HISTORICAL PAPER

MULTIREGIONAL CELL ASSEMBLIES, TEMPORAL BINDING AND THE REPRESENTATION OF CONCEPTUAL KNOWLEDGE IN CORTEX: A MODERN THEORY BY A "CLASSICAL" NEUROLOGIST, CARL WERNICKE

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Abstract

A contemporary view of conceptual representation in the brain holds that conceptual knowledge is distributed throughout the cerebral cortex, localized to cortical regions involved in their initial processing, and functionally interconnected through synchronized associative processes that are mediated through "convergence zones". The primary goal of the present paper is to point out that Carl Wernicke proposed a theory of how concepts are acquired and represented in cortex which is strikingly similar to contemporary views. Wernicke sketched his ideas on this topic in his earliest writings on aphasia. But his theory is developed most fully in the Grundriss der Psychiatrie (Outlines of Psychiatry), published in 1900 and never translated into English. We describe Wernicke's views on the distributed nature of conceptual knowledge in the brain using select quotes from his early work, and by providing a translation of relevant sections of the Grundriss der Psychiatrie.

Key words: conceptual representation, human information storage, neuroanatomy, neurology, learning and memory, cerebral cortex, neural mechanisms

Introduction

A contemporary view of how conceptual knowledge for concrete entities is represented in the brain includes four central ideas: i) the neural representation of conceptual knowledge is *widely distributed* throughout the cerebral cortex; ii) the representations involve the *same* sensory, motor, and supramodal cortical systems originally invoked in processing that information; iii) dynamic transmodal associations underlying the functional interconnectivity or *binding* of distributed representations are mediated by gateways or "convergence zones" in multimodal cortex; iv) integrative binding of the distributed information is likely achieved through *synchronization* of firing patterns of neural ensembles (Damasio, 1989; Damasio and Damasio, 1994; Mesulam, 1998; Singer, 1995; Squire, 1986). The primary goal of this paper is to point out that Carl Wernicke (1848-1905) outlined a model of conceptual representation in cortex that shares these contemporary assumptions. In what follows, we will briefly elaborate on current hypotheses concerning conceptual representation in the brain, and then show that Wernicke's early writings on aphasia foreshadowed many of these ideas. We then present Wernicke's development of his views regarding the cortical substrates of conceptual knowledge as described in a previously untranslated[1] work, the Grundriss der Psychiatrie (Outlines of Psychiatry), published in 1900.

[1] Excerpts of the Grundriss der Psychiatrie were translated in Eggert, 1977.

A Current View of the Cortical Organization for Conceptual Knowledge

Hypotheses concerning how conceptual knowledge is represented in the brain have been put forward by several researchers working in a variety of domains, including the cortical substrates of conceptual knowledge, the neural mechanisms of learning, and the neural correlates of consciousness. For example, working within a framework for developing a model of conceptual representation, Damasio and colleagues have elaborated a position which holds that concepts for concrete entities comprise a set of widely distributed neural ensembles, the components of which can nonetheless be localized to sensory and motor cortices (Damasio and Damasio, 1994). According to this view, these sensory and motor networks are the same as those involved in sensory perception (or in movement planning/execution) of the object (or action) which gives rise to the concept (Damasio, 1989).

How are these highly distributed traces associated or bound together to form unitary concepts? A common set of assumptions is that such transmodal associations i) are established during learning as a result of coincidences (e.g., in the temporal domain) in neural firing produced by an event in the various modalities, ii) that synchronization of neural activity is the mechanism for binding, and iii) that this synchronization is mediated by associative networks – "convergence zones" in Damasio's terminology – in multimodal cortex. Mesulam (1998) expresses a similar view, referring to 'transmodal areas' for the binding of modality-specific information that serve as gateways for accessing distributed conceptual information.

Empirical work by Singer and colleagues has provided support for the hypothesized role of synchronization in binding (for a review, see Engel et al., 1999). Using single- and multi-unit recording in cats, these researchers have reported spike activity in neurons that was distributed across cortical and subcortical fields and that correlated as a function of the coherence in a sensory stimulus. Observations such as these support the hypothesis that "…synchronization of neuronal discharges can serve for the integration of distributed neurons into cell assemblies and that this process may underlie the selection of perceptually and behaviorally relevant information" (Engel et al., 1999, p 128).

The view that conceptual representation is made up of widely distributed elements throughout cortex feels particularly modern, perhaps because it makes contact with developments in computational modeling of information storage, as in contemporary distributed representation architectures. For example, Hinton et al. (1986) proposed a computational correlate of the functional cell assemblies underlying neural representation of conceptual knowledge, describing these representations as patterns of activity distributed over many elements throughout cortex.

Our goal in the following sections is twofold. First we would like to show that many of the contemporary views of conceptual representation in the cerebral cortex are not new, but rather can be found in nearly identical form in Carl Wernicke's 19th century writings. Our second goal is to point out that Wernicke made contributions to cognitive neuroscience that extend beyond his well-known works on language.

Wernicke's Theory of Conceptual Representation in the Brain: Introduction and Early Work

Wernicke's theory describing a cortical processing architecture underlying the formation and retrieval of conceptual knowledge is strikingly similar to current views. Wernicke held that: i) concepts are widely distributed throughout the cerebral cortex in the form of memory images or traces; ii) individual memory traces are localized to the cortical sensory and motor fields involved in their initial processing; iii) transcortical fiber pathways provide the anatomical bases for the linking or binding of distributed cortical representations supporting conceptual knowledge; iv) synchronization of distributed activation in cell assemblies is key to the associative processes which underlie learning and concept formation.

Wernicke's views on the neural basis of conceptual knowledge are evident in his first published work, "*The Aphasia Symptom Complex: A Psychological Study on an Anatomic Basis*" (Wernicke, 1874/1977). In this monograph, Wernicke laid out his (often misunderstood[2]) model of the functional neuroanatomy of language and described several cases of aphasia, which he put forth as support for his model. Although this work is famous for its contribution to the neurology of language (which remains relevant today), Wernicke devoted a fair amount of space in this monograph describing his views on the nature of conceptual representation in the cortex:

The concept of the word "bell", for example, is formed by the associated memory images of visual, tactual and auditory perceptions. These memory images represent the essential characteristic features of the object, bell (Wernicke, 1874/1977, p. 117).

Part of the motivation for dealing with conceptual representation in a volume on the aphasia symptom complex was, presumably, Wernicke's view that the neural representations of speech processes are distinct from those supporting thought (i.e., concepts) – a view that necessitated a brief discussion on the nature of conceptual representation:

Thought and speech are two independent processes (p. 115) … The spoken or written name of an object does not impart new qualities to the object. Therefore it must be clearly differentiated from the unique sensory memory images of the object. The concept is fashioned only of the latter (Wernicke, 1874/1977, p. 117).

In a later work on aphasia, Wernicke (1885-1886/1977) elaborates his views on conceptual representation. In this work, he makes explicit his view that the different elements that unite to form a concept – such as 'bell' in his example – are both widely distributed throughout sensory and motor cortices and are localized to those processing sites where their memory traces were first established:

…we had probably found the scheme of cortical function as a whole, that memory images were the psychic elements populating the cortex in a mosaic-like arrangement as a functional development, which may very well be localized according to the regions of the nerve endings[3]*…* (Wernicke, 1885-1886/1977, p. 177).

Wernicke continues:

… the memory images of a bell … are deposited in the cortex and located according to the sensory organs. These would then include the

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[2] See de Bleser et al. (1993) for a discussion of some common misunderstandings, particularly in relation to conduction aphasia. See also Hickok (2000) for a recent description of Wernicke's model.

[3] "Regions of the nerve endings" refers to the cortical fields where peripheral sensory or motor pathways terminate: in contemporary terms, primary sensory and motor cortices.

acoustic imagery aroused by the sound of the bell, visual imagery established by means of form and color, tactile imagery acquired by cutaneous sensation, and finally, motor imagery gained by exploratory movements of the fingers and eyes (Wernicke, 1885-1886/1977, p. 179).

We have pointed out in the introduction that Wernicke's ideas concerning conceptual representation are remarkably similar to those promoted in the contemporary literature, and this should be clear in the quotes above. This point can be reinforced by comparing the quote above with one from the modern literature which appeared almost exactly 100 years later, and which highlights the current view that these ideas are relatively new:

The view of memory that has emerged recently, although it still must be regarded as hypothesis, is that information storage is tied to the specific processing areas that are engaged during learning (Squire, 1986, p. 1612).

Another important development in Wernicke's 1885 work, is that he further outlines a theory of the development and functional properties of the associative networks of memory traces underlying conceptual representation. The claim was that associative networks were established as a result of experience, and that once established, partial activation of the network could trigger activation of the entire functional unit corresponding to a given concept:

Close association between these various memory images has been established by repeated experience of the essential features of bells. As a final result, arousal of each individual image is adequate for awakening the concept as a whole. In this way a functional unit is achieved. Such units form the concept of the object, in this case a bell (Wernicke, 1885-1886/1977, p. 179).

Thus, in his early writings on aphasia, Wernicke presented a view in which memory traces underlying conceptual knowledge are both distributed and localized in cortex, with the localization corresponding to the original sensory-motor processing sites, and are linked through experience to form functional units. While Wernicke's early writings clearly outlined a theory of the neural representation of conceptual knowledge, it is in a later work that his theory describing a cortical architecture underlying concept formation and retrieval was fully developed. This work, *Grundriss der Psychiatrie* (*Outlines of Psychiatry*), was published in 1900 and has never been translated into English. In what follows, we provide a translation of relevant sections of the *Grundriss der Psychiatrie* in order to present Carl Wernicke's ideas regarding the development and retrieval of conceptual information in the cerebral cortex.

Grundriss der Psychiatrie

Wernicke's first published work, the monograph of 1874, remains his best known work and has had a major influence on the study of aphasia and language processing in the brain. However, Wernicke himself considered his writings on psychiatry to be the central focus of his research (Geschwind, 1967). In 1885, Wernicke returned to the University of Breslau, where he had originated his studies of medicine as a young man. It was during this time at Breslau that Wernicke expanded his work in psychiatry. In 1899, Wernicke published a series of case reviews that described his views on the neuroanatomic, pathologic, and neuropsychologic principles of psychic function [Krankenvorstellungen aus der psychiatrischen Klinik in Breslau (Clinical Studies from the Breslau Psychiatric Clinic), 1899]. This work was organized into three volumes: the first included a description of the psychophysiology of mental processes, the second was devoted to paranoid disorders, and the third focused on cases of acute psychosis. These case reviews formed the basis for the *Grundriss der Psychiatrie* (Outlines of Psychiatry) (1900). Here we focus on the first section of the *Grundriss*, where Wernicke outlines his views on the development of conceptual representation in the cerebral cortex in a series of lectures.

In the opening of his Third Lecture in the *Grundriss der Psychiatrie*, Wernicke begins to elaborate his view of the localization of individual memory traces in sensory cortex, and how they are established there:

As I already mentioned at the beginning of my first lecture, pathology has provided firm evidence for the fact that the central projection fields[4] *are localized to various defined places in the cortex. Furthermore, I mentioned that these places must also be the sites of memory traces, which led us to conclude that memory traces are specifically localized in the brain* (p. 20).

Here Wernicke refers to the opening of his first lecture, where he delineated areas in cortex that formed "end points for projection pathways" (p. 1) from peripheral sensory and motor areas and described these cortical areas as 'projection fields'. Wernicke then indicates that these projection fields are localized in cortex: "the occipital lobe for the optic pathway, the temporal lobe for the auditory pathway, the central gyrus for the primary motor and sensory pathways of the leg, arm, and face, and Broca's gyrus for the motor pathway of speech." (p. 1). These localized projection fields were, according to Wernicke, the site of the

[4] "Projection fields" are defined in the first lecture as the endpoints of peripheral sensory or motor pathways in the cortex. In current usage, these are primary sensory and motor cortices.

distributed memory traces. Thus while Wernicke held that concepts were not localized into a cortical conceptual center, he strongly believed that the individual memory traces that combined to form a concept were, themselves, localized in sensory and motor centers.

Wernicke next turns to the question of how memory traces are established in cortex:

The process of recognition … *requires that we already possess a set of memory traces. This leads to the question: how does such a set of memories come about? The nervous system seems to possess the unique ability to undergo permanent changes in response to temporary stimuli, a feature we usually call recognition or memory. … In the cortex we can again ascribe this role to certain cells: a transient stimulus can cause lasting modifications in these cells so that some form of residuum of the stimulus remains, which we call a memory trace. … And since the recurrence of the same external stimulus will lead to the same pattern of excitation, these perceptual elements will maintain their mutual association. In conclusion, then, we would have explained a memory trace as an acquired association of perceptual elements in the central projection field* (p. 21-22).

Wernicke's description of a proposed neural substrate for the association of distributed activation has a decided Hebbian ring to it. In fact in his earliest work, the monograph of 1874, Wernicke made explicit his strong view that is was the *coincidence of occurrence* that formed the basis for the ultimate association between activations in cortex. In this, he was clearly influenced by his teacher, Theodor von Meynert (1833-1892). Meynert's views on integrative processing in the brain were described by James Papez (1883-1958), who himself provided a seminal work on the limbic circuit in the brain:

He [Meynert] considered the cerebral cortex as a retentive recording tissue surmounting radial bundles, on which the sensory and other impulses were projected by afferent paths, each registered image being the product of a special group (pattern) of simultaneously perceived sensations. He was the first to show that central integration was dependent on this association process. (Emphasis added) (Haymaker and Schiller, 1970; p. 59-60).

And while Meynert as well as Wernicke had published fairly detailed accounts describing their view of association processes in the brain, these scientists are rarely credited when the historical roots of memory formation and conceptual representation are discussed. For example, in a letter to Jack Orbach regarding the theories of Karl Lashley (1890-1958) and David Hebb (1904-1985), Peter Milner (author of "*The cell assembly*", 1958) wrote:

*The idea that learning consists of wearing in a path goes back to the ancient Greek philosophers' views on habits, and Descartes' theory that the passage of vital spirits enlarges the passage through nerves, so it's about as dated as it can get. Even Alexander Bain (1874) knew better than to talk about the connection between two cells being strengthened by use, (*rather*) it was in consequence of two of them being independently made active at the same moment (which is the fact in acquisition), a strengthened connexion or diminished obstruction would arise between these two, by a change wrought in the intervening cell substance … This shows that Bain recognized that learning was not just doing the same thing more vigorously, but associating one stimulus with a different one by contiguity. Bain anticipated Hebb by 3/4 of a century. Both Hebb and Bain postulate that there need be no connection between the two cells initially. The connection depends upon both being fired at the same time by separate inputs"* (Peter Milner, personal correspondence to Jack Orbach, 1996, in Orbach, 1998).

In point of fact, Meynert and Wernicke – and undoubtedly many other workers of their time – should be included in the list of scientists whose work foreshadowed that of David Hebb.

Wernicke next considers how separate sensory memory traces become associated to give rise to conceptual knowledge. According to Wernicke, during the course of the development of conceptual knowledge, distributed memory traces are associated through their *simultaneous* activation patterns, ultimately becoming a functional unit, which Wernicke describes as the cortical correlate of a concept:

Since these different sensations occur simultaneously, their memory traces remain associated with each other. In this way every tangible object is related to an acquired association of memory traces of different senses, and this association is stronger the more frequently the object is perceived by our senses. We have in this manner arrived at the anatomical substrate for what psychology has long called a "concept" (p. 30).

The contents of our consciousness thus not only contain memory traces but also tangible concepts: specific complexes of memory traces that are strongly linked with each other through associations (p. 31).

This, then, is Wernicke's definition of conceptual representation, describing concepts as units or traces that are associated through experience to form complexes or assemblies that, in turn, represent the neural underpinnings of conceptual knowledge.

Next, Wernicke turned to a discussion of how these associative processes might be instantiated in the brain. Wernicke believed that white matter fiber tracts provided the anatomical basis for associative processes:

The important point is that associative processes can only be explained if we postulate functional interconnections among the anatomical regions to which the memory traces of the individual sensory modalities are localized… The established anatomical basis for this assumption is found in the immense number of fibers present in the cortical white matter tracts and in the cortex itself. The function of these fibers is to connect one cortical region to another (p. 33-34).

Having laid out in broad strokes his theory of conceptual representation in the brain, Wernicke next provides a more detailed treatment of the mechanisms of association. In a very modern sounding quote, Wernicke describes the cortical mechanism for associative learning in terms of a "resonance" of activity that leads to a 'lowered resistance to propagation':

During sensory perception] two regions within a projection field (or two regions of two different projection fields…) become activated simultaneously by the concurrent arrival of external stimuli in the projection fields. Each time this happens, the connection pathway that lies between the two areas begins to resonate, so to speak, with the active regions. The more often this process is repeated, the smaller the resistance to propagation becomes, and the pathway is ground out, or as it is called nowadays, strengthened (p. 34).

Up to this point in the lecture, Wernicke appears to assume that the associations are "mono-synaptic" (our term, Wernicke described 'nerve fibers'[5] connecting cortical regions). But a subsequent statement suggests that Wernicke had the intuition that an intermediary step is likely to exist in the association process. Continuing immediately from the quote above, Wernicke states:

I am not saying that this pathway has to be a continuous one … On the contrary, there is evidence for a layer of cortical cells, the so-called spindle cells, which by their shape and position appear to belong to the association system. Thus, it is likely that these cells are interposed in the association pathways between cortical regions. Since in my view there are no nerve fibers that do not originate from a nerve cell body, the simplest scenario I can propose will be as follows: every spindle (or association) cell has two nerve fibers which it sends out in opposite directions. The terminals of these processes connect to the cells in the projection fields which are to be associated with each other. It is not difficult to imagine that all cells in a given central projection field are interconnected with each other by way of association fibers containing one association cell per cell pair (p. 34).

Wernicke was, therefore, proposing an intermediary system that functioned as a binding mechanism for cells in different cortical fields. This proposal, of course, foreshadows the modern view of intermediary "convergence zones." Wernicke's proposal differed in two important respects from the modern concept. First, Wernicke's "association cells" were located in projection fields, which Wernicke described as sites for unimodal sensory or motor processing. Wernicke had no concept of multimodal cortex and frequently described sensory and motor projection fields as forming the majority of cortex, However, Wernicke did have an intuition that some cortical areas may be sites for associative or binding processing. For example, in his 1874 monograph, Wernicke wrote: "The parietal area, lying between (temporal and occipital lobes) represents a passageway for the transfer of processes which are still unclear" (Wernicke, 1874/1977, p. 92).

Second, according to Wernicke's hypothesis, individual association cells mediated the relation between pairs of cells in different cortical fields, and one association cell was needed for each associated pair of cells. A convergence zone (according to the framework hypothesized by Damasio and Damasio, 1994), on the other hand, contains far fewer units than are present in the cortices which project to these zones, and individual units in a convergence zone participate in multiple associations.

Wernicke did clearly recognize the computational problems associated with postulating one-to-one mappings between pairs of cells. Continuing immediately from the quote above:

The number of cells needed for this can be calculated from the number of perceptional cells and might turn out to be quite large. If we, then, step up from a simple memory trace and consider the more complicated cases of visual conceptions… or associations between visual conceptions and memory traces of another projection field, our attempt to find a structural correlate for this process runs into colossal difficulties (p. 34).

This principle of fully interconnected perceptual elements cannot possibly hold for the connectivity between memory traces. While the number of available connection fibers may be very large, it would still be dwarfed by the seemingly infinite numbers required for this purpose, as computed by a combinatorial calculation. From this we see the absolute necessity to assume additional mechanisms, which would help explain the process of association (p. 34).

[5] The Neuron Doctrine, formulated by Waldeyer and based on the work of Ramon y Cajal and others, was published in 1891. When the *Grundriss der Psychiatrie* was published in 1900, the idea of a "synapse" and mechanisms of cortical cellular connectivity continued to be debated in the scientific community.

Wernicke was not alone in being daunted by the level of complexity in the association systems in the cortex. Karl Lashley (1890-1958) wrote in his "Search for the Engram":

All this is by way of indicating the probable complexity of the memory trace of even the simplest associations. The engram of a new association, far from consisting of a single bond or neuron connexion, is probably a reorganization of a vast system of associations involving the interrelations of hundreds of thousands or millions of neurons (Lashley, 1950, p. 477).

Despite this limitation, Wernicke did manage to convey in this work some very modern views of conceptual representation and memory formation in cortex. In fact, Wernicke's theory of how conceptual knowledge is organized and retrieved in the brain embodies the same core elements of current hypotheses, holding that distributed complexes of memory traces, associated through temporally coincident activity, are functionally interconnected to form the neural substrates of unitary concepts. And this work is far from complete, as evidenced in a recent quotation by Mountcastle:

How the patterns of neural activity involved in a sensory discrimination or categorization, distributed as they are in wide areas of the brain, are unified into perceptual wholes, and how they flow through to conscious experience, remains among the great enigmas in brain science (Mountcastle, 1997, p. 719).

Influences on Carl Wernicke

The idea that separate but simultaneously occurring events may become associated in the brain is a long-standing one that dates back at least to Aristotle (384-322 B.C.). While a general notion of the association between perceptual stimulation and memory traces is an ancient one, the relation of psychological phenomena to neuroanatomy is relatively new. Throughout his career, the focus of Wernicke's work was in mapping out the relationship between behavioral findings and neuroanatomy. While it is beyond the scope of the present paper to discuss the many theoretical influences on Wernicke, it is important to highlight a few scientists who may have been influential in the establishment of Wernicke's theories of conceptual representation in the cortex.

One potential source of influence in linking brain and behavior is provided by an 18th Century associationist, David Hartley (1705-1757), who formulated an important relationship between the laws of association and contemporary knowledge of physiology. Hartley combined Newtonian mechanical (vibration) theory with Locke's associationism and formulated a theory regarding a physiological mechanism for linking perceptual sensations with their memory traces. In *Observations on Man* (1749), Hartley describes the role of separate (i.e., visual, auditory) sensations in the acquisition and retrieval of associated conceptual representations and makes clear his view that the distributed memory traces associated with conceptual representations retain their modality-specific sensory qualities (Proposition 10, p. 65-66). According to Hartley, the mechanism for encoding associated perceptions was provided by tiny particles that vibrated through the nerves and the brain (Proposition 4, p. 12). Thus, in *Observations of Man*, Hartley related psychological ideas of association to potential physiological mechanisms for their encoding, ideas that – while not correct – were truly ahead of his their time and may well have had an influence on Wernicke. While it is not known if Wernicke was directly influenced by the writings of Hartley, a German translation of Hartley's *Observations of Man* was written by Rev. Herman Andrew Pistorius, Rector of Poseritz in the Island of Rugen, and published in 1772. Therefore the possibility exists that Wernicke was familiar with Hartley's writings.

Perhaps the most famous associationist of the British Empiricist era was Alexander Bain (1818-1903). In his book *Mind and Body*, published in 1873, Bain systematically related physiology and psychology in his descriptions of cognition which, though based in large part on introspection, nevertheless paved the way for workers to follow (both David Ferrier and John Hughlings Jackson were influenced by Bain). It is unclear whether Wernicke knew of Bain's work, however Alexander Bain was a contemporary of Carl Wernicke: Bain's *Mind and Body* was published just one year before Wernicke's influential "*The Aphasia Symptom Complex*" monograph (1874), thus it is likely that Wernicke knew of Bain's work.

The greatest single influence on Wernicke was the work of the comparative neuroanatomist Theodor von Meynert. In 1870, at the age of 22, Carl Wernicke spent 6 months in Vienna working with Meynert. This brief time spent with Meynert had an enduring impact on Wernicke's approach to the study of neuroanatomy and behavior. Meynert's work was focused around two central themes: i) the study of connectivity patterns in cortical and subcortical sites through the investigation of fiber projection systems and ii) the study of specialized cortical sites for sensory and motor processing. While Meynert is perhaps best known for his work in comparative neuroanatomy, a central theme of his work was to relate his anatomical findings to the study of human cognition. It was Meynert's strong conviction that anatomy was key in the investigation into human psychology (see Meynert, 1866, in Whitaker and Etlinger, 1993). Meynert's work in mapping out sensory and motor processing centers in the cerebral cortex combined with his study of cortical fiber projection systems provided the anatomical basis for Wernicke's theoretical models. Although Meynert has never received the acclaim of his famous student, Wernicke gave him full credit in a strongly worded reference in the opening paragraphs of the 1874 monograph:

But at any event, whatever merit may be found in this work ultimately reverts to Meynert, for the conclusions here submitted issue naturally from a review of his writings and pathological studies (1874/1977, p. 92).

Wernicke was also influenced by the work of Wilhelm Griesinger (1817-1868), a German psychiatrist and neurologist, and author of the influential medical textbook, *Pathologie und Therapie der psychischen Krankheiten (Pathology and Therapy of the Psychological Diseases)*, first published in 1845. It is probable that Wernicke met Griesinger when Wernicke was serving as first assistant for Karl Westphal (1833-1890) at the Berlin Charite Hospital from 1876 until 1878. Westphal and Griesinger were lifelong friends and, along with Wilhelm Roser, co-founders of the journal "*Archiv für Psychiatrie und Nervenkrankheiten*" (Archives of Psychiatry and Nervous Diseases). In particular, in his monograph of 1874, Wernicke makes reference to an essay by Griesinger, "*Ueber psychische Reflexactionen*" (A Consideration of Psychic Reflex Action) (1843), in which Griesinger extended theories of reflex action from peripheral and spinal cord areas to the brain. Building on Griesinger's description of proposed cortical processing sites for reflexive as well as voluntary movements, Wernicke (1874/1977) proposed a language development schema that incorporated stages of acquisition from early reflex vocalization in newborns, to voluntary mimicry in infants, and to volitional speech in children and adults.

Finally, many of Wernicke's contemporaries undoubtedly had an impact on the development of Wernicke's theories regarding the functional organization of conceptual knowledge in the cortex. For example, Wernicke was close friends with Eduard Hitzig (1838-1907) who, along with Gustav Fritsch (1838-1927), performed groundbreaking work characterizing motor cortex (Fritsch and Hitzig, 1870/1960). And, in *The Grundriss*, Wernicke acknowledges the influence of several contemporary workers in the field of neuroanatomy, notably the work of Goldscheider, Sachs, Ziehen, and von Meynert. A brief list of references that provide an account of Wernicke's research life and colleagues can be found in the Appendix.

Carl Wernicke's Influence on 20th Century Neuroscience

A central aim of this work is to point out that Carl Wernicke made important contributions to the investigation of conceptual representation that have been largely unknown to the scientific community. Why is this the case? Several factors have played a role in the virtual disappearance of Wernicke's *Grundriss*. First, however, it is important to note that Wernicke's earlier works describing his language model suffered a similar fate – in spite of the fact that his model was extremely influential to the field beginning almost immediately following the publication of his first monograph, "*The Aphasia Symptom Complex: A Psychological Study on an Anatomic Basis*" (1874). Next, we turn to the factors contributing to the loss of the Grundriss to contemporary workers investigating conceptual representation in the brain.

Wernicke's language model, outlined in his 1874 monograph and expanded upon in subsequent works (Wernicke, 1885-1886/1977), proposed a schema for language processing in the brain that was well received by his contemporaries. There were some important exceptions to this favorable reception, however, and these exceptions had a role in the lack of support for – and ultimate complete dismissal of – Wernicke's model in the field during the first half of the 20th Century.

During the mid to late 19th Century, there were heated debates between two schools of thought regarding the organization of higher neural function: localizationalists, who supported the view of localized centers for neural processing in the brain, and holists, who supported a more equipotential view of cortical organization. Strong and influential attacks on the localizationalist view were led by Pierre Marie (1853-1940) of France, Constantin von Monakow (1853-1930) of Switzerland, and Kurt Goldstein (1878-1965) of Germany. Goldstein was a former assistant of Wernicke's but was nevertheless quite vocal in his critiques of the localizationalist view (for a detailed account, see Geschwind, 1964).

Another vocal critic of Wernicke's model was Sigmund Freud (1886-1939). In his work *On Aphasia: A critical study*, published in 1891 and translated in 1953 by E. Stengel, Freud took aim at the localizationist views that had been presented by the likes of Hitzig and Ferrier, Broca and Wernicke. In this work, Freud detailed a systematic and critical analysis of the localization theory of cortical organization. While *On Aphasia* had poor sales – only 142 copies sold in the first year and a mere 115 copies were sold in the next 9 years (Stengel, 1953) – nevertheless Freud's criticism of the localizationist view in general – and Wernicke's model of aphasia specifically – would prove to be damning. Of the aphasia workers of the late 19th Century, only Hughlings Jackson was spared criticism by Freud.

One aspect of Wernicke's model that was particularly criticized by Freud was the idea of a concept center.

Ironically, Wernicke never held the view that concepts – or ideas – were localized to a center in the cortex: he was explicit in his writings that while he proposed centers for the sensory and motor processing for speech, his strong view was that conceptual knowledge in the brain was not localizable to a center but was widely distributed throughout cortex. The mistaken view that Wernicke proposed a "Concept Center" in his language model remains to this day.

Another aspect of Wernicke's model for language processing has been misrepresented almost since its inception. Wernicke's language model – described in his 1874 monograph and expounded upon in his later works on aphasia (1885-1886) – has been incorrectly interpreted to represent a serial model for language processing. This, however, was not the case. Specifically, Wernicke described two association pathways during the activation and subsequent production of a word concept. One path led from the region component he termed "conceptualization" ("*B*", which was the distributed conceptual representation for the concept) to the "motor speech center" ("*b*", Broca's area in present day terminology). A second, more complex pathway led from the conceptualization region component ("*B*") and made contact first with the "acoustic speech center" ("*a*", Wernicke's Area), and then on to the "motor speech center" ("*b*"). During the production of a word concept, this second pathway "*B-a-b*" provided contact with the acoustic speech center, thus providing a sound-based constraint for the production of the word. This is an important element of Wernicke's model – one which is well supported by both his pathological data at the time as well as present day research findings in aphasia – that has been misunderstood and misinterpreted from the time of his writing to the present day. It is important to note that Lichtheim (1845-1928), who provided elaborations of Wernicke's model (Lichtheim, 1885), did not agree with this aspect of Wernicke's model and did not include it in his versions of the 'house' model. Wernicke was well aware that Lichtheim had a differing viewpoint on this aspect of the model:

On this basis, I hypothesize that centrifugal innervation of the word-concept from the area (of sensory perception) of the concrete object follows a double path, namely the simple path B-b and the more complicated route B-a-b. … In this matter I differ with Lichtheim who explains these facts another way (Wernicke, 1885-1886/1977, p. 181).

This difference of opinion coupled with the similarity between the early Wernicke model and later versions of the Wernicke-Lichtheim 'house' model may have played a role in the subsequent misinterpretation. In any event, most present day psychology textbooks include a figure of the 'house' model that fails to include the bi-directional arrows between the acoustic speech center ("*a*") and the conceptualization region ("*B*") that Wernicke included in his original writings (1874/1977; 1885-1886/1977) and that was key to understanding his schema for language processing.

In addition to the criticism by Freud, Marie, Goldstein, and von Monakow, as well as the general misinterpretations of key aspects of Wernicke's language model, a third, and perhaps the most deadly, factor for the discrediting of Wernicke's early work came from Sir Henry Head (1861-1940). In his 1926 review *Aphasia and Kindred Disorders of Speech*, Head, a holist, was scathing in his criticism of Wernicke. Head referred to Wernicke and other modelers of his time with scorn as "map-makers", given to carving up the cerebral cortex into more and more circumscribed regions of functional specialization resembling mosaic like patterns (Head, 1926). Head's review of aphasia and his anti- localizationist views had a huge effect on discrediting the Wernicke model. Head's work stood alone as the key review of aphasia work at this time and his expertise was largely undisputed. However, Head's criticism of Wernicke includes many inaccuracies in Head's interpretation of Wernicke's work (Eggert, 1977). The inaccuracies present in Head's review are surprising in that Head was fluent not only in his native language of English but also in French and German. Therefore, Head most certainly had access to the primary sources of Wernicke's writings in the native German.

Nevertheless, the damage caused by Head's review was near fatal and Wernicke's model for language processing would not re-emerge until the 1960's. This re-emergence was due in large part to the efforts of Norman Geschwind (1926-1984) and his detailed descriptions of Wernicke's contribution to aphasia research and his model for language processing (Geschwind, 1963, 1967).

How do we explain the loss of *The Grundriss* to the neuroscience community? The obscurity of *The Grundriss* was, no doubt, affected by the misunderstandings and criticisms of Wernicke's earlier works, detailed above. And while Wernicke was well respected in his time, his academic career was unspectacular and his influence diminished at the time of the writing of *The Grundriss* (Eggert, 1977; Geschwind, 1963, 1967). These factors, coupled with his untimely death in 1905 in a bicycle accident at the age of 57, may have contributed to the relative obscurity of *The Grundriss*. However, perhaps the major factor contributing to the obscurity of Wernicke's early works on aphasia as well as *The Grundriss* has to do with global politics at the beginning of the 20^{th} Century. Germany was undergoing unification at this time and, as we now know, was arming for warfare which would ultimately lead to World War I. Following World War I, the seat of neuroscience moved from Europe to the United States and English became the primary language of neuroscience. Wernicke's early writings on aphasia would not be translated into English until the 1960's (Geschwind, 1963, 1967) and a complete translation was not available until 1977 (Eggert, 1977), thus key primary sources were not available at this time to the largely English speaking neuroscience community. And, *The Grundriss* was not translated into English at all, until the present effort.

While Wernicke's direct influence on science at the start of the 20th Century was clearly minimal, many of his students went on to become highly influential leaders of their fields. Otfrid Foerster (1873-1941) became the leading neurosurgeon in Germany of his day. Another of Wernicke's assistants, Karl Bonhoeffer (1868-1948), was the prominent academic psychiatrist of his time and went on to write the seminal description of alcoholic delirium and other psychoses in Korsakoff's syndrome (Geschwind, 1963). Other students of Wernicke's went on to have prestigious academic and scientific careers, among them Liepmann, Goldstein, Dejerine, and Lissauer. While Liepmann is best known for his work on apraxia (Liepmann, 1900, 1905), his research efforts included a broader based investigation of brain-behavioral relationships than is generally known (for a recent historical review, see Goldenberg, 2003). Lissauer provided the seminal work on apperceptive and associative agnosia (Lissauer, 1890) that continues to influence workers in the field today (e.g., Carlesimo et al., 1999; Warrington and McCarthy, 1987).

Wernicke's model for language processing – still in wide use today – and the contributions of his many students have formed the large part of Wernicke's legacy to modern science. In the present work, we hope to add Wernicke's views on conceptual representation to that legacy.

Conclusions

As we suggested above, Wernicke does not often surface as a theorist whose ideas foreshadowed modern concepts of associative learning and distributed representational systems. Rather, Hebb is often cited as the major source of influence on modern theorists working within the framework of distributed representations:

We already have noted Hebb's contribution of the Hebb rule of synaptic modification; he also introduced the concept of cell assemblies – a concrete example of a limited form of distributed processing – and discussed the idea of reverberation of activation within neural network. (McClelland et al., 1986, p. 41).

But in fact, these views were promoted by Wernicke decades prior to Hebb, as we've shown above. Furthermore, even when modern researchers consider the 19th century precursors to Hebbian approaches, Wernicke's name fails to surface, and instead is typically lumped into a category of neurologists with simplistic, non-dynamical views of brain function.

Some of the earliest roots of the PDP approach can be found in the work of the unique neurologists, Jackson (1869/1958) and Luria (1966). Jackson was a forceful and persuasive critic of the simplistic localizationist doctrines of late nineteenth century neurology, and he argued convincingly for distributed, multilevel conceptions of processing systems (McClelland et al., 1986, p. 41).

It is a mistake to consider Carl Wernicke's views of cortical function as simplistic and localizationist. This should be clear from the above discussion. True, he did hypothesize (probably correctly, it turns out) that "components" of a neural circuit can be localized to specific cortical fields, but these localized representations interacted with other localized components of the network forming dynamic, multi-level, widely distributed processing systems. Even his model of language organization in the brain had dynamical properties, including parallel and bi-directional processing (Hickok, 2000). It is our view, then, that Wernicke should be considered alongside of Hebb and Jackson as one of the theorists who foreshadowed modern concepts of distributed dynamical representations in learning and memory.

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References

Bain A. *Mind and Body: The Theories of their Relation*. New York: D. Appleton and Company, 1873.

Carlesimo GA, Casadio P, Sabbadini M and Caltagirone C. Associative visual agnosia resulting from a disconnection between intact visual memory and semantic systems. *Cortex, 34:* 563-576, 1998.

Damasio A. The brain binds entities and events by multiregional activation from convergence zones. *Neural Computation, 1:* 123-132, 1989.

Damasio AR and Damasio H. Cortical systems for retrieval of concrete knowledge: The convergence zone framework. In C Koch and JL Davis (Eds), *Large-scale Neuronal Theories of the Brain*. Cambridge, MA: The MIT Press, 1994, p. 61-74.

de Bleser R, Cubelli R and Luzzatti C. Conduction aphasia, misrepresentations, and word representations. *Brain and Language, 45:* 475-494, 1993.

Eggert GH. *Wernicke's Works on Aphasia: A Sourcebook and Review*. The Hague: Mouton, 1977.

Engel AK, Fries P, Konig P, Brecht M and Singer W. Temporal binding, binocular rivalry, and consciousness. *Consciousness and Cognition, 8:* 128-151, 1999.

Freud S. On aphasia: A critical study. In Stengel E (Ed), *Freud on Aphasia*. New York: International Universities Press, 1891/1953.

Fritsch G and Hitzig E. Ueber die elektrische Erregbarkeit des Grosshirns (On the electrical excitability of the cerebrum), *Arch. f. Anat., Physiol. und wissenschaftl. Mediz.*, Leipzig, 37: 300-332, 1870. In von Bonin G (Ed), *Some Papers on the Cerebral Cortex,* 73-96 (Thomas, Springfield, 1960).

Geschwind N. Carl Wernicke, the Breslau School and the History of Aphasia. In Carterette EC (Ed), *Brain Function, Volume III: Speech, Language, and Communication.* University of California Press: Berkeley, 1963.

Geschwind N. The paradoxical position of Kurt Goldstein in the history of aphasia. *Cortex, 1:* 214-224, 1964.

Geschwind N. Wernicke's contribution to the study of aphasia. *Cortex, 3:* 449-463, 1967.

Goldenberg G. Apraxia and beyond: Life and work of Hugo Liepmann. *Cortex, 39:* 509-524, 2003.

Hartley D. *Observations on Man: his Frame, his Duty, and his Expectations. In two Parts*. London: Richardson S, 1749.

Haymaker W and Schiller F. *The Founders of Neurology* (2nd Ed). Springfield: Charles C. Thomas, 1970.

Head H. *Aphasia and Kindred Disorders of Speech* (in 2 volumes). London: Cambridge University Press, 1926.

Hickok G. Speech perception, conduction aphasia, and the functional neuroanatomy of language. In Grodzinsky Y, Shapiro L and Swinney D (Eds), *Language and the Brain*. San Diego: Academic Press, 2000, pp. 87-104.

Hinton GE, McClelland JL and Rumelhart DE. Distributed representations. In DE Rumelhart and JL McClelland (Eds), *Parallel Distributed Processing: Explorations in the Microstructure of Cognition, Volume 1: Foundations*. Cambridge, MA: MIT Press, 1986, pp. 77-109.

Lashley K. In search of the engram. *Symposia of the Society for Experimental Biology, 4:* 454-482, 1950.

Lichtheim L. Ueber aphasie. *Deutsches Archiv fur Klinische Medicin, 36:* 204-268, 1885.

Liepmann H. Das Krankheitsbild der Apraxie (motorische Asymbolie) auf Grund eines Falles von einseitiger Apraxie. *Monatschrift fur Psychiatrie und Neurologie, 8:* 15-44; 102-132; 182-197; 1900.

Liepmann H. Der weitere Krankheitsverlauf bei dem einseitig Apraktischen und der Gehirnbefund auf Grund von Serienschnitten. *Monatschrift fur Psychiatrie und Neurologie, 17:* 289-311, *19:* 217-243, 1905.

Lissauer E. Ein Fall von Seelenblindheit nebst einem Beitrage zur Theorie derselban. *Archiv fur Psychiatrie und Nervenkrankheit, 21:* 220-270, 1890.

McClelland JL, Rumelhart DE and Hinton GE. The appeal of parallel distributed processing. In Rumelhart DE and McClelland JL (Eds), *Parallel Distributed Processing: Explorations in the microstructure of cognition, Volume 1: Foundations*. Cambridge, MA: MIT Press, 1986, pp. 4-44.

Mesulam M-M. From sensation to cognition. *Brain, 121:* 1013-1052, 1998.

Mountcastle VB. The columnar organization of the neocortex. *Brain, 120:* 701-722, 1997.

Orbach J. *The neuropsychological theories of Lashley and Hebb*. Lanham: University Press of America, 1998.

Singer W. Development and plasticity of cortical processing architectures. *Science, 270:* 758-764, 1995.

Squire LR. Mechanisms of memory. *Science, 232:* 1612-1619, 1986.

Warrington EK and McCarthy RA. Categories of knowledge: Further fractionation and an attempted integration. *Brain, 110:* 1273-1296, 1987.

Wernicke C. Der aphasische Symptomenkomplex: Eine psychologische Studie auf anatomischer Basis. In Eggert GH (Ed), *Wernicke's works on aphasia: A sourcebook and review*. The Hague: Mouton, 1874/1977.

Wernicke C. Einige neuere Arbeiten ueber Aphasie. In Eggert GH (Ed), *Wernicke's works on aphasia: A sourcebook and review*. The Hague: Mouton, 1885-1886/1977.

Wernicke C. *Grundriss der Psychiatrie*. Leipzig: Verlag von Georg Thieme, 1900.

Whitaker H and Etlinger S. Theodor Meynert's contribution to classical 19th century aphasia studies. *Brain and Language, 45:* 560-571, 1993.

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