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Ideas and Instruments in Social Context

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SYMPOSIUM S48 : NETWORKS OF INSTRUMENTATION IN THE NEUROSCIENCES

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Technical advances in neurochemistry: histofluorescence and immunohistochemistry, their influence on sleep physiology

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Starting from the mid sixties, sleep physiology could develop in the biochemical direction thanks to several advances in neurochemistry : radioactive labeling of monoamines inducing a better knowledge of brain metabolism ; histofluorescence leading to the first localization of monoamines in nuclei of the brain stem and thus to physiological models of the sleep cycle ; immunohistochemistry coming later on, in the late seventies and early eighties, provided a much detailed view of the plurality of neurotransmitters and of their localization in/on the neuron, with much better physiological implications. More recently, immunohistochemistry played an important role in helping to localize several neurotransmitters involved in sleep regulation, and thus in providing evidence to build much improved models of sleep mechanisms.

Epilepsy, a disease between the fields of clinics and surgery in the twentieth century

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The epilepsy is a disease which between 1850 and 1960 follows many different theoretical ways of thinking within medicine and/or neurosciences. From researches of John Huglings Jackson considered the father of modern epileptology, to surgical techniques developed by Jean Talairach and electroencephalographic representations, we will analyze the ways the epileptic symptom becomes a pathological and clinical entity: epilepsy.

Many questions should be answered: In what manners electroencephalographic studies, surgical developments and clinics contribute to the renewal of the medicine of epileptic disorders?

Through this vast problematic, we will examine the works of Antoine Rémond, Jean Talairach, Henri Gastaut and Robert Naquet.

Action potentials and the “digitization” of the Nervous System by European scientists between 1900 and 1950

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At the beginning of the XXth century, Gotch (1853-1913), Lucas (1879-1916) and Adrian (1889-1977) established two fundamental laws, the all-or-none response (Gotch 1902, Lucas 1909) and the absolute and relative refractory period between two stimulations (Adrian and Lucas 1912). These laws demonstrated that the nervous conduction corresponded to a "digitization" of its activity. Nervous activation seemed to correspond to a conversion of the information into a digital format. These trains of action potentials were recorded both in motor and in sensory nerves. The signal was similar in amplitude with a very short duration; the intensity of the phenomenon was expressed by the frequency and the duration of the discharge. This expression of motor and sensory conduction, with frequency coding, unified the vision of the central nervous system (CNS). The metaphor comparing the CNS with a telephone system was confirmed, nervous centers corresponding to central offices.

It was not easy to record such very short and very rapid activities. In US, Gasser and Erlanger (1922) were using the cathodic oscillograph very early which allowed a fine analysis of complex waves. In Europe, apparatus were more primitive, using capillary electrometer or string galvanometer. However some new apparatus were built and gave the possibilities of better recordings (Matthews 1928, Fessard 1933).

The following work confirming this "CNS wiring vision" was done mainly by the Cambridge school. They isolated single sensory as motor fibres, demonstating the ubiquity of digitization. The responses were recorded from specific mechanoreceptors like the Pacini corpuscle (Umrath and Adrian, 1929) or like the muscle spindle (Matthews 1931). Concerning motor command, Adrian and Bronk (1929) recorded motor neurones, confirming the reflex activation (Liddell and Sherrington, 1926).

Around 1930, the description of the cortical brain waves seemed a global responses of these isolated fibres. At that time, the CNS was in fact considered as completely "electrical", rigid and composed of an ensemble of inputs and outputs. Arvanitaki (1901-1983) studied the activities of the invertebrate nerves with Fessard (1900-1982) and Cardot (1886-1942). In 1942, she demonstrated that large cuttlefish fibres could communicate by electrical connection, confirming the nervous electrical synaptic hypothesis developed mainly by Eccles (1903-1997).

First studies on synaptic contents were not accepted easily and induced fighting between "the soups and the sparks" (Valenstein, 2005). It ceased abruptly, in 1950, when Eccles recorded intracellularly the spinal cat motorneurones. Recording excitatory and inhibitory postsynaptic potentials, he was admitted electrical conduction at the level of the synapse was not possible. Further developments in electrophysiology and on neurochemistry demonstrated analog signals seemed the law in the CNS and that actions potentials corresponded to digital signals necessary to relay information throughout the body!

A Fine Balance: The Cultural Implications of Indirect Measurement

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This talk describes a mid nineteenth century controversy over the interpretation of experiment. It concerns the claim of the Berlin physiologist Emil du Bois-Reymond (1818-96) to have arrived at a technique of manifesting nerve signals in living human subjects. Du Bois-Reymond's method was based on two tenets of classical physics: first, that absolute measurements can be inferred from relative measurements, and second, that parts can be integrated into wholes. The *Académie des sciences* in Paris, however, rejected du Bois-Reymond's findings when he was invited to demonstrate them. Here I will discuss why, along with what this controversy between French and German scientists implies about contemporary practices of cultural history.

The PPI Network : From Spiritual Brain to Future Antipsychotics?

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Measured by San Diego Instruments' Startle Response System SR-LAB, prepulse inhibition (PPI) of the startle reflex is a widely used operational measure of sensory motor gating in biopsychiatric and neuropsychopharmacological research. PPI is based on the nineteenth-century idea that the brain filters out an overabundance of external stimuli. In the 1950s, the British writer Aldous Huxley interpreted mystical states of mind, including his own hallucinogen intoxications, as the perception of an ethereal reality caused by an impairment of this cerebral "reducing valve": detrimental to biological survival, but spiritually enriching. Since the 1970s, the inhibition of the startle reflex through non-startling prepulses has been taken as an instantiation of such filtering mechanisms. But instead of pursuing Huxley's neurotheology, the psychopharmacologists Mark Geyer, David Braff, and Neal Swerdlow demonstrated PPI deficits in schizophrenics and began to use hallucinogen-induced PPI deficits in rodents as an animal model of

psychosis that could help to screen for new antipsychotic drugs. By marketing a standardized version of their startle response system, Geyer managed to build an extensive research network around PPI. However, until today no novel antipsychotic has been discovered through PPI. The measure and its network are also in crisis since discrepancies between the animal model and its human counterpart have recently come to the fore. This presentation explores the formation (and, possibly, the beginning disintegration) of the PPI network in the context of hallucinogen research and the secularization of Huxley's conception of the spiritual brain.

Electric fish discoveries in Modern Age: complex networks of scientific endeavour and historical intricacies.

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Research on electric fish played a fundamental role in our understanding of physical and physiological electricity. It contributed to Luigi Galvani's discovery of the electric nature of nervous signals (in 1780) and also to invention of the electric battery by Alessandro Volta (designated as *organe électrique artificiel* to acknowledge the inspiration from the natural organ of fish). Earlier studies on the history of electric fish research had focused mainly on the investigations carried out from 1772 to 1776 by John Walsh, first on torpedoes at La Rochelle in France, and afterwards on electric eels imported from Surinam to London. Although Walsh's endeavours played a crucial role in indicating that electricity could be involved in animal economy, the electric nature of shocks from fishes had first emerged from observations of electric eels and the African electric catfish. Recently, in collaboration with Stanley Finger, Peter Koehler and Jean-Gaël Barbara, I have been investigating the pre-Walsh phase of electric fish research. Electric eels were studied by Dutchmen, and they profited from complex social and cultural networks, particularly those expressed in the Low Countries. These involved many factors including: interests in voyages to exotic countries, colonialism, strong commitment to collecting natural specimens and their systematic classification, great development of natural philosophy and experimental science, presence of an important publishing houses, foundation of scientific societies with their associated scientific journal and magazines. The historical pathway that brought the relatively neglected electric catfish to the attention of Western literati was even more complex. In addition to some of the factors mentioned above other, more specific factors were involved. The blossoming of Catholic missions and specifically those of Jesuits in Ethiopia were significant. Ethiopia was considered a mysterious country that had attracted the interest of Europeans because of its religion and its legends (and mainly that of its mythical Emperor, the so called Prester John). The initial important contact between Ethiopia and Europe occurred in the first half of the sixteenth century, in a particularly dramatic phase of Ethiopian history which resulted in a glorious epic of the Portuguese army. One consequence was that Jesuits were allowed into Ethiopia and eventually, at the beginning of the next century, they seemed to have great success in converting members of the local high class to orthodox Catholicism, including the Emperor himself. In this context a controversy exploded among the Dominicans and the Jesuits regarding the importance of their respective roles in the Christianization of Ethiopia. This led to the publication in 1610-1611 by the Dominican Luis de Urreta of one of a most fanciful work in which old legends of Ethiopia were presented as true historical facts. The first printed descriptions of the electric catfish emerged within the climate of this controversy and in this way news about the “African torpedo” spread throughout Europe. Much later (in 1757) this led to the first proposal of the electric nature of its discharge by the French naturalist Michel Adanson during his voyage in Senegal.

Beyond the Synapse
On the Impact of Adult Cerebral Plasticity on the Neurologically Human

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The paper deals with the quite recent emergence of the claim that plasticity (broadly defined as any morphogenetic change of the cerebral tissue) is a major feature of the adult human brain – and it elaborates on the significance of this emergence for contemporary neurocultures.

The approach is historical: The aim is to show that (and how) the emergence of plasticity research has mutated the *neurologically possible* – the space of possibilities within which neurologists have to organize/arrange their ideas about the brain – and how this mutation has in turn transformed the *neurologically human* – the space of possibilities within which those existing under the spell of the brain have to live their lives.

The particular case I focus on in order to map these changes is depression/anxiety: The paper shows how plastic conceptions of the brain and its disorders depart from previous synaptic conceptions of the brain and its disorders (i.e., from a focus on neurotransmitters as cause and remedy of, e.g., depression) that have become predominant with the invention of psychopharmacology.

From Leipzig to Cambridge, from Wundt to James: Hugo Münsterberg and his Laboratories for Experimental Psychology

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Hugo Münsterberg (1863 - 1916) is often referred to as a pioneer of applied psychology. Münsterberg is also well-known for his philosophy of values and his early theory of the cinema (*The Photoplay*, 1916). Less familiar is Münsterberg's role as a creative experimenter and energetic director of psychological laboratories – in Germany and the United States. In this role, Münsterberg contributed significantly to the transition from a cognitive and/or idealist "Physiological Psychology" in the sense of Wilhelm Wundt to the pragmatist and/or functional "Science of Mental Life" as advocated by William James and others.

The paper argues that this transition was not only grounded in theory and epistemology but corresponded to significant changes in the material culture of Münsterberg's psychological laboratories. In particular, Münsterberg collaborated with the Freiburg based precision mechanic Hermann Elbs (1861-1936) for setting up innovative experiments that transgressed the tight conceptual and practical boundaries of Wundtian chronometry. Instruments such as the “Muscle Sense Apparatus” and devices for investigating the power of the eye to compare lengths (“Augenmassapparat”) permitted Münsterberg to investigate the psycho-physiological periphery of the body, whereas Wundt and his research school had remained focused on centralized, i.e. conscious phenomena. Based on unpublished sources, this paper shows how Münsterberg developed and used these instruments and transferred them from Europe to the US.

‘Ex-radar folk with biological leanings’: models, electronics and the nerve impulse at WWII

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Around 1945, the ‘nervous impulse’ ascended as a premier scientific problematic and a great many accounts, representations, theories, and models were floated in matters of fundamental bioelectric mechanisms underlying nervous activity. If the ideological lure of basic science and the worrisome state of the mental health of the world provided much of the rationale, war-induced advances in instrumentation, notably electronics, provided the means that shaped mid-century approaches to nerve. In the post-war world, the ‘behaviour’ of nerve was zeroed in with a vengeance from the vantage points of biophysics, biochemistry, cybernetics, energetics, biomolecular structure, or colloidal science.

Arguably the most consequential of these approaches transpired in Cambridge, UK, and would be handed down to posterity as the Hodgkin-Huxley ‘model’ of the action potential: a complex assemblage, in fact, of ‘theory’ and ‘hypotheses’, differential equations, circuit-diagrammatic representations, organismic preparations, computational practices, and a set of novel experimental technologies – electronically controlled recording techniques, microelectrodes, and radioactive tracers. Despite its eventual hegemony, it wasn’t obvious at the time that the model should exhaust the issue: indeed it was, in many ways, a model without referent. The ‘mechanism’ it gestured at remained shrouded in microphysical darkness, its mathematical splendor meant horrors to the average nerve physiologist, and it blissfully ignored the metabolic dimensions of nervous activity.

Explaining the relative success of this relatively particularistic vision of the nerve cell, or so I argue here, requires taking into account the broader mid-century transformations in attitudes towards biological research and modelling practices. This paper presents an account and contextualization of the model’s relative success by examining the impact of the ‘radio war’ on the state of British biological science. This paper analyses first, Britain’s war-time radar training schemes – including large-scale ‘conversion’ efforts at imparting non-physical scientists with electrical engineering skills - and how biologists, exposed to an ideology of science suffused with ‘teams’, ‘mixing up’, and crossing boundaries, in the process came to appropriate engineering modes of research, and their emphases on ‘design’, ‘prototypes’ and ‘models’. Second, it attempts to gauge the subsequent transfer of such frame of mind, skills, instrumentation and its impacts on the state of post-war neuro-physiology. The model, the argument goes, derived its persuasiveness from a historical context that not only or merely saw the diffusion of electronics-based research techniques, but the incipience of a model biological persona who prioritized schematic simplicity to exhaustive complexity. It attained critical mass not least thanks to what one may think of as a generational effect: the post-war emergence of a small but influential population of electronics-and-models-minded biological scientists - 'ex-radar folk with biological leanings'.

"What was in their Luggage? German Refugee Neuroscientists and the Emergence of Interdisciplinary Research Networks in North-America, 1933 to 1963"

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It is a well established fact of 20th century history of science and medicine that with the seizing of power of the Nazi party in Germany, numerous anti-Semitic laws became established, which aimed at the expulsion from service of most Jewish scientists and doctors at universities and other state-funded medical and research institutions. The neurosciences (broadly understood to include neurologists, psychiatrists, and neuropathologists, etc.) were one of the areas, which were most strongly affected by the political pressures that eventually led to the expulsion from Central Europe of up to a third of the leading doctors in this medico-scientific field.

As a result of their holistic, healing-oriented approach, many of the protagonists of the emerging neuroscientific and psychiatric cultures in the early 1930s – such as the Goldstein group in Frankfurt, the Munich neurohistologists, or the private clinicians of Berlin – were faced not only with expulsion from academic work circles, but also prohibited from pursuing their career as medical doctors. Many of them searched to escape this and establish a new professional life elsewhere. Those who were socially adaptable and economically well-off were able to react quickly when political conditions deteriorated; they decided that it was better to leave Germany before things worsened, often with nothing more than suitcases filled with clothes, a little seed money, and the addresses of relatives, friends, or international colleagues in their pocket.

Until recently, this exodus of German-speaking scholars is frequently portrayed in the historical research literature by the “brain gain” theory of the forced-migration of academics, intellectuals, and scientists, when most notably the United States (in North America) and Great Britain (in Europe) were “enriched” through receiving the émigré neuroscientists, and German-speaking science underwent the loss.

The perspective presented in this paper challenges this received historical view, by drawing attention to the often neglected immigration rules, social relations, and contingent patterns of re-adaptation into scientific working groups. By focusing on the travelling ideas and instruments of the émigrés, during what many saw as a process of “parachuting from Europe into the new world of North American psychiatry” (Heinz Lehmann, 1911-2000), some new light will be shed on the difficult re-integration of the German-speaking refugees in the North-American neurosciences. When taking books, journal articles, brain slides, microscopes, etc. as essential utensils of modern neuroscientific research, the luggage of such individuals as Hans Lehmann, Martin Silberberg (1895-1969), or Kurt Goldstein (1878-1965), etc. shall historically be unpacked and scrutinized as to its role and influence in the process of re-integration of the exiled neuroscientists in North America.

Travels of a bioassay: the eserinized leech muscle in Henry Dale's lab and beyond

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In 1933 a young German refugee physiologist, Wilhelm Feldberg, arrived in Sir Henry Dale’s lab at the National Institute of Medical Research (NIMR) in North London. He brought with him the ‘key’ (in his own words) to a series of successful experiments in the lab, which contributed to the award of the Nobel Prize to Dale, and the adoption of his experimental technique in physiology and pharmacology labs around the world. What was that ‘key’? It was the use of the acetylcholinesterase inhibitor eserine on the dorsal muscle of the leech as a bioassay to detect minute quantities of acetylcholine. In 1918 the German pharmacologist Fühner had noted that adding eserine to an organ bath in which a leech muscle was suspended made the muscle extremely sensitive to acetylcholine, and he used the system as an assay for eserine (Führer, H, 1918, 'Ein Vorlesungsversuch zur Demonstration der erregbarkeitssteigerndend Wirkung des Physostigmins' Archs exp Path Pharmak 82:81-85). Feldberg merely reversed the procedure and used the eserinized muscle as a sensitive and simple assay for acetylcholine.

As early as 1914 Dale had suggested that acetylcholine, then known only as a synthetic molecule, was an ideal candidate as an endogenous mediator in the parasympathetic nervous system. However it was not until 1929, after his chance discovery that it occurred naturally in animals, that research in Dale's lab focussed on the physiology and pharmacology of acetylcholine. Feldberg's arrival with his eserinized leech muscle heralded a period of enormous scientific productivity – 14 full papers in the Journal of Physiology alone in just three years, and the first direct experimental evidence for acetylcholine in ganglionic transmission, at the parasympathetic post-ganglionic junction and at the neuromuscular junction of the voluntary nervous system was soon available (see Tansey, E M , 1991 'Chemical neurotransmission in the autonomic nervous system: Sir Henry Dale and acetylcholine' Clin. Auton. Res. 1:63-72 for a summary).

Dale's lab, known by its room number 'F4' attracted people from around the world (Tansey, E M, 1995, An F4-vescent episode: Sir Henry Dale's laboratory 1919-1942 Brit J Pharm 115: 1339-1345). Visitors and co-workers took away techniques and concepts they had learned in F4, and the eserinized leech muscle travelled via G L Brown, W S Feldberg, J G Gaddum, F C MacIntosh, W D M Paton, Marthe Vogt and others, to, inter alia, many British labs including Cambridge, Edinburgh, Oxford, and UCL, and further afield to Australia, Belgium, Canada and New Zealand.