Neural basis of neuropsychological rehabilitation

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Summary

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Neuropsychological rehabilitation is often guided by pragmatic approaches. There is, however, a strong belief that models of recovery derived from cognitive and basic neurosciences may yield more efficient strategies. This paper summarises evidence from neuropsychological, activation and anatomical studies, which supports a model of parallel distributed processing of human cognitive functions. Parallel distributed processing models can account for recovery after brain damage and may prove useful for designing new rehabilitation strategies in future.

Keywords: neuropsychology, neurorehabilitation, plasticity, cerebral cortex, cognitive functions, visual, auditory, connectivity, Talairach coordinates, human, adult

Introduction

Since Broca's seminal paper [1], much of neuropsychological research has been devoted to clarify the anatomical substrates of deficits observed after cerebral lesions (e.g. [2, 3]). This review paper addresses a complementary question, namely that of anatomical substrate underlying cognitive recovery following acute lesions. In particular, it highlights those organisational principles of the human brain which may play an important role in recovery and which should thus guide rehabilitation strategies.

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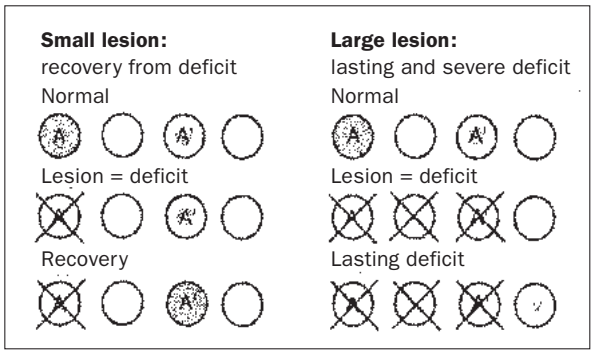
Models of recovery from brain damage are certainly not a new venture. Based on his clinical observations, Kurt Goldstein (for historical review see [4]) introduced the distinction between restitutive and compensatory therapy. The former tries to restore the patient's earlier capacities, while the latter concentrates on the development of substitutive strategies for lost or impaired functions. Goldstein did not believe in assigning individual functions to strictly delimited areas of the brain, but he assumed a co-operation between different brain structures for a given function. If only part of this structure was damaged, restitutive therapy would be successful, but if all parts were damaged, compensatory therapy should be used. During Goldstein's active period, relatively little was known about the functional organisation of structures underlying cognitive functions. The cerebral cortex, e.g., was subdivided into primary areas and association cortex; although the latter was believed to contain different hierarchical levels of association, precise data and models were sparse (for review see e.g. [5]).

Current neuropsychological rehabilitation is often guided by pragmatic approaches. At the same time, there is a strong belief that efficient rehabilitation should be based on understanding the basic mechanisms of recovery; much hope is given today to cognitive models (see e.g. [6]) and to the combination of cognitive models and basic neuroscience [7].

Parallel distributed processing

A simple model of what may happen during recovery is represented in figure 1. Following a small lesion, recovery is accompanied by functional reorganisation. A given function, represented by *A* in figure 1, is then supported by a different cerebral region than in normal subjects. Such a reorganisation was demonstrated in cases of recovery from hand paralysis and from aphasia; recovered functions activated foci which were not or only partially activated in normal subjects [8, 9].

Figure 1



Recovery after small (on the left) or large lesions (on the right). A function, represented here by A, activates in the normal subject a distinct region, represented by the shaded circle, and marginally also A'. A lesion restricted to circle A is first accompanied with the corresponding deficit. Later function A recovers, activating a region, or a set of regions, normally only marginally (here A') or not at all activated in this function. A much larger lesion is not accompanied with such a recovery.

Several questions remain open in relation to the functional reorganisation underlying recovery. First, the nature of functional units is very poorly understood. Although language is known to depend critically on specific regions within the left hemisphere, the precise organisation of these areas is still unknown. Evidence summarised below indicates that speech areas are likely to consist of several specialised subareas. If so, new rehabilitation strategies could be designed for cases with specific lesions. Second, the flow of information between functional units is almost entirely unknown. Work on non-human primates showed repeatedly that parallel processing occurs at different levels of analysis. The same principle seems to apply to man and existence of parallel pathways was confirmed by human tracing studies (see below). Third, the degree of functional plasticity within the adult central nervous system is not determined. Recent evidence shows that a lesion limited to a specialised region is not accompanied with a lasting and severe deficit in the corresponding function; the latter occurs only in case of much larger lesions (see example of colour vision below).

Multiple visual areas in non-human primates

The last three decades of neurophysiological and neuroanatomical studies transformed what was previously believed to be a rather homogenous association cortex into a wealth of functionally and anatomically different cortical areas. The visually-related cortex of macaque monkeys was shown to consist of over 30 functionally defined visual areas. Some of these areas contain a high proportion of functionally selective neurons, such as the colour specific neurons in V4 and the motion specific neurons in V5 (for review see [10]). Other, less precisely defined areas have been described more rostrally in the parietal and temporal cortices (for review see [11]). E.g., neurons selectively responsive for faces have been found in the inferotemporal cortex and the superior temporal sulcus.

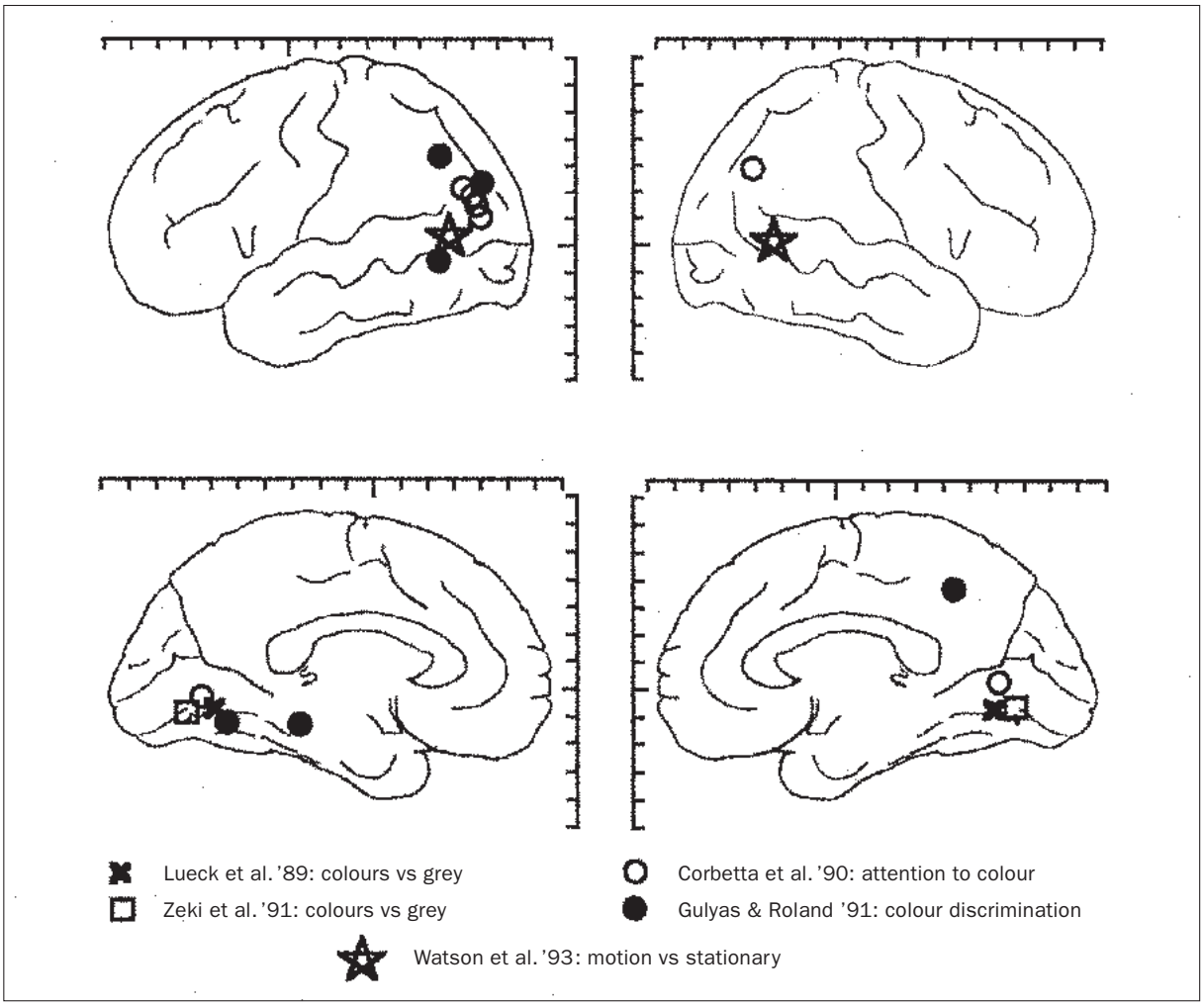
Specialised visual areas in man

Case reports of selective loss following focal brain damage, and activation studies with positron emission tomography, have suggested the existence of extrastriate regions specialised in motion perception, colour vision or face recognition in man (for review see [10]). It has been proposed that these deficits result from lesions of human equivalents of V5, V4 or inferotemporal cortex [12, 13]. Anatomical studies in man identified several extrastriate areas [14–16] and strengthened thus evidence from neuropsychological and activation studies.

The relationship between specialised areas as observed in the normal human extrastriate cortex and the corresponding deficits observed after lesions is far from clear. One of the best understood examples is colour vision. A series of activation studies showed that colour tasks activate selectively specific regions (fig. 2; [17–20]). The most heavily activated region was at the inferior occipitotemporal junction, corresponding to putative human area V4, and additional foci were on the parieto-occipital convexity, predominantly on the left side. The foci activated by colour tasks were anatomically distinct from a region at the posterior part of the superior temporal sulcus that was shown to be selectively activated by visual motion stimuli [21]. Evidence from clinical reports predicted a separation of colour and motion processing: lasting achromatopsia was most often reported in association with relatively large inferior occipitotemporal lesions [12], whereas akinetopsia was reported in association with lesions of the occipital convexity [22].

We have investigated the role of the human extrastriate cortex in colour perception by testing a series of patients with circumscribed posterior lesions. In most cases reported in the literature, achromatopsia was associated with prosopagnosia following large occipitotemporal lesions. We examined two patients with severe and lasting prosopagnosia of whom one was achromatopsic and the other not [23]. Both patients had bilateral, almost symmetrical lesions within the posteroinfe-

Figure 2



Centres of foci selectively activated by colour or motion tasks, represented on the lateral and medial views of the hemispheres. Bars indicate Talairach and Tournoux [39] coordinates.

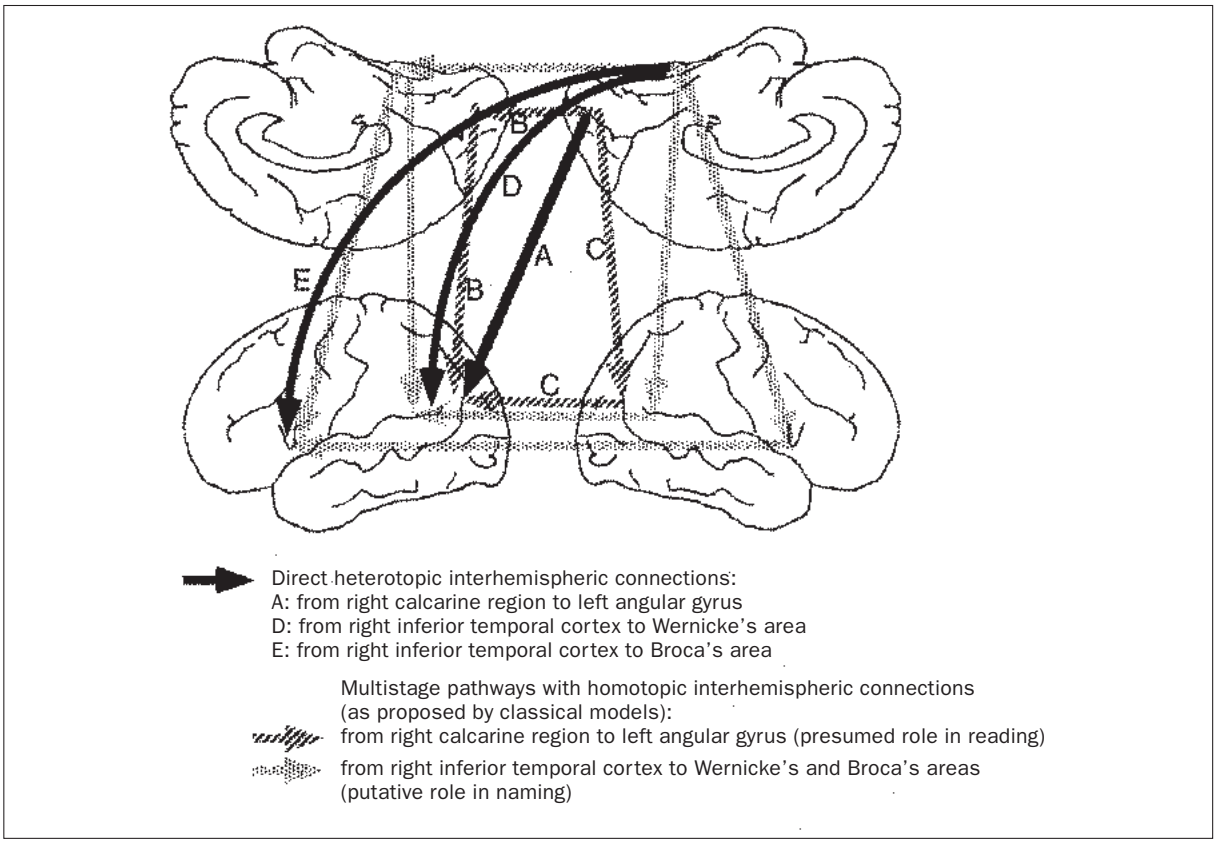
rior parts of the hemispheres. Comparison of the lesions by means of the Talairach and Tournoux coordinate system showed that the lesion associated with achromatopsia included the inferior occipitotemporal junction (site of putative V4), whereas the other one did not. This finding suggests that V4 lesion is necessary for achromatopsia to occur. In another series of experiments, we tested patients with relatively small circumscribed lesions of which some were limited to V4. In the chronic stage, patients with bilateral lesions limited to V4 were not at all or only very little impaired in colour discrimination and colour short-term memory tasks [24]. This finding shows that V4 lesion is not sufficient for lasting and severe achromatopsia to occur.

Heterotopic interhemispheric connections

Many influential models of human cognitive functions have presumed that human interhemispheric connections link predominantly symmetrical parts of cortex (e.g. [25, 26]). Our recent work shows that, in addition to homotopic connections, there is a wide array of heterotopic connections, some of which may be specific to man. In many instances, the heterotopic connections may represent alternative pathways and thus substrate for compensatory strategies developed following brain damage.

In a recent study, we traced interhemispheric connections originating in the medial part of the right occipital lobe using the Nauta method for anterogradely degenerating axons [27]. Serial coronal sections from the posterior third of the hemisphere contralateral to the lesion were stained and analysed for anterogradely degenerating axons, i.e., interhemispheric afferents from the damaged site. Callosal afferents were found within early stage visual areas, and also in the posterior parietal and temporal cortices. The latter regions received medium to high density of callosal afferents originating in the contralateral medio-occipital cortex. Among the callosal-recipient regions was the (left) angular gyrus.

Figure 3

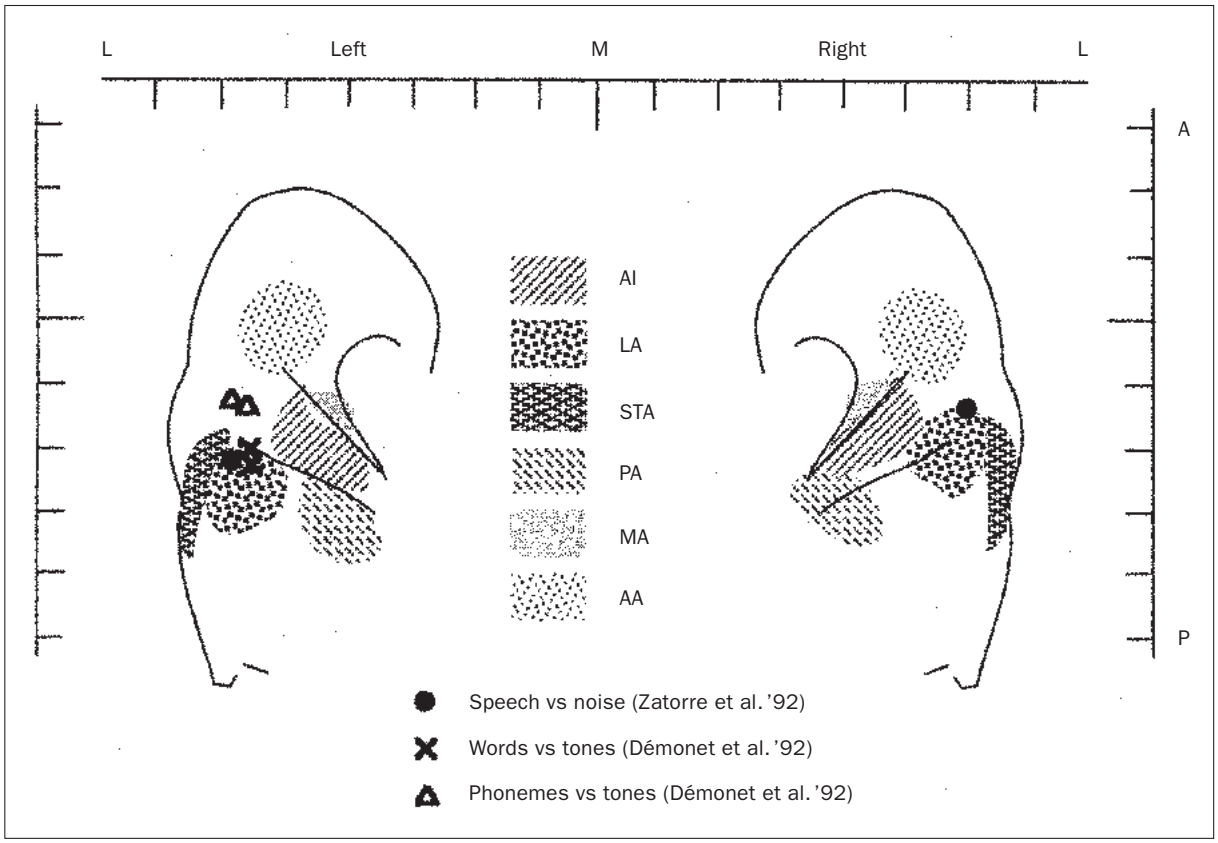


Heterotopic interhemispheric connections demonstrated in man (black arrows) and the alternative pathways that were proposed in classical models (shaded arrows). A: direct, monosynaptic connections were found to link the right calcarine region to the left angular gyrus [27]; it may be one of several pathways (B, C) involved in reading (see text). D, E: direct, monosynaptic connections were demonstrated from the inferior temporal cortex to Wernicke's and Broca's areas [30]; it is part of a most likely large network linking higher order visual and speech areas and sustaining visuo-verbal functions.

In cases of left calcarine and splenial lesions, pure alexia was attributed to disconnection of the right, non-injured calcarine region from the left angular gyrus, which was proposed to be involved in reading [28]. At least three routes link right calcarine region to left angular gyrus (fig. 3): (A) heterotopic callosal connection from right calcarine region directly to left angular gyrus; (B) combination of homotopic callosal connections from right calcarine region to the left one and then association connections from left calcarine region to left angular gyrus; (C) combination of association connections from right calcarine region to right angular gyrus and then a homotopic callosal connection from right angular gyrus to its homologue on the left side. Neuropsychological evidence showed that the ability to read does not rely critically on route B [29]. Route A, i.e. a monosynaptic pathway from right calcarine region to left angular gyrus was demonstrated in man [27], but its role in reading is presently unknown. Our current hypothesis is that it may underlie spared reading capacities that are present in some alexic patients.

The second example of heterotopic connections is that of monosynaptic interhemispheric input from right inferior temporal cortex to Wernicke's and Broca's areas [30]. The connections were traced in a brain with a right inferior temporal infarction by means of the Nauta method. The lesion from which the interhemispheric connections were traced was within a region known to be activated selectively in tasks of recognition of known faces (comparison of lesion site with activation foci reported by others [31]). Afferents were found both in Broca's and Wernicke's areas, with a higher density in the latter. These interhemispheric pathways are part of what is most likely a large network linking higher order visual and speech areas. When parts of this network are damaged, processing within the remaining parts determines spared capacities. It is conceivable that connections from right inferior temporal cortex to the speech areas may account, e.g., for successful phonemic cueing in otherwise anomic patients (see e.g. [32]): simultaneous activation of auditory and visual inputs in both Wernicke's and Broca's areas may be strong enough to initiate correct naming.

Figure 4



Human auditory areas and putative specialisation for speech processing. Anatomical studies [33] identified five distinct areas on the supratemporal plane outside the primary auditory cortex (AI) and two on the insula (not shown here). These areas may be involved in specific aspects of auditory processing, similarly to the functional specialisation of some extrastriate visual areas. Here we compare the sites of anatomically identified auditory areas (hatched; from Rivier and Clarke [33]) and activation foci to speech-related auditory tasks [34,35]. Areas lateral to AI, but not those anterior, medial and posterior to it, show specialisation for speech processing. Bars indicate Talairach and Tournoux [39] coordinates.

Multiple auditory areas in man

The human auditory cortex is the entry to the most powerful communication system and yet relatively little is known about its functional organisation. Most current beliefs are derived from work on non-human primates or extrapolated from work on the human visual cortex. It is often assumed that the auditory cortex outside the primary auditory cortex contains several, perhaps functionally specialised areas. Such a view is supported by recent anatomical and functional studies (fig. 4). We have studied the functional subdivision of the human supratemporal plane and insula using stains for cytochrome oxidase and acetylcholinesterase activity [33]. Seven distinct areas outside the primary auditory area were identified (for their relative positions see figure 4). Comparison with activation and electrophysiological studies (by others) showed that all these areas respond to auditory stimuli. Some of these areas may belong to specialised processing streams, such as area LA (lateral to the primary auditory area) shown to be selectively activated by speech-related sounds [34, 35], or anterior insula, by auditory motion [36]. Neuropsychological studies confirm further a putative functional specialisation, since different aspects of e.g. non-verbal auditory recognition can be disrupted independently [37].

Human primary auditory area contains anatomically distinct compartments that may be involved in processing of specific functions. The cytochrome oxidase staining revealed in the supragranular layers a pattern of dark and light stripes [38]. Comparison with tonotopic maps of human primary auditory area obtained by activation studies suggests that these cytochrome oxidase stripes are perpendicular to isofrequency lines. They may be related to particular binaural or ampliotopic domains, whose presence is suggested by evidence from animal experiments and from magnetoencephalographic studies in man, or else to specifically human functions, such as speech.

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