Overview

After injury the brain is capable of a large degree of self-repair. The mechanisms underlying this, so-called, spontaneous recovery are not completely understood. The only well-established idea is that these mechanisms are based on brain plasticity, the brain’s ability to change its structure and function as a result of autonomous recovery processes. In addition, plasticity is fostered by learning and environmental stimulation.

Three main plasticity mechanisms are important in spontaneous recovery: the resolution of diachisis, functional network recovery and more behaviourally oriented compensatory readjustments after brain damage. The concept of ‘diaschisis’, coined in 1914 by von Monakow (1914) to explain the loss of excitability occurring distant from a focal brain region, has experienced mixed fortunes. However, the recent development of new methods to investigate brain function has revitalised the concept. Functional network recovery has been intensively studied in patients with motor deficits and aphasia, whereas behavioural compensatory mechanisms have been found in several domains after acquired brain injury (Lee et al., 2015; Meinzer et al., 2011; Nudo, 2013; Robertson and Murre, 1999).

As mentioned, brain plasticity also underlies recovery processes based on experience and learning, commonly referred to as ‘experience-dependent’ recovery. These changes in cerebral organisation are most evident in sensory impaired persons (e.g. congenitally deaf or blind) in the, so-called, cross-modal plasticity phenomenon (Frasnelli et al., 2011), but rehabilitation-induced plastic remapping of lesioned brain areas should also be present in people with acquired brain injury. In this chapter we describe a few rare studies that have investigated adaptive cerebral reorganisation after cognitive training. The most frequently used method to foster recovery after brain damage is the teaching of compensatory strategies. In this case, recovery is not pursued by restoring a lost function, but by offering patients with acquired brain injury strategies to compensate for their impairments. These strategies can be broadly subdivided into external and internal strategies. External strategies are material aids that help patients in overcoming cognitive deficits in everyday life. Internal strategies are verbal and non-verbal methods for improving the processing and retention of information, problem-solving and self-regulation (e.g. mnemonics and self-instructional training). In the case of compensatory strategy training the mechanisms of recovery are well known at task level, but there are no studies to date that investigate recovery at cerebral level.
Introduction

Acquired brain injury often affects large portions of cortical areas, but may also damage subcortical brain regions, as in stroke or traumatic brain injury (TBI). However, in most individuals, spontaneous recovery almost invariably occurs within a period that may vary from weeks to months after injury. This functional recovery process can be defined as spontaneous when subjects – patients or experimental animals – have not been submitted to formal rehabilitation training procedures and the recovery is experience-independent.

Such a definition of spontaneous recovery, however, raises two problems. As argued by Mogensen (2012) it is difficult to assume that recovery, even in the absence of formal training, is independent of experience. Patients recovering from brain damage, for example, are constantly exposed to the demands of everyday life. Activities such as walking, communicating, feeding, dressing and taking medication are not experience-independent and may be considered as informal types of training. Second, it is often difficult to distinguish true spontaneous recovery processes from recovery due to behavioural compensation (Nudo, 2013). After stroke, for example, pointing movements can be made even by individuals with very severe motor impairment. However, most subjects use the trunk instead of the arm to achieve these movements (Cirstea and Levin, 2000). The use of these compensatory strategies is related to the degree of motor impairment; while severely impaired subjects recruit these strategies to a great extent in an effort to compensate for their motor deficits, mildly impaired subjects tend to employ more conventional arm movement patterns.

Despite these caveats, several older studies, which were conducted when rehabilitation was not as common, point to considerable spontaneous recovery of cognitive processes, mainly during the first six months after brain injury. In a cross-sectional study, Bond (1976) found that, even without rehabilitation interventions, the IQ of TBI patients with a post-traumatic amnesia (PTA) of less than 11 weeks recovered substantially within the first six months post onset and stabilised to within one standard deviation of the mean. After this period a slower rate of recovery was observed that reached a maximum after 24 months. In another study of that epoch (Bond and Brooks, 1976), performed longitudinally with a subset of the patients of the Bond (1976) study, it was also found that most of the improvement in IQ scores occurred during the first six months, with only a slight change from six months to two years after injury. Although both studies can be criticised for several reasons, amongst others for the absence of a control group, the learning effects due to the repeated use of the same IQ test, the absence of premorbid IQ scores and other confounding factors, they support the idea that the brain is capable of a large degree of self-repair. Another clear example of spontaneous recovery is the study of reaction times. Van Zomeren and Deelman (1978) charted the recovery curves of reaction times in untreated patients with closed head injury of varying degrees of severity. In this case, the reaction times of all the severity groups improved swiftly during the first six to eight months, while progress slowed during the subsequent 18 months.

Research indicates that it is not only patients with TBI who improve spontaneously during the initial stages of their illness; spontaneous recovery has also been consistently reported in stroke patients. The natural course of aphasia, for example, has been frequently mapped. Lendrem and Lincoln (1985), for instance, followed the spontaneous recovery of language abilities in 65 stroke patients randomly allocated to the no-treatment group of a study designed to evaluate speech therapy, and assessed at six-weekly intervals. Thirteen other patients identified as having aphasia on admission had already recovered so well after four weeks that they were excluded from further participation. The language abilities of the remaining 52 patients improved the most between 4 and 10 weeks after stroke, with little change thereafter. More recently, Farnè et al. (2004) followed the natural course of recovery of visuospatial neglect in a group of 23 stroke patients, using several tests for personal and extrapersonal neglect. The results show that during the acute stage (1–6 weeks after onset and 1 and 2 weeks later) both types of neglect recover significantly in a majority of patients. A subset of eight
patients showed even greater improvement in the chronic stage (> three months after stroke). In a more recent neglect study, Nijboer et al. (2013) followed the course of recovery of visuospatial neglect in a sample of 51 patients who received no specific neglect training. The results showed that the most significant recovery takes place during the first 12–14 weeks. After this period the recovery curves, as measured in line bisection and letter cancellation tests, grow flat and recovery from neglect is negligible.

To sum up, there is enough evidence to assert that substantial spontaneous recovery occurs in the weeks and months following the sudden onset of a brain injury. However, the exact mechanisms underlying these self-repair capacities of the brain are still poorly understood. Understanding these mechanisms would allow for the planning of treatments that further stimulate and reinforce spontaneous recovery. Such therapies might have a cumulative effect and improve recovery and long-term outcomes. Three of these mechanisms have been extensively studied: resolution of diaschisis, functional network recovery and the already mentioned behavioural adaptation mechanisms.

**Diaschisis**

The concept of diaschisis was introduced by von Monakow in 1914 to indicate the temporary loss of excitability or the functional standstill of neurons in regions distant from a lesion. This process was described as dynamic and was supposed to resolve over time. At the time of introduction, the experimental methods were not advanced enough to verify this process and therefore it disappeared in neuroscience research. Not until the 1950s did Kempinski (1958) show that unilateral cortical ablation engendered depressed electrical activity in homotopic points of the contralesional hemisphere. Some years later Høedt-Rasmussen and Skinhoj (1964) noticed a significantly low blood flow in a clinically and angiographically normal cerebral hemisphere of a patient whose contralateral middle cerebral artery was occluded. Despite this paucity of evidence, diaschisis was used for many years to interpret clinical symptoms that could not be directly related to a brain lesion, in the absence of a better explanation.

However, the development of new imaging techniques, especially those measuring metabolic changes in brain tissue, has led to a revival of the concept of diaschisis. When defined as any remote alteration in brain functioning directly caused by a lesion inducing abnormal behaviour and resolving over time, diaschisis has been identified in an increasing number of studies. For example, Carrera and Tononi (2014) made a distinction between several types of diaschisis. Focal diaschisis concerns changes in well-defined brain areas at a distance from a focal lesion, whereas connectional diaschisis regards changes in connectivity between the affected area(s) and distant brain regions.

Focal diaschisis has been shown at rest as well as in the case of stimulation. Focal diaschisis at rest was first detected by Kuhl et al. (1980) and by Baron et al. (1984) by means of positron emission tomography (PET). In the Baron et al. study, a significant reduction of metabolism (glucose and oxygen) was found in the contralesional cerebellum of five stroke patients with a unilateral supratentorial infarction. In a subsequent PET study, Baron et al. (1992) discovered that in patients with thalamic lesions, global neuropsychological impairment was significantly correlated with ipsilateral cortical hypometabolism and that subsequent recovery from hypometabolism was accompanied by cognitive improvement in a subgroup of neuropsychologically impaired patients. However, the behavioural consequences of diaschisis are different in cortical and subcortical lesions. Whereas patients with subcortical lesions and cortical diaschisis tend to display clinical deficits similar to those of cortically injured patients, in cortical lesions different patterns of diaschisis have been found, but their relation to behavioural change is less clear. After cortical stroke, for example, hypometabolism in the ipsilateral thalamus and striatum has been frequently found, but with no clear behavioural consequences.
Activation paradigms can also reveal negative distant effects after focal brain damage, in which case it is appropriate to speak about functional diachisis (Carrera and Tononi, 2014). In 1990 Di Piero et al. showed that contralesional cerebellar diachisis was still visible in a patient one month post-stroke during a finger activation task, even though at the same time resting cerebellar blood flow was symmetrical. This study showed that areas of diachisis may still be present in response to stimulation but not at rest. This phenomenon may be due to the absence of input from a damaged area rather than unresponsiveness as such, as demonstrated by Price et al. (2001). These authors administered a reading task to four patients with speech output problems and damage to Broca’s area. This task elicited abnormal activations, not only in the damaged inferior frontal cortex but also in the undamaged inferior posterior temporal cortex. Yet, in one of the patients the latter region could be activated by another task, which provoked widespread temporo-parietal activations. Activation research has also brought to light that increases of activity in brain regions distant from a lesion may be secondary to a loss of inhibition from the lesioned area (e.g. Mohajerani et al., 2011), a form of diachisis not foreseen in von Monakow’s original definition.

Connectional diachisis refers to distant changes in connectivity within and between cerebral hemispheres after focal injuries. These selective changes in coupling occur between the nodes of a defined brain network distant from an injury and entirely resolve after time. He et al. (2007), for example, found disrupted functional connectivity within two separate attention networks, located in dorsal and ventral dorso-parietal areas in 11 stroke patients with visuospatial neglect. Connectivity within the lesioned, predominantly right hemisphere ventral network was disrupted and showed no recovery after time. In the structurally intact bilateral dorsal network, on the contrary, interhemispheric connectivity was only transiently disrupted in the acute stage after stroke but fully recovered after approximately 40 weeks. The behavioural consequences of this interhemispheric functional connectivity interruption, in particular stimulus detection and attentional reorienting in the left visual field, had also recovered completely at the chronic stage. Diaschisis can also be studied in the human connectome, the comprehensive map of all neural connections in the brain. Lesions in the, so-called, brain graphs provide a way of modelling injury to the nervous system, defined as a set of nodes (denoting anatomical regions) and interconnecting edges (denoting connections). The simulation of focal lesions has highlighted the widespread effects that these lesions can have on brain functional connectivity (for a recent review see Fornito et al., 2015). Lesions affecting areas with high topological centrality (with densely connected hub nodes) cause widespread changes of inter-regional functional connectivity characterised by a complex pattern of inter-regional increases and decreases in connectivity, unlike the effects of lesions to less central regions. Whole-brain computational modelling has thus determined that focal lesions can have diffuse effects on inter-regional brain dynamics, based on the connection topology of the injured region (Alstott et al., 2009). Therefore, Carrera and Tononi (2014) have proposed a new subtype of diachisis, namely, ‘connectomal diachisis’ defined as the ‘remote changes in the structural and functional connectome, including disconnections and reorganization of subgraphs’ (p. 2414).

**Functional network recovery**

After brain damage, spontaneous cognitive and behavioural recovery might also be achieved by a reorganisation of intact neural circuits. The first to suggest that such a remodelling of neuronal networks could underlie functional recovery was Luria (1963). More recently, particularly during the last two decades, functional imaging studies have revealed evidence for cerebral reorganisation mechanisms by shifts of activity toward perilesional brain areas and toward homologue areas of the contralesional hemisphere. These reorganisation processes have mainly been investigated in aphasia and deficits in motor function.
Recovery after acquired brain injury

The longitudinal PET study of de Boissezon et al. (2005) illustrates these reorganisation processes after aphasia. The authors scanned seven patients with a subcortical aphasia twice: two months and one year after stroke, both while the patient was at rest and during a word-generation task. Aphasia had considerably improved after one year and the differences in rCBF (regional cerebral blood flow) for the language-rest contrast in session two relative to session one are shown in Figure 3.1.

As shown in Figure 3.1, the recovery of language not only engages language-specific perisylvian areas of the left hemisphere, but also (to a much lesser extent) of the right hemisphere. Both these regions, the dominant hemisphere perilesional regions for language-related tasks and the language homologue areas in the non-dominant hemisphere, are the subject of the two main theories explaining recovery of aphasia (Cappa, 2008; Hamilton et al., 2011).

There is considerable evidence that perilesional areas of the left hemisphere can take over language functions in the weeks and months following a stroke. Saur et al. (2006) used repeated fMRI to study the dynamics of language recovery in 14 patients with aphasia. In the first days after stroke, there was very little activation of left hemisphere perilesional regions and none in the right hemisphere, with varying degrees of language impairment. In the peri-acute stage (about two weeks after stroke), however, a large increase of activation was seen in the language regions of both hemispheres, with peak activation in the right hemisphere Broca-homologue region. These upregulated areas also showed a high correlation with improved language. Finally, in the chronic stage a normalisation of activation with a re-shift of peak activation to left-hemispheric language areas was observed, associated with further language improvement. These neuroplastic changes after aphasia, namely the activation of spared left hemisphere language areas and new left hemisphere areas coupled with activations of homologue right hemisphere areas, is consistent across aphasic patients (Kiran, 2012; Turkeltaub et al., 2011). Although the role of intact perilesional regions in aphasia recovery has been firmly established, the recruitment of contralesional areas in the right hemisphere is more controversial. According to several authors, right hemisphere recruitment may only be partially adaptive (Szafarski et al., 2013; Thiel et al., 2006; Winhuisen et al., 2005) and it has been suggested that activation of the right pars triangularis may even limit the recovery process, especially in the chronic stage (Naeser et al., 2011; Turkeltaub et al., 2012).

Similar results have been found in motor recovery after stroke. After traumatic focal injury or stroke, perilesional areas are responsible for neurological recovery. Follow-up studies over several months with stroke patients with an ischaemic brain infarction have revealed that such a stroke results in a reduced excitability of brain tissue adjacent to the lesion. The regression of this perilesional inhibition, as well as intracortical disinhibition of the motor cortex contralateral to the infarction, were the mechanisms related to recovery (Bütefisch et al., 2006). Studies examining the affected upper limb have described a shift in laterality of activation after stroke such that, early after stroke, brain activation during limb stimulation is mainly ipsilateral in the unaffected hemisphere; later after stroke, activity shifts toward the normal pattern, being contralateral, that is, in the perilesional areas (including secondary somatosensory areas) of the affected sensorimotor cortex (Chen et al., 2014; Feydy et al., 2002; Nhan et al., 2004).

Figure 3.1  rCBF increase for the language-rest contrast between sessions one (two months post-onset) and two (one year after stroke).

Source: de Boissezon et al., 2005.
Altered patterns of neural recruitment have also been found in patients with traumatic brain injury when performing working memory tasks (McAllister et al., 2001; Turner and Levine, 2008). This increased activity is found either in homologous regions of the contralateral prefrontal cortex (PFC) in comparison with healthy subjects or in small areas of the ipsilateral PFC adjacent to those used by healthy controls (Christodoulou et al., 2001). In an fMRI study, Turner, McIntosh and Levine (2011) investigated if these patterns of neural recruitment in working memory tasks are truly compensatory or if they are also present in an undamaged or under-challenged brain. They found that response accuracy at different levels of working memory load was related to the recruitment of several brain regions in patients with TBI and healthy controls. It appeared that ‘compensatory’ right PFC regions were, in fact, recruited in both groups, as working memory task demands increased. However, the levels of working memory load at which these right PFC networks were engaged was clearly lower in TBI patients when compared with healthy controls, consistent with an altered functional engagement hypothesis rather than with neural compensatory activity.

**Behavioural compensation**

Even in the absence of training or rehabilitation, spontaneous behavioural compensation may occur after brain damage. This compensation entails the unintentional use of different neuropsychological systems in the performance of a task, compared with non-brain-damaged controls (Robertson and Murre, 1999). Changes in kinematics due to cognitive problems are a typical example of compensatory mechanisms of this kind. Goodale et al. (1990), for example, studied a group of nine patients with fully recovered visuospatial neglect five months after they had sustained a stroke. These patients were asked to point to targets on a bar and to bisect pairs of targets on the same bar. Although the accuracy of the movements was comparable to healthy controls, a kinematic analysis revealed that the patients started by making a much wider arc than controls. This arc was then corrected ‘in flight’ to reach the final target. Apparently a distortion in a body-referenced spatial system was still present in the patients, but this was spontaneously compensated for by visual feedback during the pointing movements. Another example of behavioural compensation comes from an eminent neuropsychologist (Kolb, 1990) who sustained an occipital stroke with a left upper quadrantanopia as the main symptom. He reported having difficulties in fixating objects directly because he had rapidly learnt to compensate for the foveal loss by shifting fixation point. Overcompensation for the field defect even led to a skiing accident when he bumped into an obstacle in the intact field while trying to avoid another obstacle on the affected side.

Kolk’s theory of preventive adaptation in people with Broca’s aphasia (Kolk, 1995) exemplifies behavioural compensation remarkably well. This author put forward the idea that producing a grammatically correct sentence requires time and that agrammatic sentence production by aphasic patients might be due to a timing problem (Kolk and van Grunsven, 1985; Kolk et al., 1985). According to this idea, the elements needed to build a sentence need time to be activated and this activation is subject to decay over time. Another assumption is that elements in a sentence are interdependent, in other words the activation of one element requires the activation of another element, like the subject of a sentence which has to be active in order to activate the right conjugation of a successive verb. In daily situations this time problem is perceptible in the large differences in type of speech output by people with Broca’s aphasia. In free conversations, for example, aphasic patients tend to produce agrammatic speech; that is, language that lacks much of the required grammatical morphology but contains few erroneously produced morphemes. In elicited conversations, on the contrary, the speech of aphasic patients is more paragrammatic, with a high number of wrongly selected morphemes and relatively few omissions. Kolk and his collaborators (Haarmann and Kolk, 1992; Hofstede and Kolk, 1994; Kolk and Heeschen, 1990) have convincingly shown that elicited speech mainly reflects the just-described timing problem, whereas the agrammatic character of
spontaneous speech is primarily an adaptation to this underlying deficit. In spontaneous speech, aphasic patients have the opportunity to create simpler sentence forms and this message simplification is an adaptive reaction to the capacity overload. In elicited speech and other time pressure situations, preventive adaptation is hardly possible, resulting in more morphological and constructional errors.

**Experience and learning**

Although spontaneous recovery, network recovery and behavioural compensation adaptation processes after brain injury may lead to functional improvements, the most powerful booster of cortical and functional progress is obviously experience-dependent recovery. Cortical and functional changes are most striking in, so-called, cross-modal plasticity, in which the loss of a sensory function due to disease or brain damage strengthens other sensory functions and induces extensive plastic reorganisation of brain areas.

In congenitally blind people, for example, the otherwise idle visual cortex is progressively recruited for a wide range of other sensory and cognitive tasks, like auditory and tactile processing (Pascual-Leone et al., 2005), language processing (Bedny et al., 2011; Röder et al., 2002) or verbal memory (Amedi et al., 2003).

Although the effects of sensorimotor skills training on plasticity processes after brain damage have been extensively investigated (for a review see Nudo, 2013), the impact of cognitive rehabilitation and practice on cerebral reorganisation after brain damage has only received scant attention. Only in the treatment of aphasia with speech and language therapy a substantial number of studies has been undertaken. A PET-investigation by Musso et al. (1999) concluded that a brief, intense language comprehension training administered to four patients with Wernicke’s aphasia resulted in significant improvements in performance. The brain areas that correlated with the training-induced improvement in verbal comprehension were the posterior part of the right superior temporal gyrus and the left precuneus. This study emphasised the role of the right hemisphere in recovery from aphasia.

Subsequent studies (see Abel et al., 2015) found therapy-induced increases as well as decreases in activation, both in the left and in the right hemisphere, with high inter-individual variability of the right hemisphere as a ‘backup’ resource (Cappa, 2000).

In a rare study involving both language and memory, Blasi et al. (2002) have shown that patients with left frontal lesions and partially recovered aphasia can learn a novel word stem completion task that normally requires the damaged left cortex, at a rate comparable to that of healthy controls. This improvement was evident from improved verbal reaction times and a reduction of errors. fMRI data acquisition showed that these patients activate, to an abnormally high degree, homologous regions in the right frontal cortex during word stem completion, especially when the task is novel. This right frontal compensatory activity clearly subsides as performance improves during the learning stage. According to the authors, this decrement in activation resembles the normal modulation induced by word retrieval practice in the left frontal cortex. Frontal compensatory activity in the non-damaged hemisphere has also been demonstrated to be dynamic, or dependent on cognitive load (Voytek et al., 2010). In an EEG experiment these authors manipulated working memory load and attentional load in two separate groups of patients with unilateral frontal damage. The intact prefrontal areas of the non-damaged hemisphere rapidly and flexibly compensated on a trial-by-trial basis for the damaged hemisphere, dependent on the cognitive load. This compensatory activity of the undamaged hemisphere not only increased as demands on the damaged hemisphere increased, but was also related to behavioural accuracy.

Hebbian learning and neural reconnection have been repeatedly proposed as mechanisms that might explain rehabilitation outcomes, by coupling learning on a behavioural level with changes on the physiological level, in particular the increase in synaptic strength between neurons that fire together as a result of learning experiences (Hillis, 2005; Robertson and Murre, 1999). However,
empirical support for this explanation is still lacking, most probably due to the same reasons that
diaschisis has been a lingering concept for many years: the absence of sophisticated imaging methods
that allow verification of the principles of Hebbian learning. Progress in medical imaging, especially
in the fine-grained mapping of brain connectivity patterns, might foster empirical support of this
theory of recovery in the near future.

Finally, recovery from brain damage has been facilitated by teaching patients compensatory
strategies (see, for example, Chapter 15 on memory rehabilitation). In this case, recovery is not
achieved by restoring or substituting impaired neuropsychological functions but by offering patients
strategies to compensate for their impairments at task level. These strategies are aimed at improving
behaviour by replacing ineffective task achievement with a behavioural bypass in order to accomplish
tasks successfully. To this end, both external and internal cognitive strategies can be utilised. External
strategies have been successfully used to improve cognitive problems in domains as diverse as
attention, organisation and planning, calculation, time management, memory retrieval, emotion
regulation and self-awareness (for a review see Gillespie et al., 2012). Studies using internal
compensatory strategies following TBI have recently been described in a series of evaluative reviews
by an international group of researchers and clinicians (INCOG). These reviews cover the domains
of attention and information speed (Ponsford et al., 2014), memory (Velikonja et al., 2014), executive
function and self-awareness (Tate et al., 2014) and cognitive communication (Togher et al., 2014).
Other reviews evaluating the effectiveness of internal strategies after acquired brain injury are those
of Cicerone (Cicerone et al., 2000, 2005; Rohling et al., 2011).

Although in the strategic approach the mechanism of action of both internal and external strategies
is well understood at task level, to this date no studies have investigated how strategies effective at
task level might influence brain organisation and functioning.

Summary and conclusions

The occurrence of spontaneous recovery after brain damage has been well established nowadays,
both from a behavioural and an imaging point-of-view. Processes such as diascisis, functional
network recovery and the presence of behavioural compensation mechanisms have been repeatedly
shown to occur after acquired brain damage. However, their exact time-course and working
mechanisms are still a matter of debate. In the case of functional network recovery, for example,
alternative hypotheses, such as altered functional engagement, have been proposed. Similar to
diaschisis, the development of more sophisticated behavioural and imaging methods may answer
some of these riddles in future research. Further, marked effects of experience-dependent recovery,
including cognitive training, have been repeatedly found at behavioural and task levels. The
explanation of these effects at the level of the brain is still in its infancy, but here also the use of new
imaging and neurophysiological investigation methods may explain how experience-dependent
training influences brain reorganisation in the near future. In turn, these insights might foster better
targeted rehabilitation methods.

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Recovery after acquired brain injury


Luciano Fasotti


Recovery after acquired brain injury


