyperproteinorachy (80 mg/dl); very high tau protein at 1339 pg/ml (nl <381 pg/ml) with normal P-Tau at 23 pg/ml (nle <61 pg/ml) => neuronal destruction
- Brain MRI : bilateral (L>R) swelling of the hippocampi and parahippocampal gyri : probable encephalitis (retrospectively already present on the MRI scan 6 months before)
- PET scan FDG full body : absence of neoplasia. Intense hypermetabolism in the striatum and moderate hypermetabolism in the hippocampi/para-hippocampi (G>R), consistent with limbic encephalitis.
- AB research (antimembrane and onconeuronal antibodies) : **positive for anti VGKC LGI1**

Diagnosis : **autoimmune limbic encephalitis**

Case 3 : 52 years old, masculin

R/plasmapheresis, corticoides, immunosupressors, antiepileptics

Followed up for 2,5 years

Marked improvement, but :

- could not return to work
- persistence of brief episodes of "crisis“ :

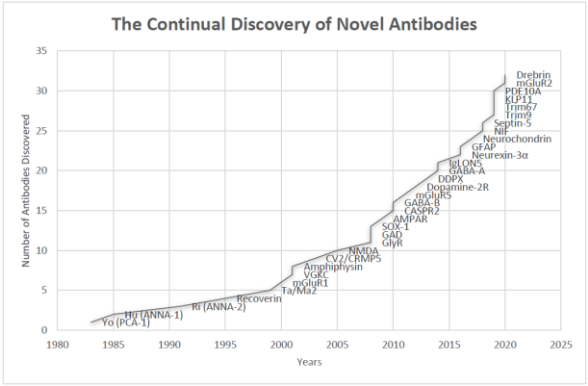
“It always starts as an overexcitement, then an acceleration of the rate of speech until stuttering, then feeling of shivering last the head, goosebumps which go from the top of the skull to the toes, at the end the fingers which stiffen, tense mouth and face +++, crying ++, still conscious (no CP). To stop the crisis, you have to stop the current thought process.”

- ac. his wife : the behavioral problems persist, she describes him as being "unfiltered", with a low tolerance threshold.
- examination : a logorrheic tendency and great emotivity (with piloerection).
- *no evidence of disease activity (brain MRI, anti VGKC LGI1 becoming negative)*

Autoimmune Encephalitis: A Physician's Guide to the Clinical Spectrum Diagnosis and Management

Arpan Patel [1,*], Yue Meng [2], Amanda Najjar [3], Fred Lado [4] and Souhel Najjar [4]

Brain Sci. **2022**, *12*, 1130. https://doi.org/10.3390/brainsci12091130



- The most common form of encephalitis of noninfectious origin
- Caused by autoantibodies targeting neural epitopes such as synaptic surface structures (e.g., receptors, ionic channels, or supporting proteins) or intracellular antigens such as onconeural antigens
- Psychiatric presentations of autoimmune encephalitis are common : more than 80% of patients with NMDA encephalitis initially presented with psychiatric symptoms requiring psychotropic medications and, in some instances, psychiatric hospitalization
- Personality changes, bizarre behaviors, agitation, anxiety disorders, depressive or manic symptoms, auditory or visual hallucinations, delusions, or catatonia
- They can be mistaken for primary psychiatric illnesses such as new-onset primary psychosis, schizoaffective spectrum disorder, and acute mania
- Antipsychotics are often not effective and associated with higher incidence of significant side effects such as neuroleptic malignant syndrome
- Autoimmune psychosis : autoimmune encephalitis presenting with isolated psychosis (including delusion, hallucination, thought disorganization, agitation, and aggression)

Case 4 : 41 years old, masculin

After an unremarkable childhood, the situation deteriorates from adolescence onwards, with a tendency to social withdrawal, lack of empathy, difficulty adjusting on the relational level.

However, he remains able to complete his studies and train as a caregiver. He worked as caregiver until he was 29.

Dg. Autism spectrum disorder (Asperger sdr ?)

Case 4 : 41 years old, masculin

The situation continues to deteriorate, he cannot keep a job, he isolates himself more and more and his autonomy is gradually lost.

At 30, he is no longer able to manage his household, his budget, the administrative aspects as well as his medication.

He lives alone in an apartment but under the supervision of parents who must come every day.

Dg. Anxio-depression

Case 4 : 41 years old, masculin

Familial history

Frontotemporal dementia in the father whose onset of symptoms is estimated around the age of 40

Notion of probable dementia in the paternal uncle (around 60 years old a priori).

However, the neurologist does not believe in the hypothesis of dementia

Case 4 : 41 years old, masculin

He is seen for a second opinion

He spends his days watching NBA basketball games, playing on the PlayStation or on websites.

The patient reports a few symptoms that he describes himself as abnormal, such as going around in circles in his apartment, regardless of the activity he performs (reading, television, etc.). These round trips have resulting in numerous knocks followed by hematomas. At the same time, he says that he flees the company for several years. He has moved away from his acquaintances and currently has no friends.

Case 4 : 41 years old, masculin

Neuropsychological examination :

The patient is cooperative but impulsive. Bradypsychia.

MMSE : 28/30

Relatively normal : verbal fluency and memory borderline; slow processing speed in executive tests

Case 4 : 41 years old, masculin

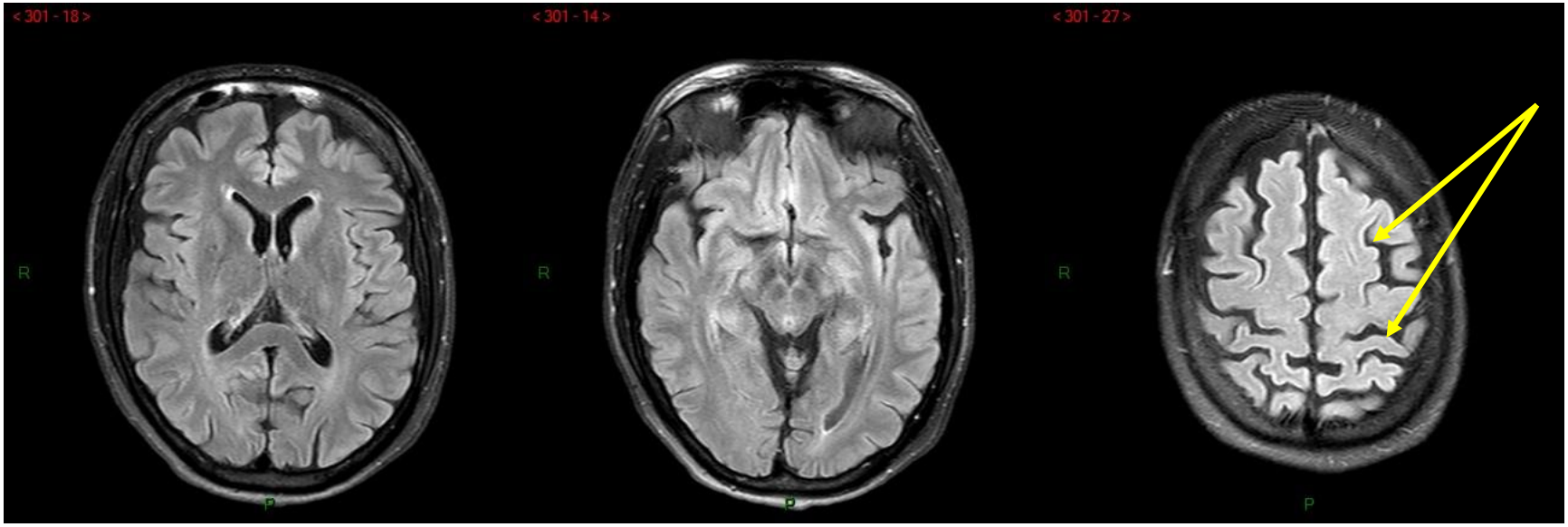
Complementary exams:

- PET FDG : some abnormalities, but no clear-cut cortical involvement
- Brain IRM : moderate and non-specific global cerebral atrophy
- Genetic analysis : C90RF72 mutation is identified.

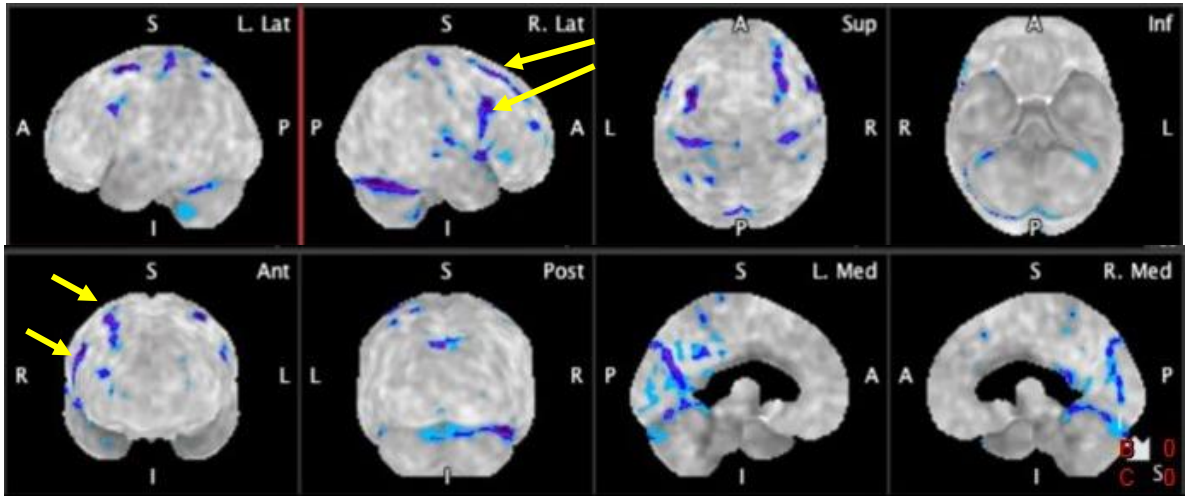
Dg. Frontotemporal dementia ?

Case 4 : 41 years old, masculin

MRI scan



Brain PET
FDG scan



Posterior frontal/upper parietal heterogeneity associated with some abnormal voxels at the level of the precuneus. Some lateral frontal sulci are also a little more marked - AD Score: 1,24 (normal < 1.0)

Case 4 : 41 years old, masculin

Evolution

- +3yrs : some worsening is reported by the family; MMSE : 25/30
- +5yrs : same, MMSE : 24/30
- +7yrs : MMSE : 18/30; an increase in frontal syndrome (apathy, inappropriate behavior, appearance of prosopagnosia), accompanied by a drastic reduction in one's autonomy. Living alone in an apartment under parental supervision is no longer possible and a decision to be placed in a rest and care home has been taken.

Ccl : progressive evolution towards dementia

Current Neurology and Neuroscience Reports (2019) 19: 93
https://doi.org/10.1007/s11910-019-1017-9

DEMENTIA (K.S. MARDER, SECTION EDITOR)

Links Between the *C9orf72* Repeat Expansion and Psychiatric Symptoms

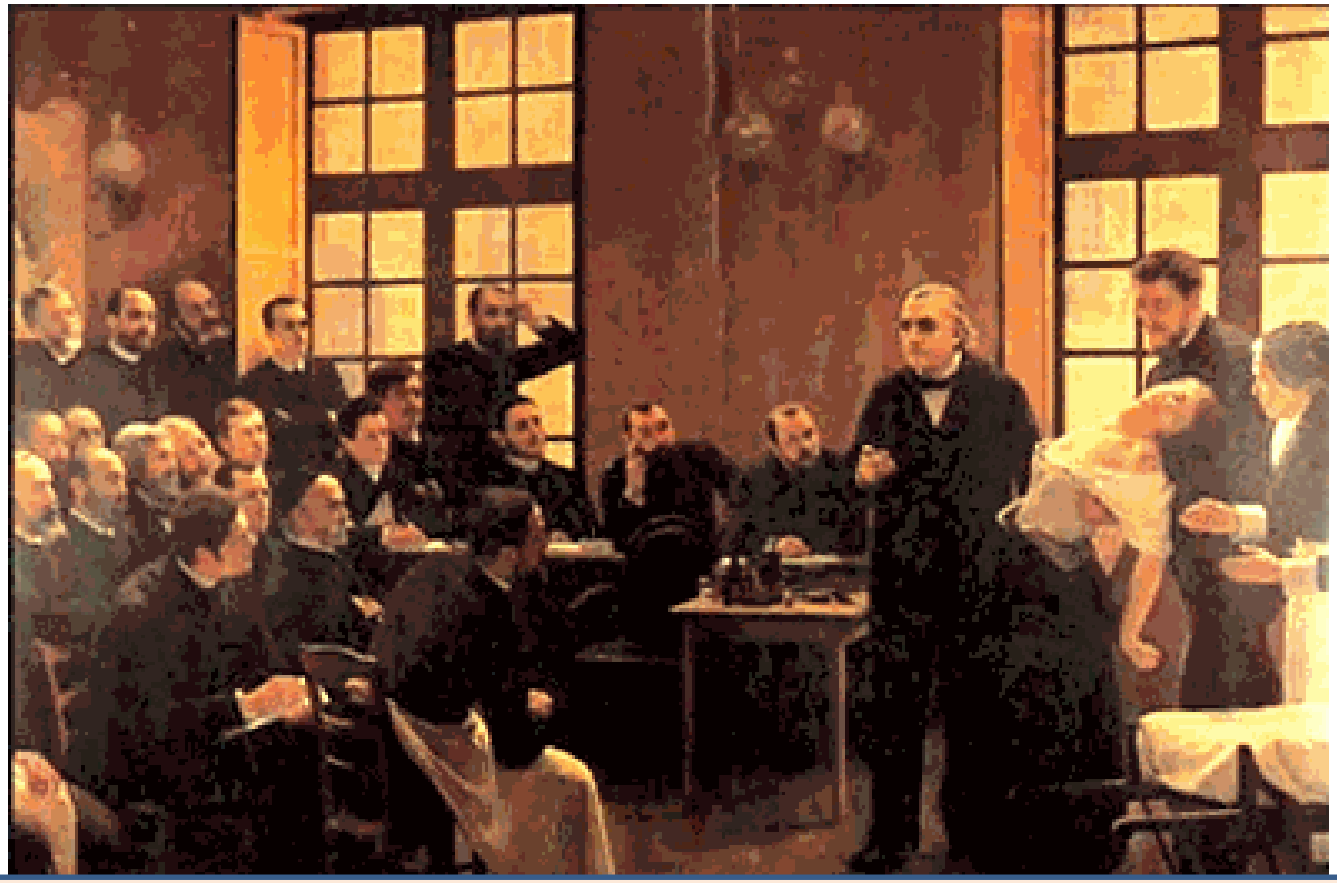
Hannah E. Silverman[1,2] · Jill S. Goldman[1,2] · Edward D. Huey[1,2,3]

- In 2011, a hexanucleotide repeat expansion in the C9orf72 gene was identified as a pathogenic cause of amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD), and the mixed phenotype, FTD-ALS. The implications of an intermediate number of repeats (generally considered 20–30) are undetermined
- The **psychotic phenotype in C9orf72-linked FTD**
  - ✓ carriers have higher rates of psychotic symptoms than non-carriers
  - ✓ case reports demonstrate that psychotic symptoms may occur prodromally years prior to formal diagnosis of FTD, which can lead to misdiagnosis of a psychiatric disorder such as schizophrenia

Ccl : psychotic symptoms may be an early sign of neurodegeneration in mutation carriers (ex. C9orf72)

From Hysteria to Functional Neurological Disorders (FND)

Jean-Martin Charcot (1825-1893) : Leçons de mardi à la Salpêtrière



Hysteria = brain (neurodegenerative) disorder
“Only hysterics could be hypnotized”

Functional neurological disorder: new subtypes and shared mechanisms

Mark Hallett, Selma Aybek, Barbara A Dworetzky, Laura McWhirter, Jeffrey P Staab, Jon Stone

Lancet Neurol 2022; 21: 537–50

New classification :

- Functional seizures (also called dissociative or psychogenic non-epileptic seizures)
- Functional movement disorders, including paresis
- Chronic dizziness (functional vestibular disorder of persistent postural perceptual dizziness)
- Cognitive dysfunction as part of a functional disorder
- Other :
  - somatosensory (functional anaesthesia)
  - visual symptoms (functional blindness)
  - other motor disorders (eg, speech and swallowing disorders)

Common etio-pathogenesis : **primary pathophysiological processes are alterations in functioning of brain networks rather than abnormalities of brain structures.**

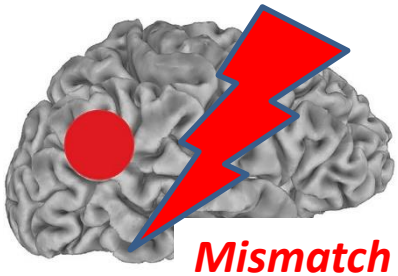
Functional neurological disorder: pathophysiology

1) Predisposing factors :

- Genetics
- Developmental (trauma, abuse during childhood)
- Psychological disorders (anxiety & depression) & stress
- Neuro diseases (epilepsy, Parkinson etc.)
- Other sdrs. functional (chronic pain etc.)
- Socio-cultural norms
- Sometimes: unknown

2) Precipitating factors :

- Loss of consciousness,
- True vertigo,
- Trauma,
- Infection and Vaccine
- Medications
- Stressful events
- Sometimes: none



Temporo-Parietal Junction (TPJ)

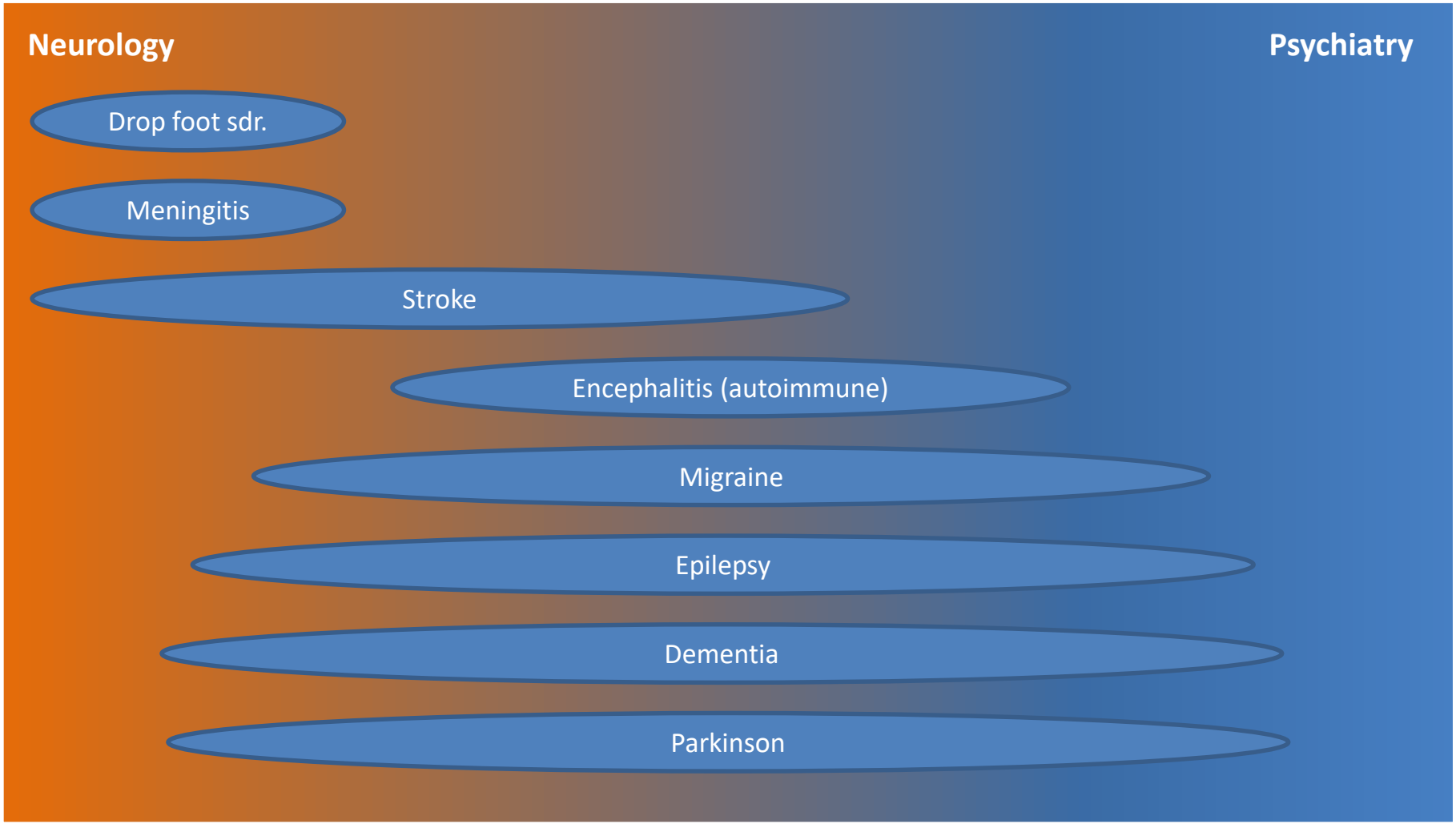
3) Comorbidities :

- Anxiety,
- Depression,
- Borderline personality,
- Other tr. functional (irritable colon, fibromyalgia etc.)

4) Perpetuation factors :

- Diagnostic error
- Diagnostic uncertainty ("shopping medical")
- Poor doctor-patient communication
- Litigation in progress (ex. accident)
- Secondary benefits (income, "sick" status)

Neuro-psychiatric continuum



J Neuropsychiatry Clin Neurosci. 2018 ; 30(4): 271–278. doi:10.1176/appi.neuropsych.17100200.

Bridging the Great Divide: What Can Neurology Learn from Psychiatry?

David L. Perez, MD, MMSc[1,2,*], **Matcheri S. Keshavan, MD**[3], **Jeremiah M. Scharf, MD, PhD**[4,5], **Aaron D. Boes, MD, PhD**[6], and **Bruce H. Price, MD**[1,7]

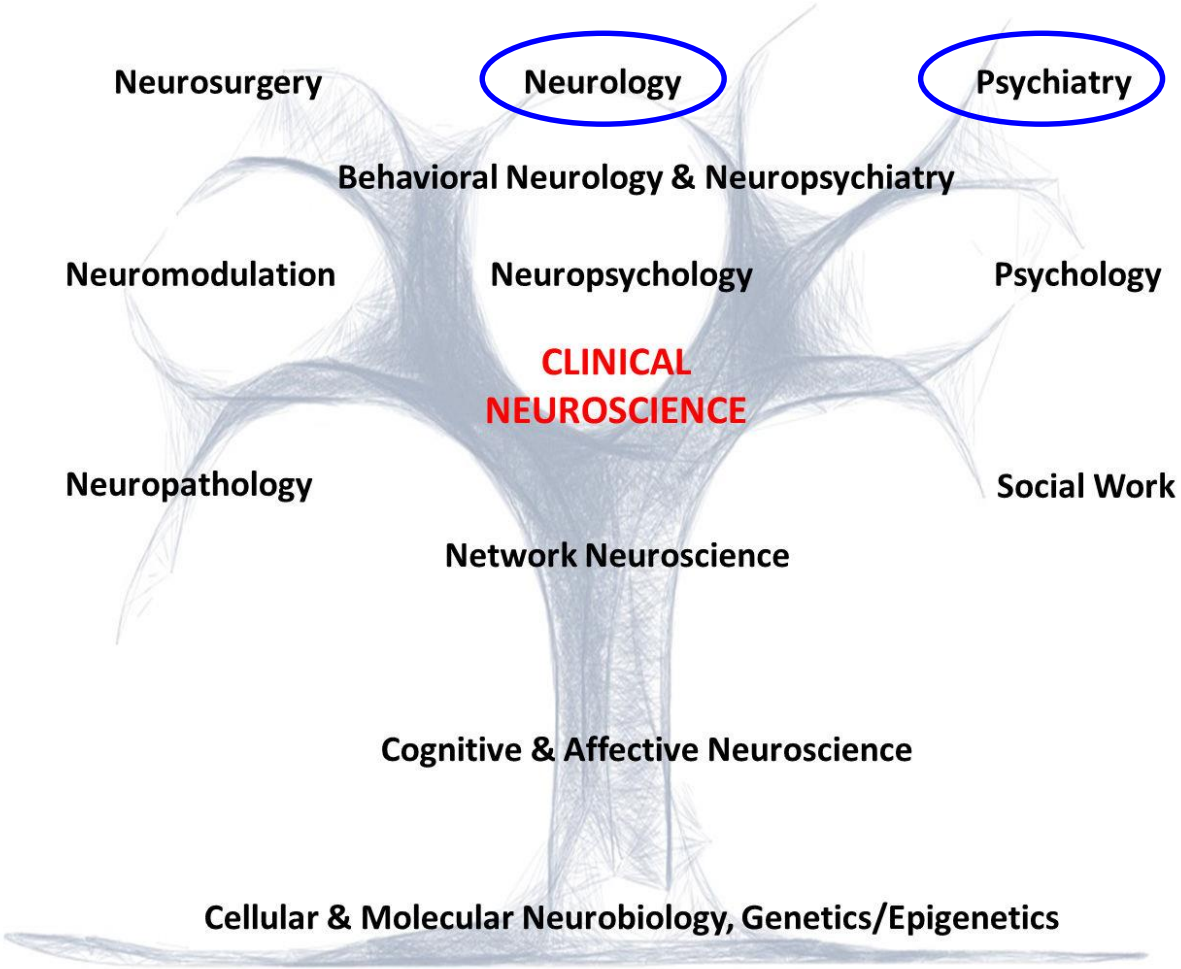


Figure 1.

An Integrated Clinical Neuroscience Approach for the Assessment, Management and Investigation of Brain Disease.

Une « convergence forcée » ? Ethnographie d'une collaboration entre neurologie et psychiatrie dans un centre de neurosciences en France

A "forced convergence" ? Ethnography of a collaboration between neurology and psychiatry in a French neuroscience center

Baptiste Moutaud

https://doi.org/10.4000/anthropologiesante.927

Biological and cognitivist perspective of a natural or "brain" subject

⇔

Dynamic approach, valuing individual biography and a socialized subject (sociological and anthropological perspective)

Criticism :

Biological reductionism

"The brain secretes thought like the liver secretes bile."
Cabanis, Pierre Jean Georges (1757-1808)

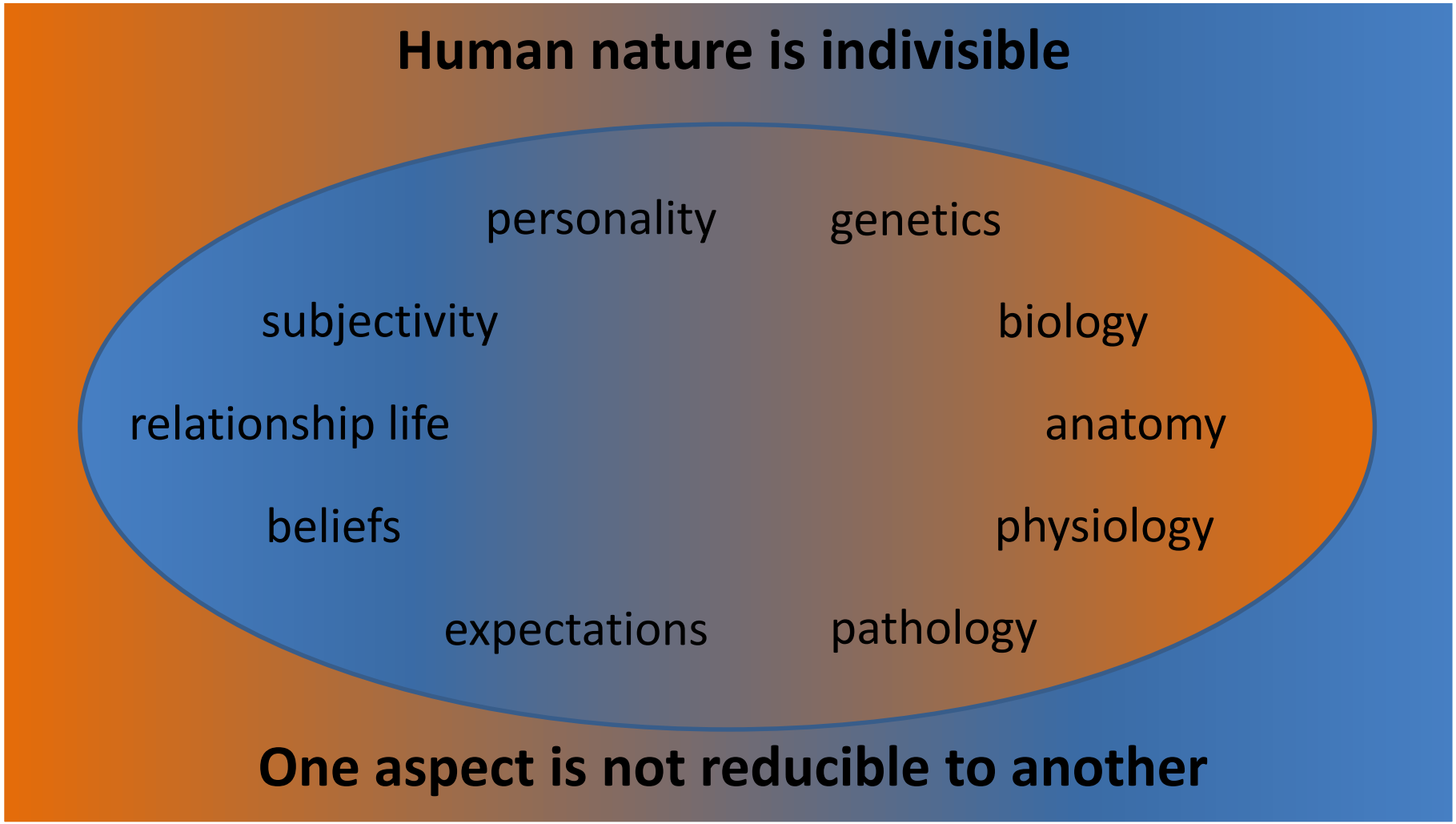
⇔

Criticism :

The "Blank slate" fallacy

"Behavior is not just emitted or elicited, nor does it come directly out of culture or society. It comes from an internal struggle among mental modules with differing agendas and goals"
The Blank Slate: The Modern Denial of Human Nature
Steven Pinker, 2003

How to succeed in convergence?



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"In the last analysis, we see only what we are ready to see, what we have been taught to see. We eliminate and ignore everything that is not a part of our practices."

Jean-Martin Charcot 1825–1893

Thank You !