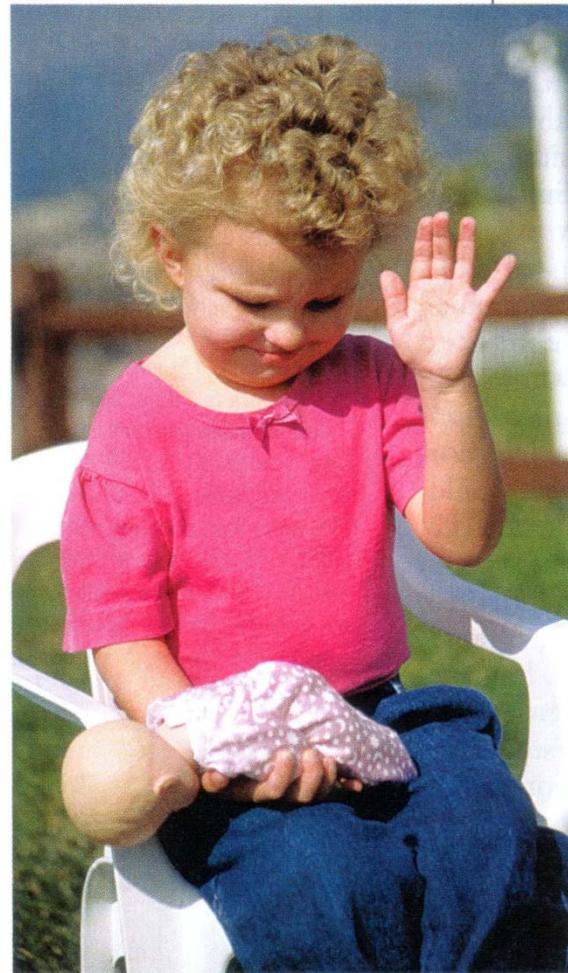


Terminplan KLE 2016

- 07.01.16 Emotionales Lernen und Gedächtnis (AM)
- 14.01.16 Motivation und Lernen (AM)
- 21.01.16  Neuronale Plastizität (AM)
- 28.01.16 Fähigkeiten und Fertigkeiten: Learning by doing (AM) & QUALIS
- 04.02.16 Neurofeedback: Lernen von Hirnkontrolle (AM)
- 11.02.16 Hubert Zimmer: Kognitives Training und dessen neuronale Korrelate

Bestrafung?

- Körperliche Züchtigung von Kindern ist gesetzlich verboten.
- Nutzen von Bestrafung ist umstritten (Bestrafung als Verstärker für ungewolltes Verhalten) .
- Lösungen?
Aufmerksamkeitsentzug
Gewünschtes Verhalten gezielt verstärken.
- Nicht im Widerspruch zu Bobo doll Studien zum Modell-Lernen (Bandura)

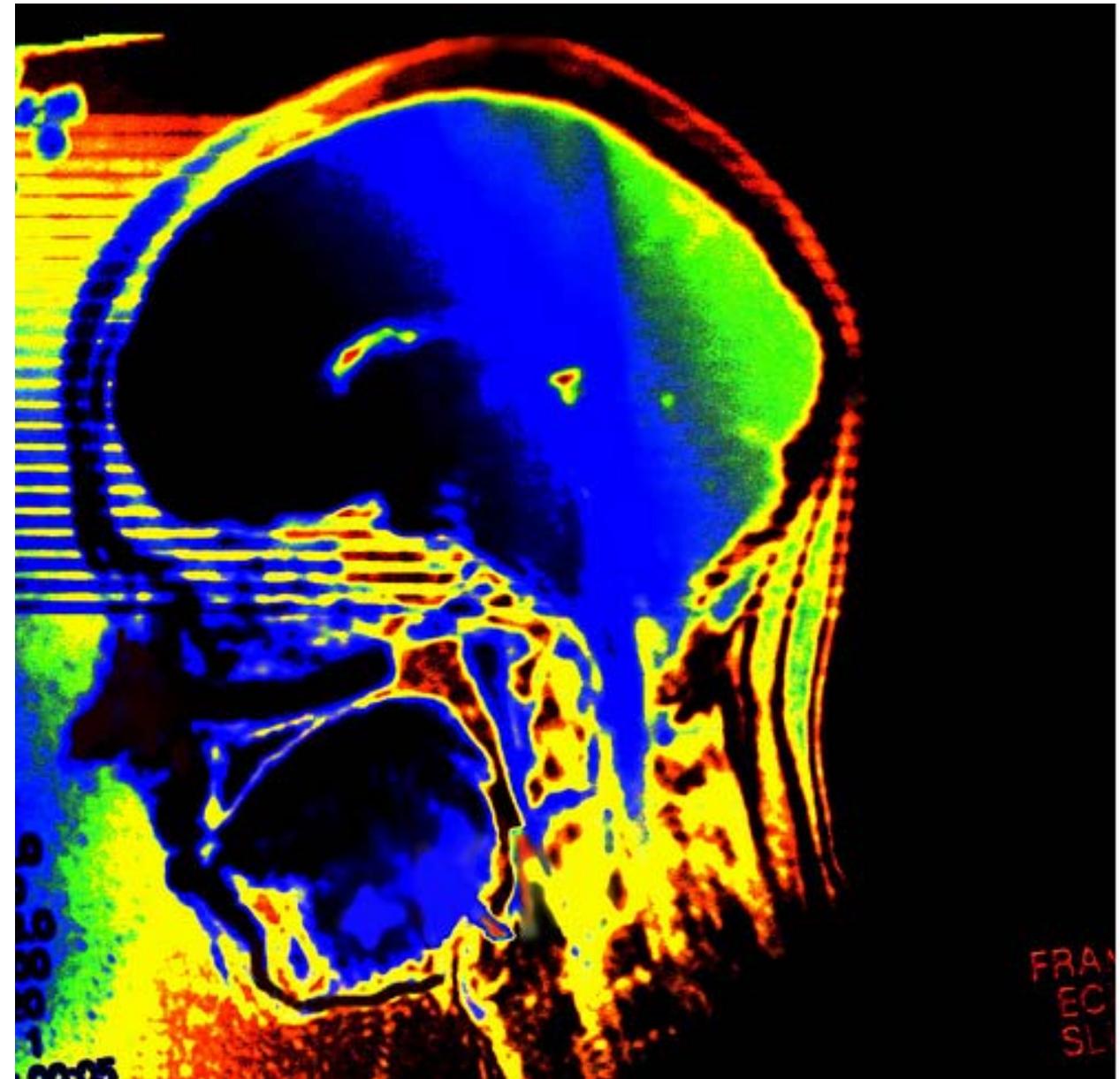


Myrleen Ferguson/Cate/PhotoEdit

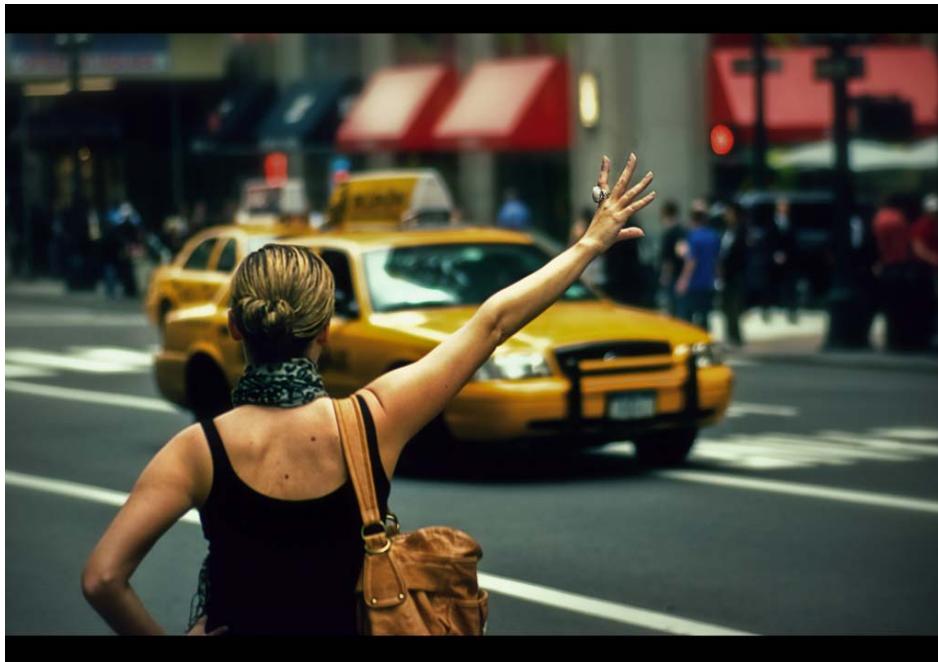
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Neuronale Plastizität



21.01.2016
Axel Mecklinger



Navigation-related structural change in the hippocampi of taxi drivers

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Navigation requires the ability to remember environmental cues and to respond rapidly to unexpected changes in the environment. Navigation is a complex skill that requires the acquisition of large amounts of spatial memory and the development of navigational skills. It seems that there is a capacity for plastic changes in the brain that support such human learning in response to environmental demands.

The hippocampus is involved in facilitating spatial memory and navigation. Previous studies have found that hippocampal volume relative to brain size has been reported in taxi drivers to be larger than in non-taxis drivers (1). Some specific hippocampal regions have been implicated in spatial memory, such as dorsal striatum (2). In some species hippocampal volume is correlated with spatial memory demand for spatial ability is greater (2,3). In humans hippocampal volume is correlated with memory performance (4). In humans, hippocampal volume is correlated with memory performance in tasks such as memory for faces (5), memory for objects (6), memory for locations (7), and functional neuroimaging studies have shown increased hippocampal activity in spatial memory and navigation, thus it is often claimed that hippocampal volume is increased in taxi drivers due to spatial memory and navigation. One prediction was that the hippocampus would be enlarged in taxi drivers compared to non-taxi drivers.

Taxi drivers in London must undergo extensive training. This training is colloquially known as "Swing The Knowledge" and involves memorizing the streets of London. To operate, it is necessary to pass a very stringent set of written examinations. These examinations test the driver's knowledge and with navigation experience were detected anywhere in the body of knowledge. The examination consists of a series of procedures that identifies regional differences in relative gray matter volume between taxi drivers and controls. The point in the brain to be considered in an unbiased way, with no

bias or preconceived notion.

Image Acquisition. Structural MRI scans were obtained with a 1.2 T scanner (Siemens Magnetom Vision, Siemens, Erlangen, Germany) using a standard three-dimensional gradient echo sequence (TR = 2500 ms, TE = 30 ms, flip angle = 9°, field of view = 256 mm, matrix = 256 × 256 mm, slice thickness = 3.5 mm, voxel size = 1 × 1 × 3.5 mm).

Image Processing. Statistical Parametric Mapping (SPM99, Wellcome Trust, London, United Kingdom) was used to analyze the data. This training is colloquially known as "Swing The Knowledge" and involves memorizing the streets of London. To operate, it is necessary to pass a very stringent set of written examinations. These examinations test the driver's knowledge and with navigation experience were detected anywhere in the body of knowledge. The examination consists of a series of procedures that identifies regional differences in relative gray matter volume between taxi drivers and controls. The point in the brain to be considered in an unbiased way, with no

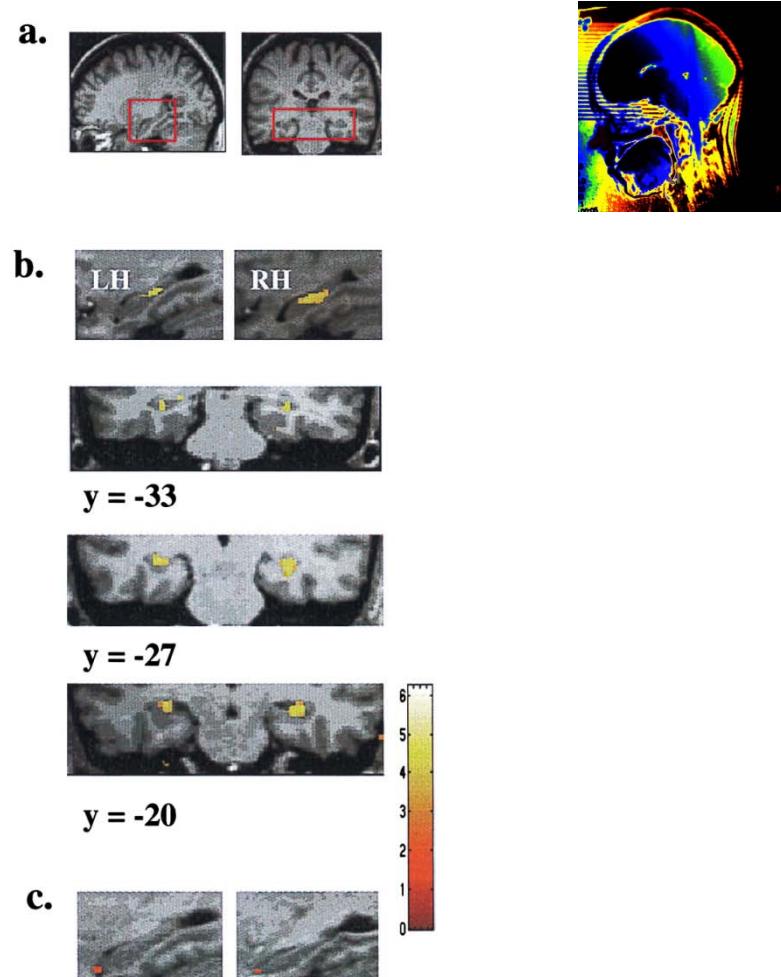


Fig. 1. VBM findings. (a) Left) Sagittal section of an MRI scan with the hippocampus indicated by the red box. (a Right) Coronal section through the MRI scan, again with the hippocampi indicated. (b) The group results are shown superimposed onto the scan of an individual subject selected at random. The bar to the right indicates the Z score level. Increased gray matter volume in the posterior of the left and right hippocampi (LH and RH, respectively) of taxi drivers relative to those of controls, shown in the top of the figure in sagittal section. Underneath, the areas of gray matter difference are shown in coronal sections at three different coordinates in the y axis to illustrate the extent of the difference down the long axis of the hippocampus. (c) Increased gray matter volume in the anterior of the left and right hippocampi of controls relative to those of taxi drivers, shown in sagittal section. Note that, although the Talairach and Tournoux (11) coordinate system was used to describe the locations of VBM differences in stereotactic space, the images were normalized with respect to a template based on a large number of brains scanned in the same scanner used to collect the current data (see Methods). Thus, the coordinates given refer to our brain template and only approximately to the Talairach and Tournoux template.

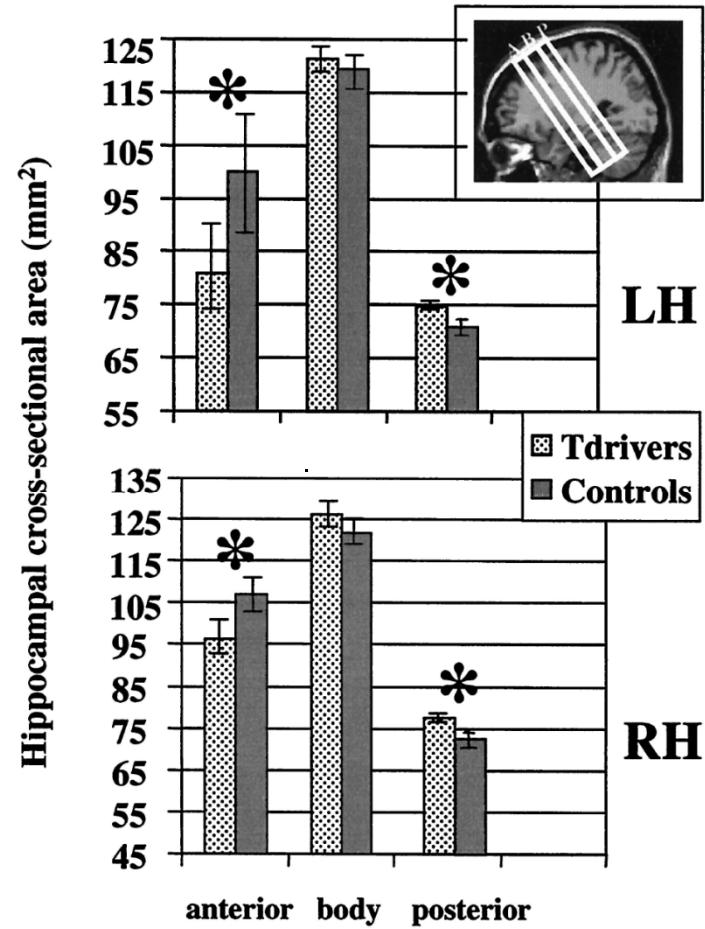
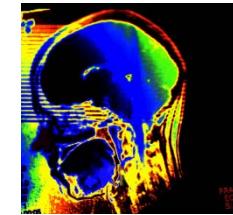


Fig. 2. Volumetric analysis findings. The orientation of the slices measured in the volumetric analysis with respect to the hippocampus is shown (*Top Right Inset*). A, anterior; B, body; P, posterior. (*Upper*) The mean of the cross-sectional area measurements (uncorrected for ICV) for the three regions of the left hippocampus (LH). (*Lower*) The means for the right hippocampus (RH). Taxi drivers had a significantly greater volume relative to controls in the posterior hippocampus, and controls showed greater hippocampal volume in the anterior. There was no difference between the two groups in the hippocampus body. *, $P < 0.05$.



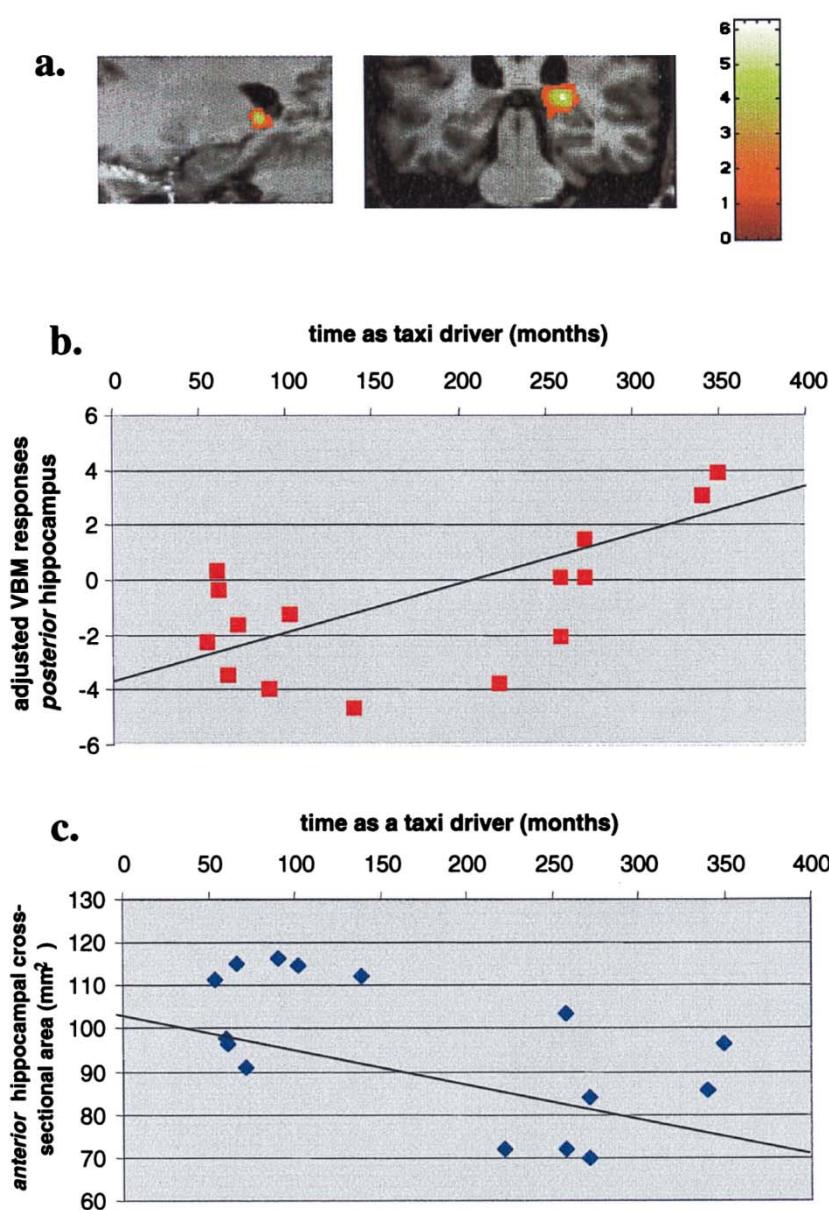
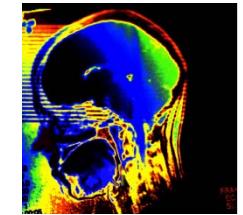


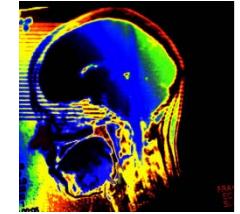
Fig. 3. Correlation of volume change with time as a taxi driver. (a Left) Sagittal section. (a Right) Coronal section. The VBM group results are shown superimposed onto the scan of an individual subject selected at random. The bar to the right indicates the Z score level. The volume of gray matter in the right hippocampus was found to correlate significantly with the amount of time spent learning to be and practicing as a licensed London taxi driver, positively in the right posterior hippocampus (b) and negatively in the anterior hippocampus (c).

Inhalt



- 😊 Neuronale Entwicklung
- 😊 Auswirkung von Erfahrung auf die neuronale Entwicklung
- 😊 Neuroplastische Reaktionen des adulten ZNS
- 😊 Neuroplastizität nach kognitivem Training

Fünf Phasen der neuronalen Entwicklung



- Induktion der Neuralplatte
- Neuronale Proliferation
- Migration und Aggregation
- Axonwachstum und Synapsenbildung
- Neuronentod und Neuanordnung der Synapsen

1) Induktion der Neuralplatte

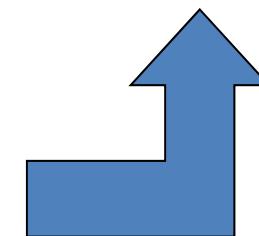
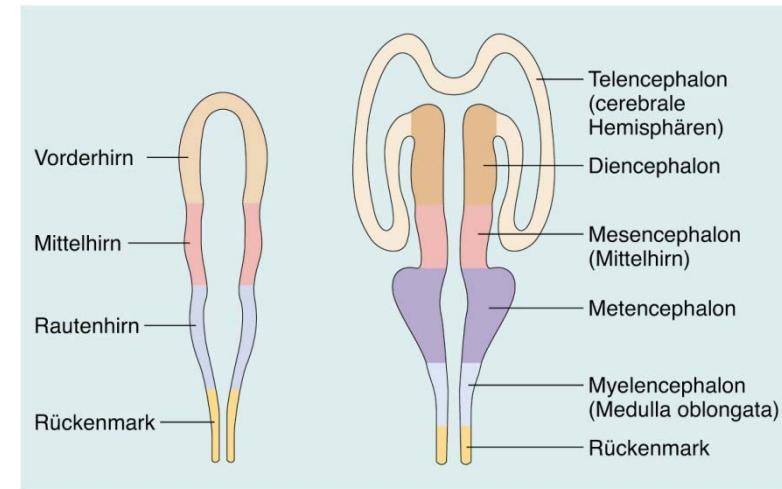
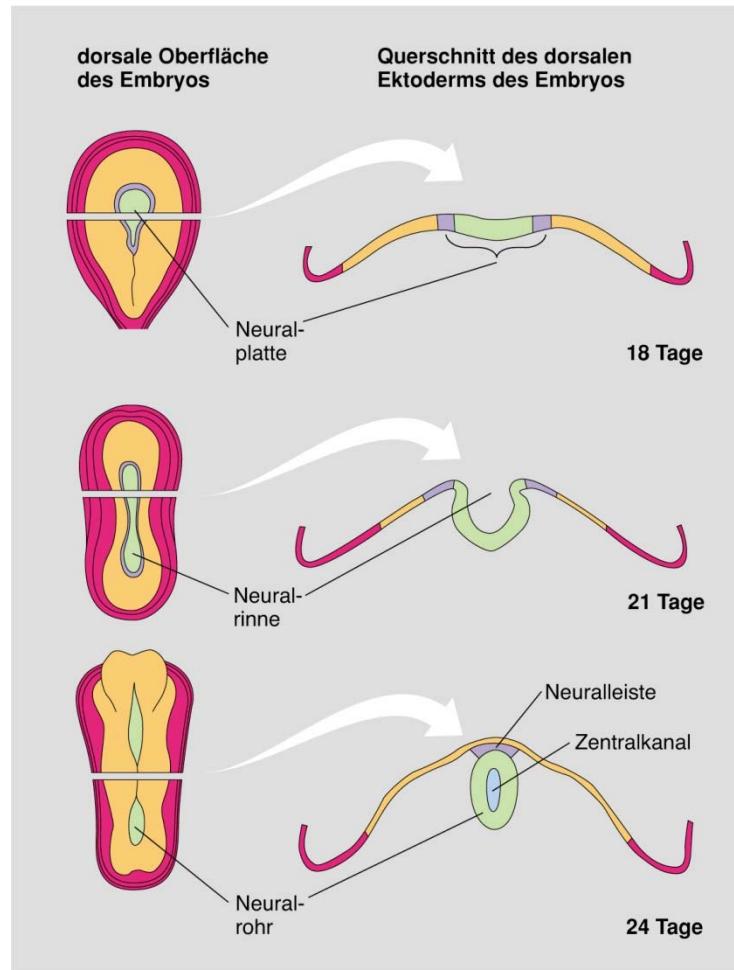
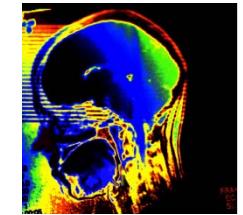


Abbildung 9.1: Hier ist dargestellt, wie sich die Neuralplatte während der dritten und vierten Woche der menschlichen Embryonalentwicklung zum Neuralrohr ausbildet (adaptiert nach Cowan, 1979).

2) Neuronale Proliferation (ab 30 Tage)

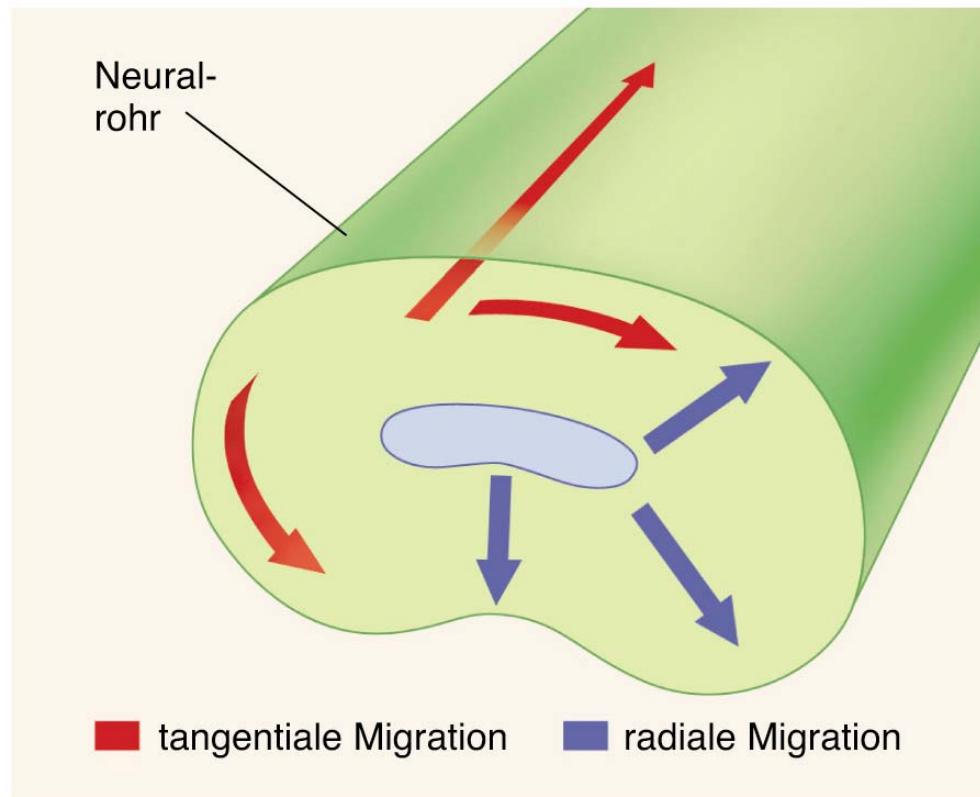
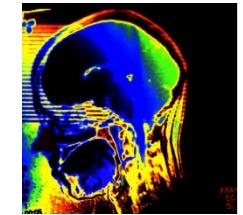
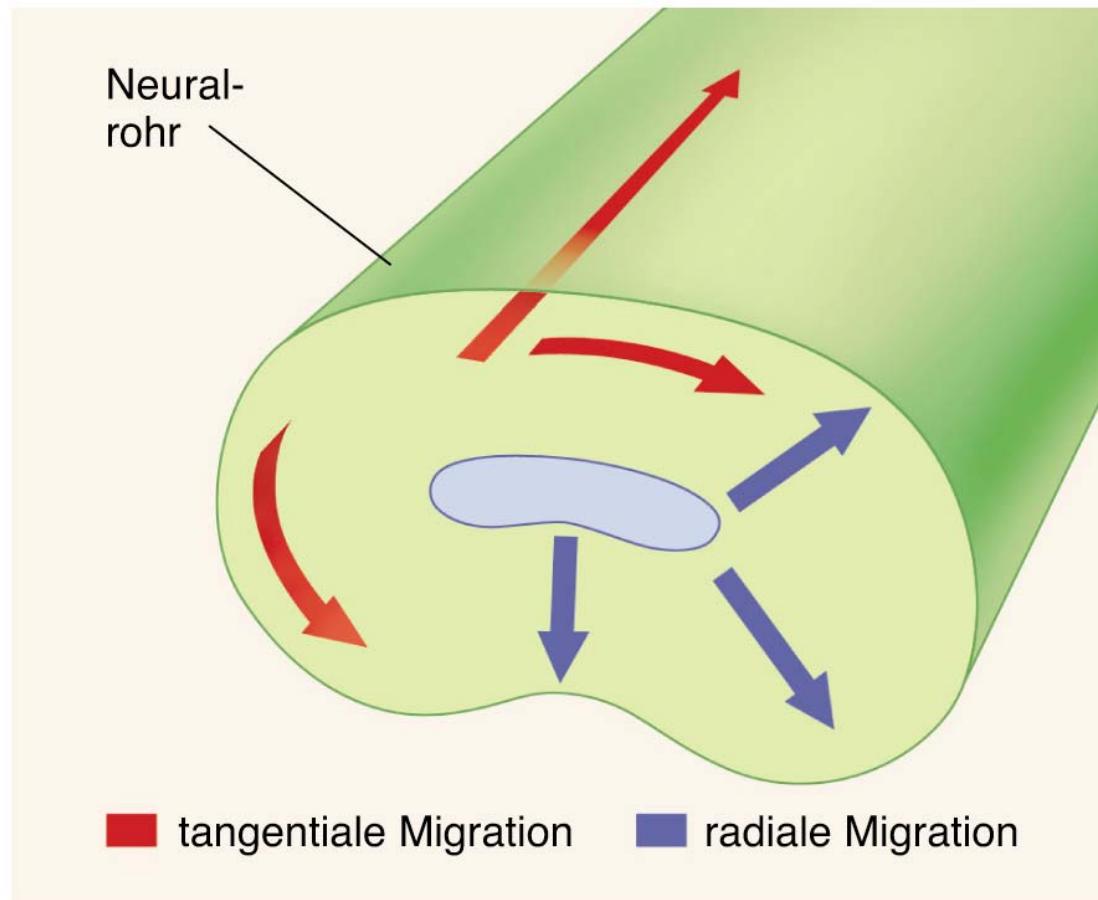
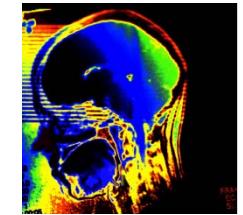
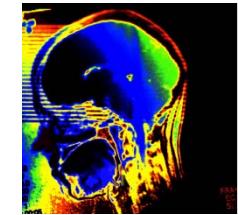


Abbildung 9.2: Die zwei Arten der neuronalen Migration: die radiale Migration und die tangentiale Migration.

3) Migration und Aggregation: Vermittelt durch neuronale Zelladhäsions- moleküle (NCAMs)



4) Axonales Wachstum und Synapsenbildung



XX Wachstumskegel. Die fingerförmigen cytoplasmatischen Fortsätze (Filopodien) der Wachstumskegel scheinen nach der richtigen Route zu tasten (Abb. 15.4).

Die Chemoaffinitäts-Hypothese

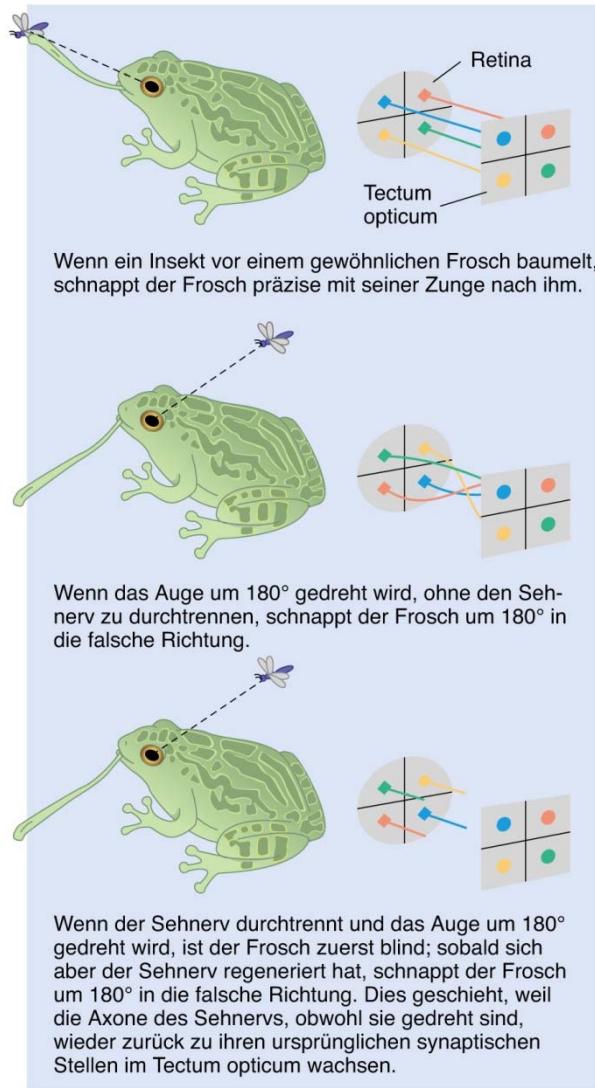
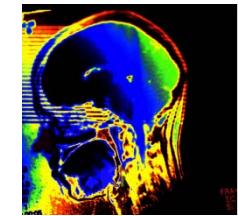


Abbildung 9.5: Sperrys klassische Untersuchung zu Augenrotation und Regeneration.

Hypothese der topographischen Gradienten

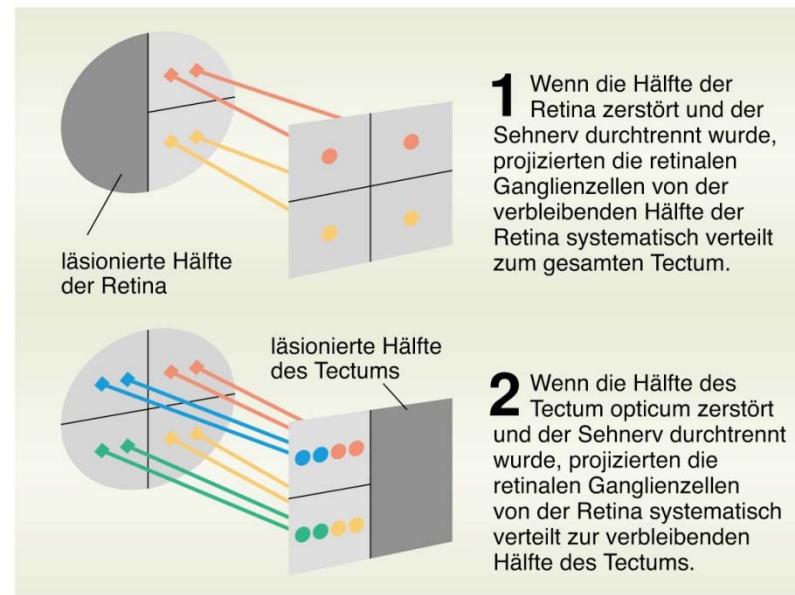
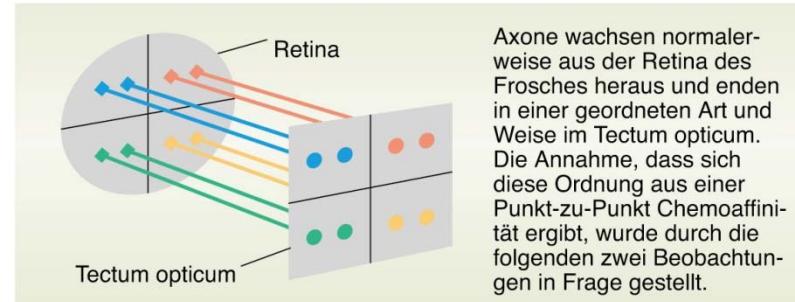
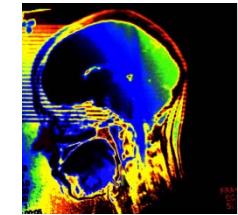
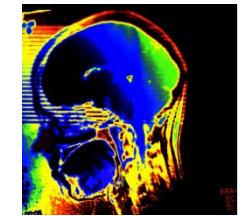


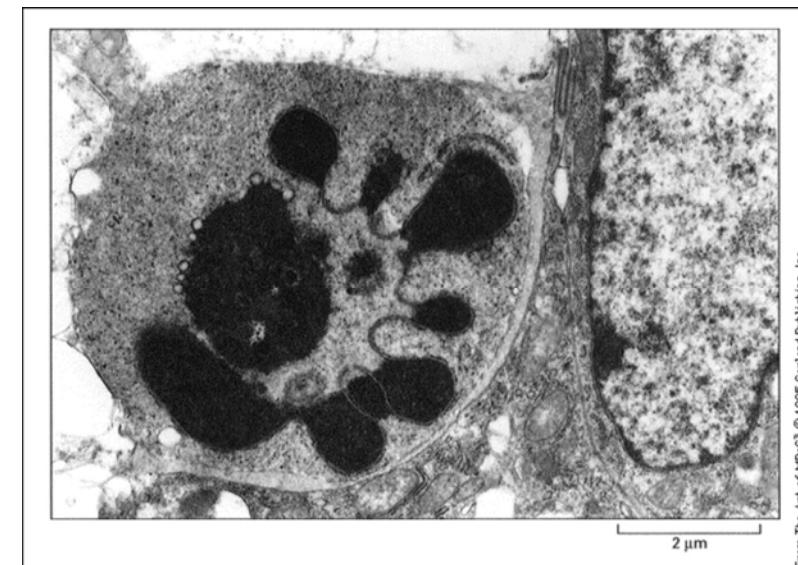
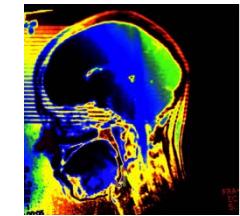
Abbildung 9.6: Die Regeneration des Sehnervs des Frosches, nachdem entweder Teile der Retina oder des Tectum opticum zerstört wurden. Diese Befunde unterstützen die topographische Gradientenhypothese.

Neuronentod

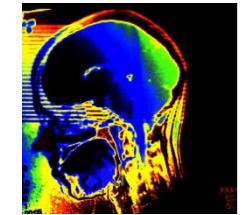


- „Survival of the fittest“
- Neurotrophine
 - Der Nervenwachstumsfaktor (NFG)
 - Fördern Wachstum und Überleben von Neuronen
 - Leitsignale für Axone
 - Stimulieren Synaptogenese
- Apoptose
 - Aktiver Zelltod
 - Entfernt überschüssige Zellen (zu wenig Neurotrophine)
- Nekrose
 - Passiver Zelltod
- Synapsenneuanordnung

Apoptose



Neuronentod



- „Survival of the fittest“
- Neurotrophine
 - Der Nervenwachstumsfaktor (NGF)
 - Fördern Wachstum und Überleben von Neuronen
 - Leitsignale für Axone
 - Stimulieren Synaptogenese
- Apoptose
 - Aktiver Zelltod
 - Entfernt überschüssige Zellen (zu wenig Neurotrophine)
- Nekrose
 - Passiver Zelltod
- Synapsenneuanordnung

Synapsenneuanordnung nach Neuronentod

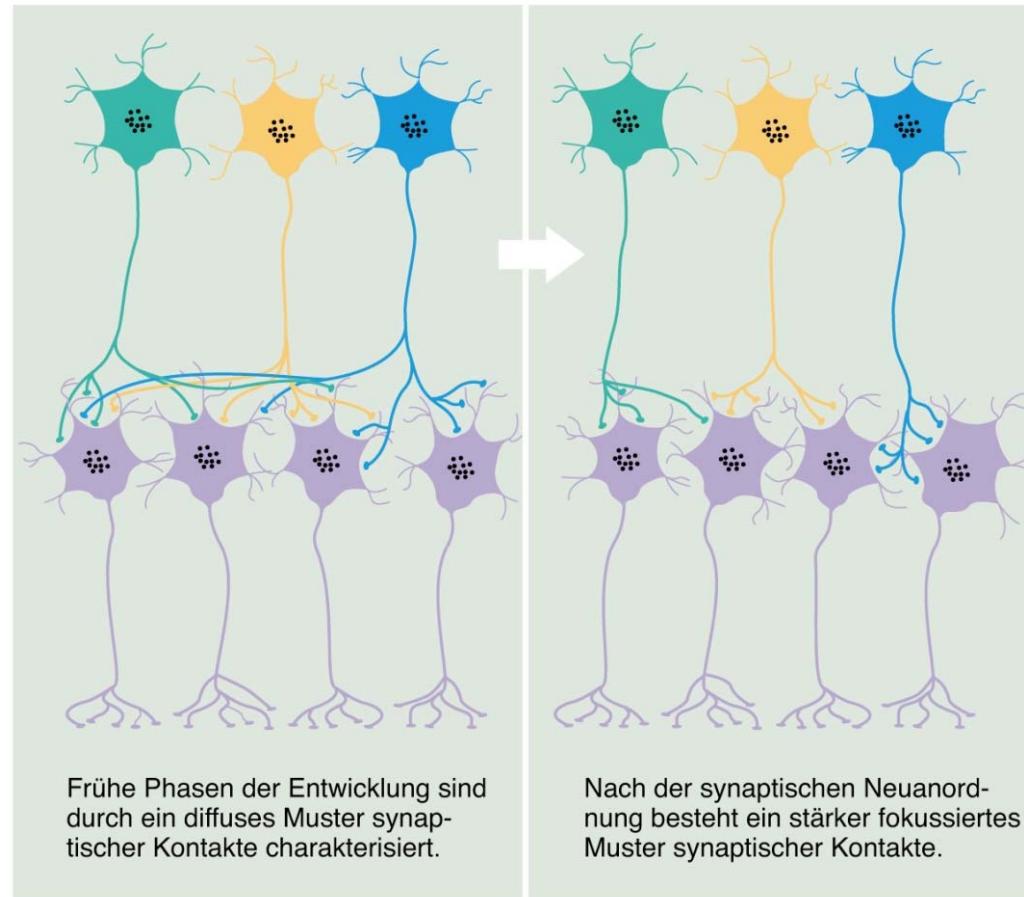
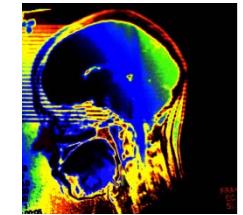
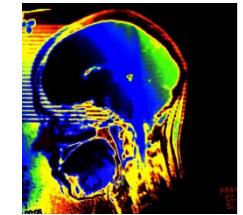


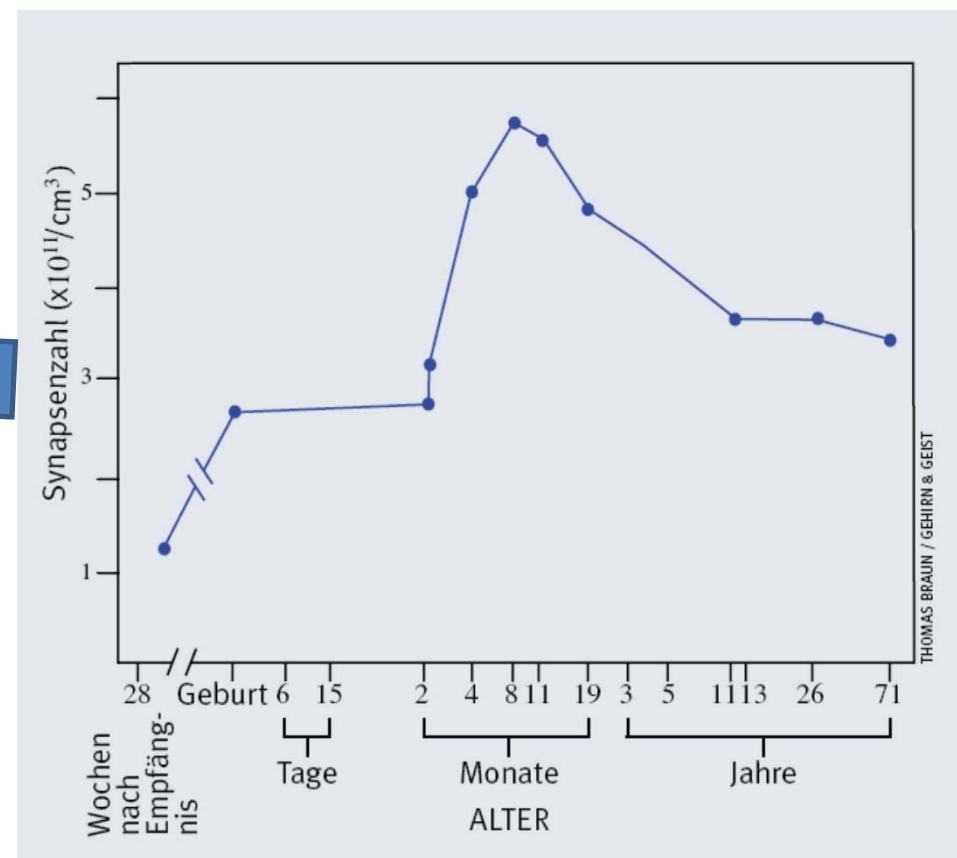
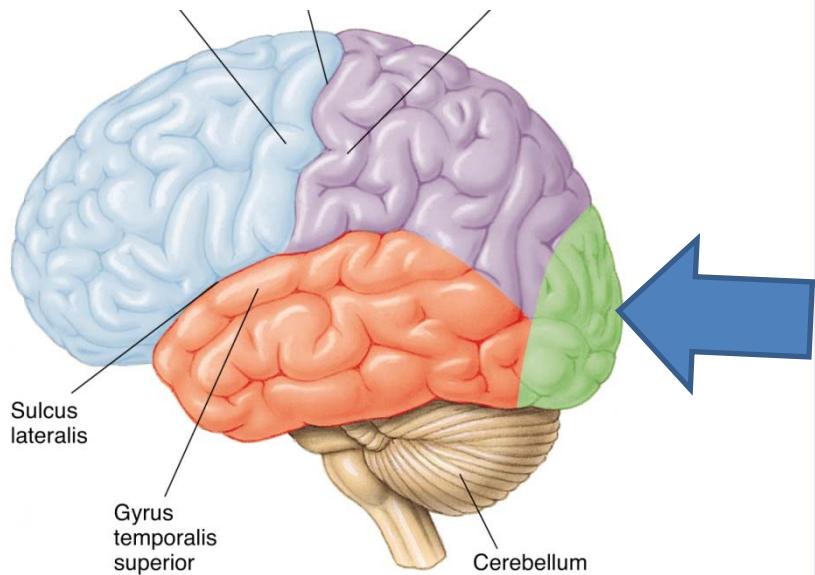
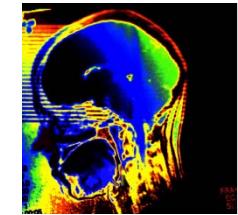
Abbildung 9.8: Die Auswirkung von Neuronentod und Synapsenneuanordnung auf die Selektivität der synaptischen Übertragung. Die synaptischen Kontakte jedes Axons werden auf eine kleinere Anzahl von Zellen konzentriert.

Inhalt

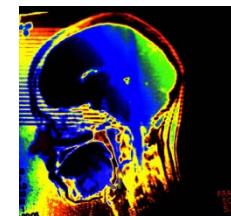


- 😊 Neuronale Entwicklung
- 😊 Auswirkung von Erfahrung auf die neuronale Entwicklung
- 😊 Neuroplastische Reaktionen des adulten ZNS
- 😊 Neuroplastizität nach kognitivem Training

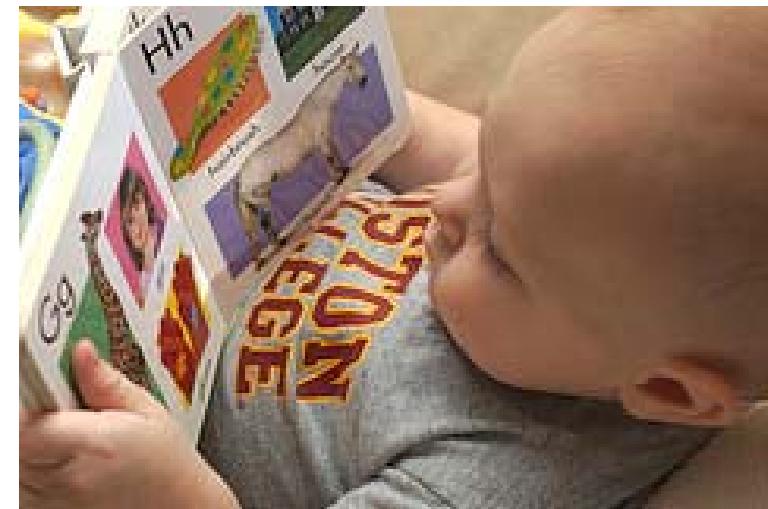
Postnatale Gehirnentwicklung bei Kindern: Abbau überschüssiger Kontaktstellen aufgrund von Lernerfahrungen („use it or lose it“) In der Sehrinde ab 6 Monate



Erfahrung und frühe Entwicklung



- „Use it or loose it“
- Pruning:
Abbau überschüssiger
Kontaktstellen aufgrund
von Lernerfahrung



Die Auswirkung von Erfahrung: Monokulare Deprivation

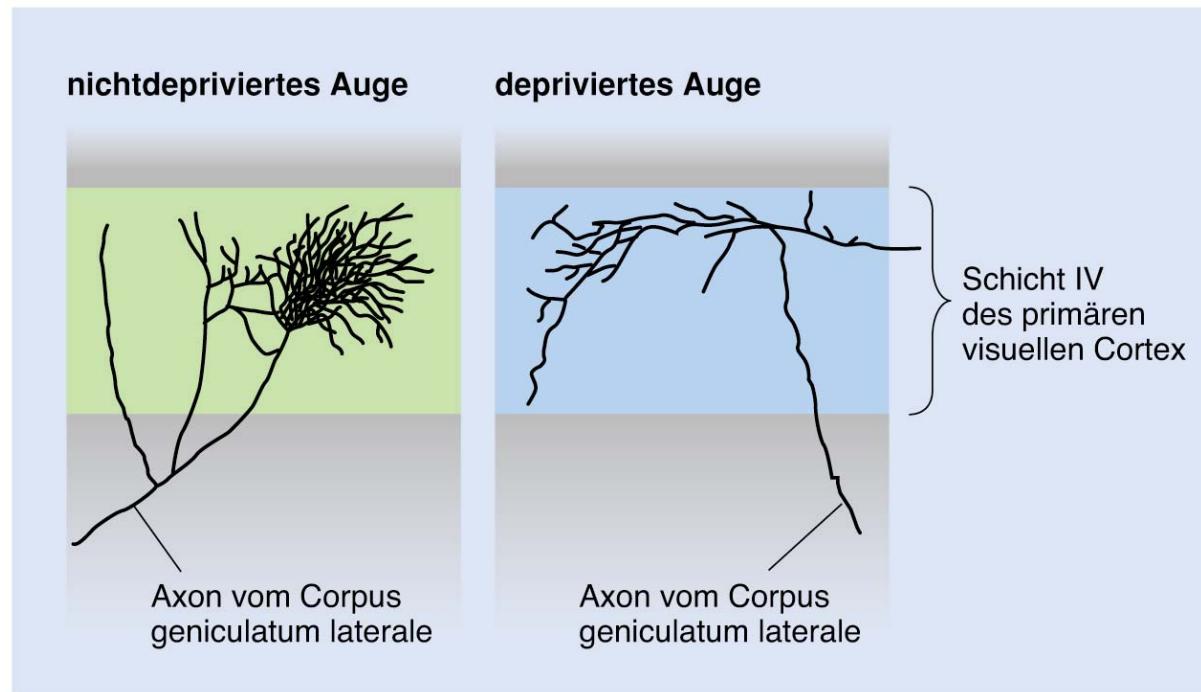
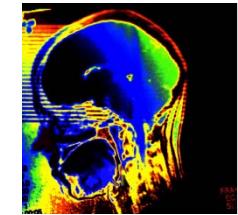
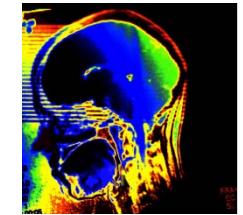


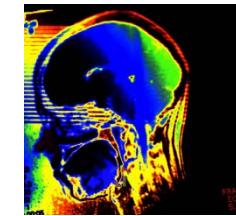
Abbildung 9.9: Die Auswirkung einiger weniger Tage früher monokularer Deprivation auf die Struktur der Axone, die vom Corpus geniculatum laterale in die Schicht IV des primären visuellen Cortex projizieren. Axone, die Information vom deprivierten Auge übertragen, zeigten eine wesentlich geringere Verzweigung (adaptiert von Antonini und Stryker, 1993).

Postnatale Gehirnentwicklung bei Kindern

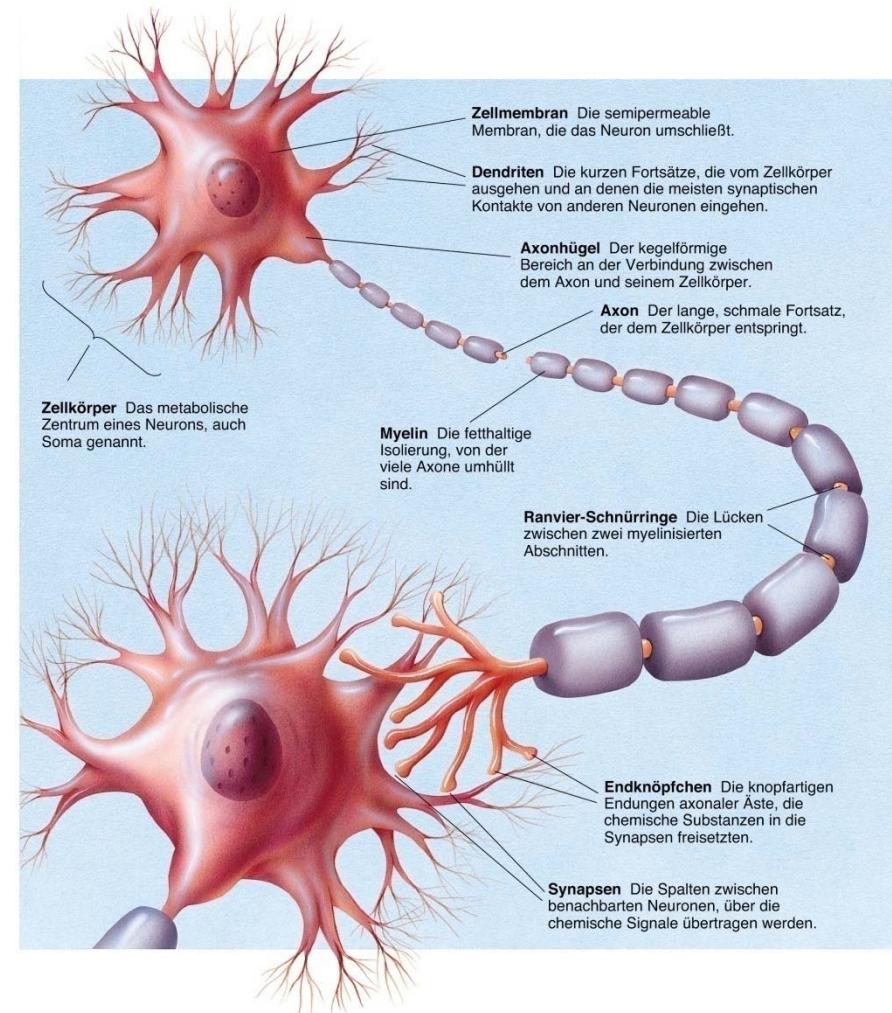


- Vervierfachung des Gehirnvolumens von Geburt bis zum Erwachsenenalter.
- Aber:
 - Alle Neurone sind bereits im 7. pränatalen Monat vorhanden
- Drei Wachstumsformen:
 - Myelinisierung
 - Dendritenverzweigung
 - Synaptogenese

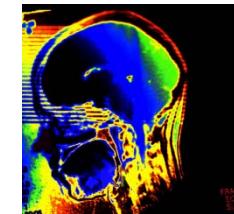
Myelinisierung



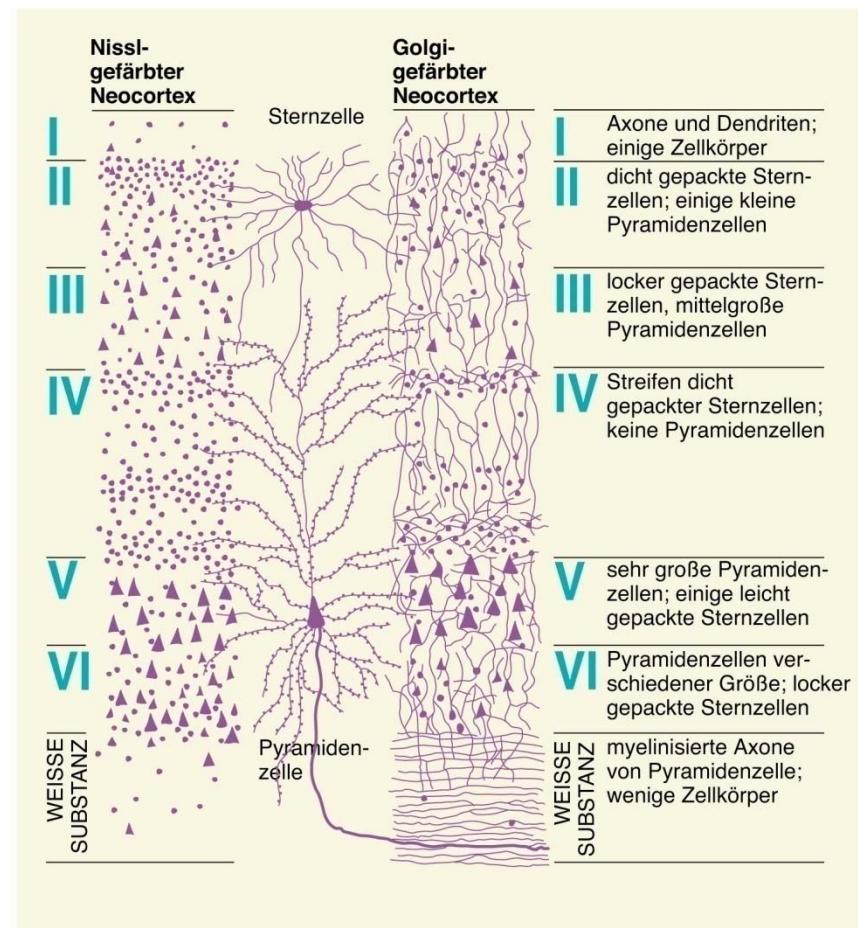
- Sensorische / motorische Bereiche:
0-10 Monate
- Präfrontaler Kortex:
bis Adoleszenz



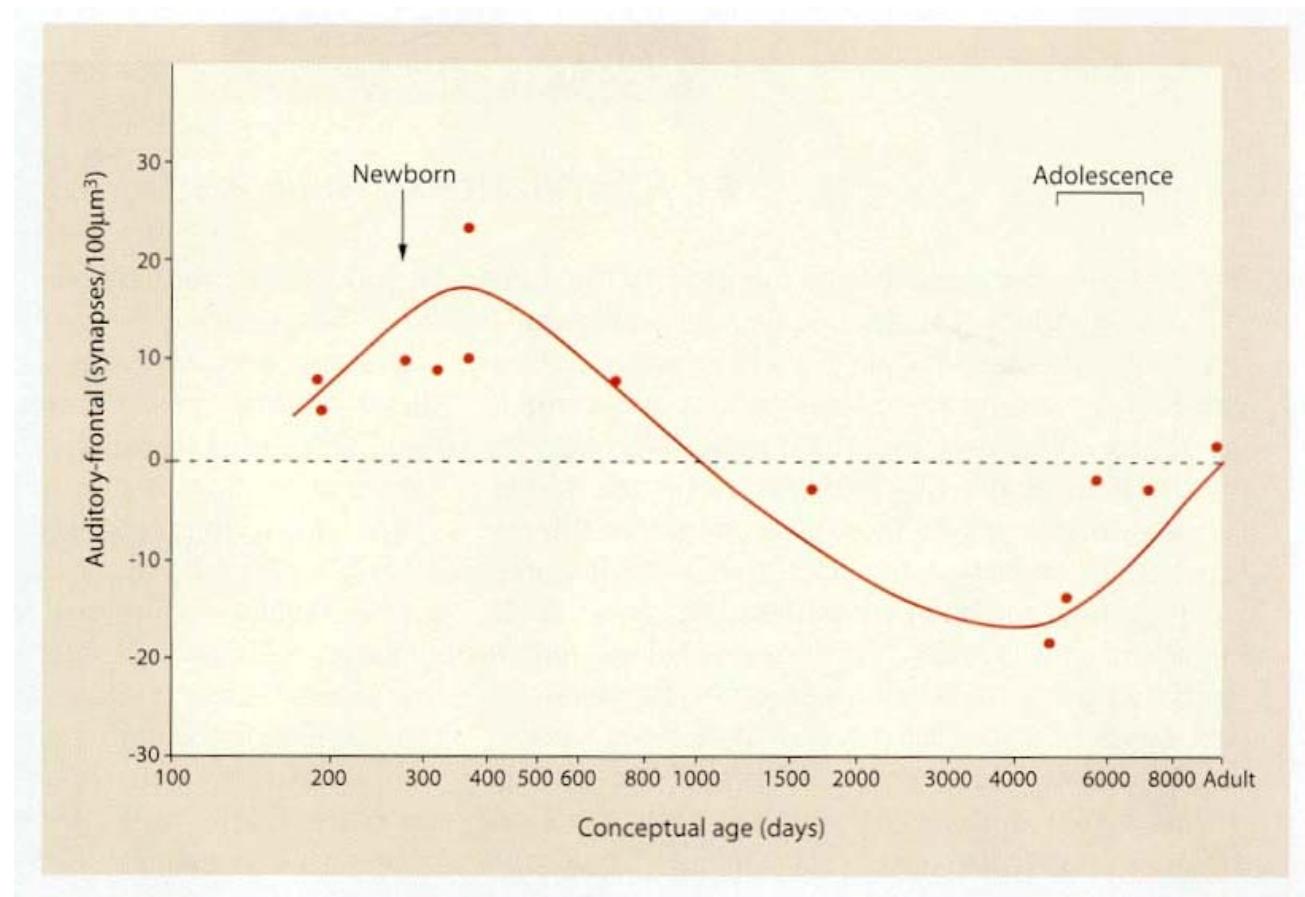
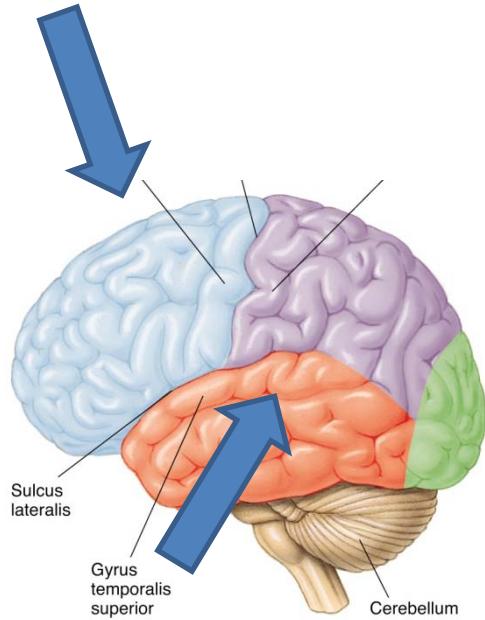
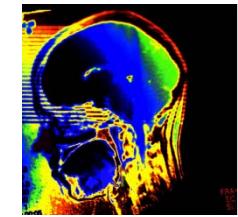
Dendritenverzweigung



- Folgt dem Muster der Migration von tiefen zu oberflächennahen Schichten (inside-out)



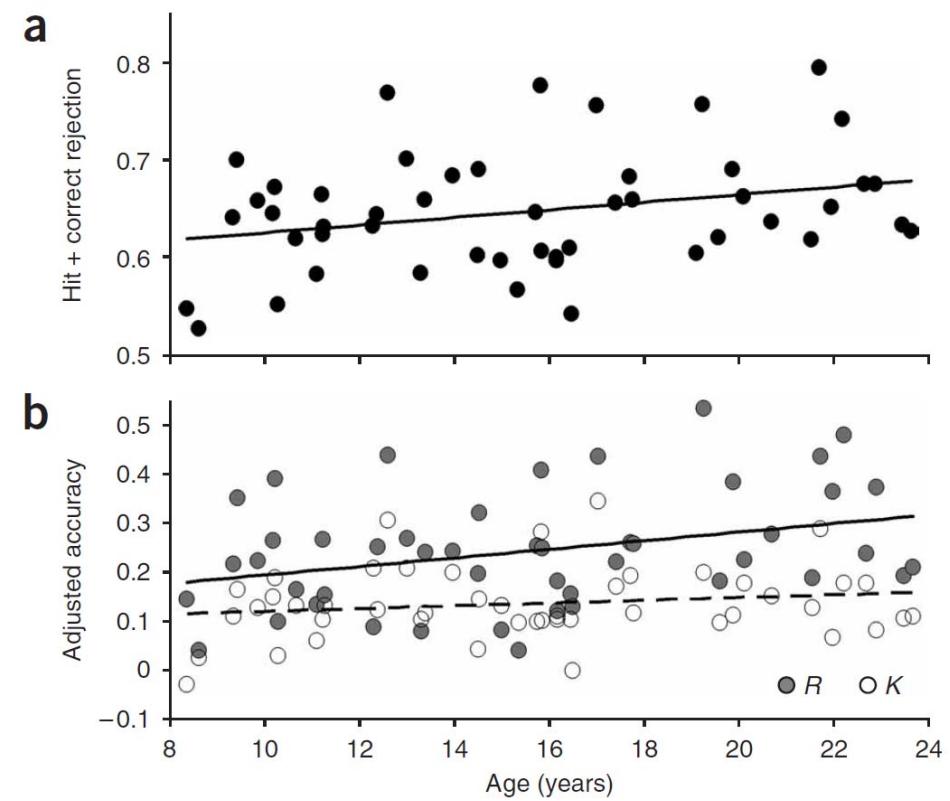
Synaptogenese im auditorischen und präfrontalen Cortex (postmortem)



Verzögerte Reifung des präfrontalen Cortex (PFC) und die Entwicklung von Gedächtnisleistungen



- N = 52;
- Alter: 8 -24 Jahre
- 250 Bilder mit innerhäuslichen und außerhäuslichen Szenen
- Rekognitionstest mit R/K Instruktion



Ofen et al. 2007

Verzögerte Reifung des präfrontalen Cortex (PFC) und die Entwicklung von Gedächtnisleistungen



- Subsequent Memory Effekte
(R > F) über alle Altersgruppen

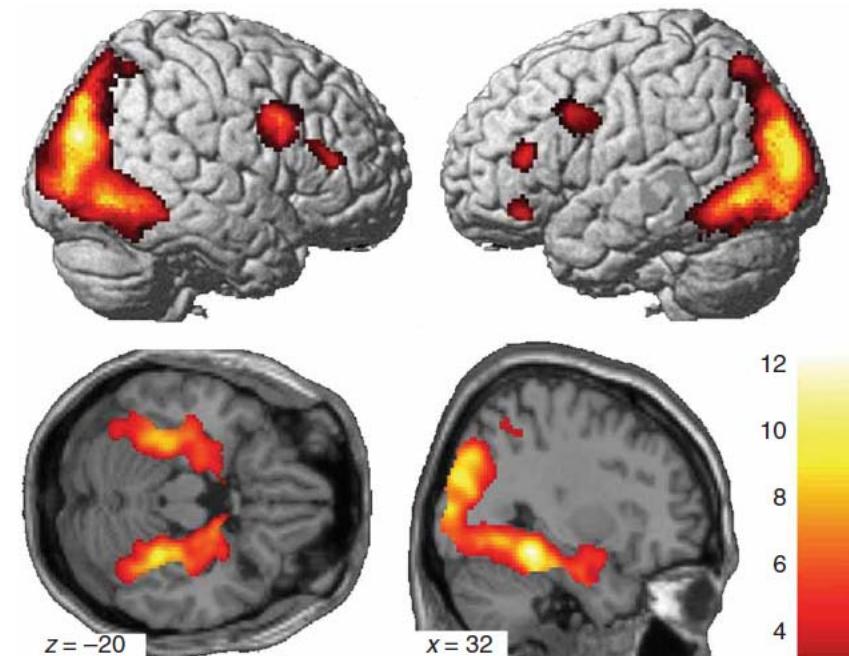
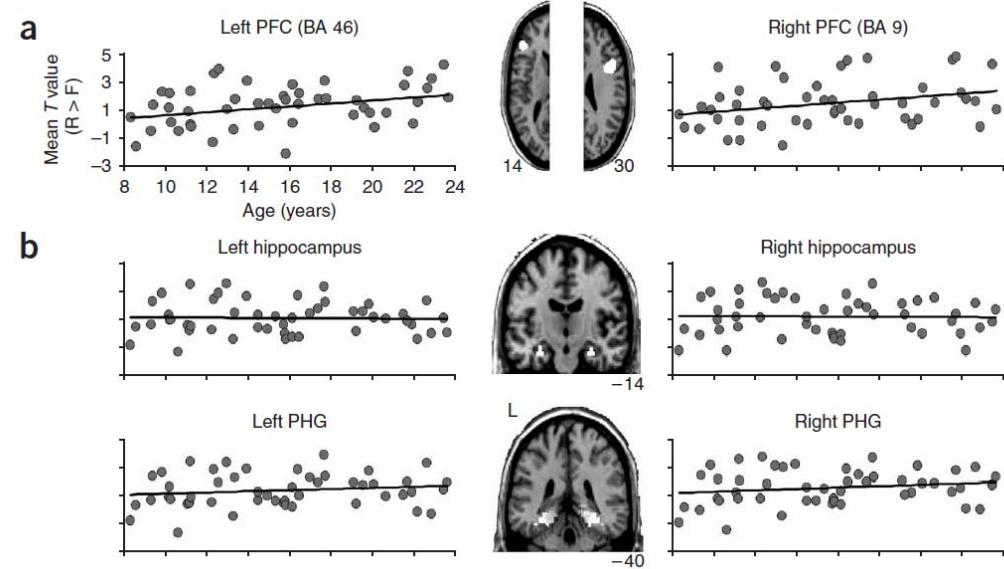
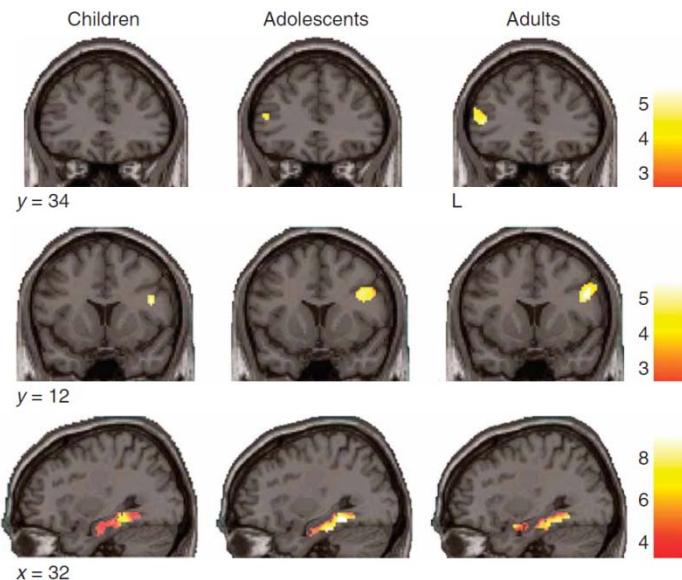


Figure 2 Subsequent memory activations (R > F) across all 49 participants, ages 8–24 years. Activation maps are rendered on standard brain right and left lateral views (top), and on horizontal and coronal sections (bottom). MNI coordinates presented at the bottom of each section. $P < 0.001$, uncorrected; cluster threshold ≥ 80 contiguous voxels. T value scale presented on the bottom right.

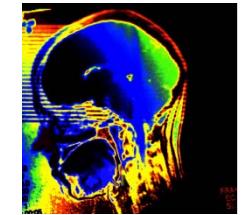
Verzögerte Reifung des präfrontalen Cortex (PFC) und die Entwicklung von Gedächtnisleistungen



- Subsequent Memory Effekte im PFC nehmen mit dem Alter zu.
- Keine Alterseffekte im medialen Temporallappen

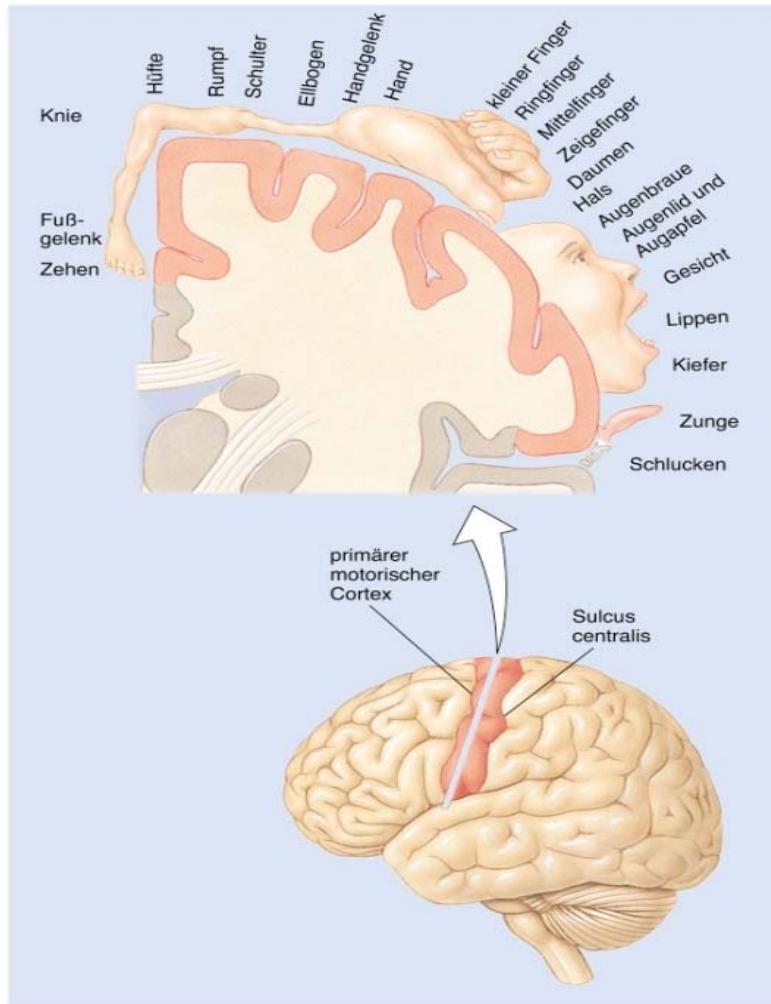
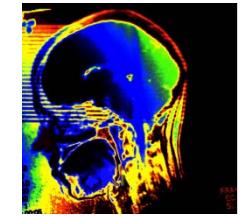


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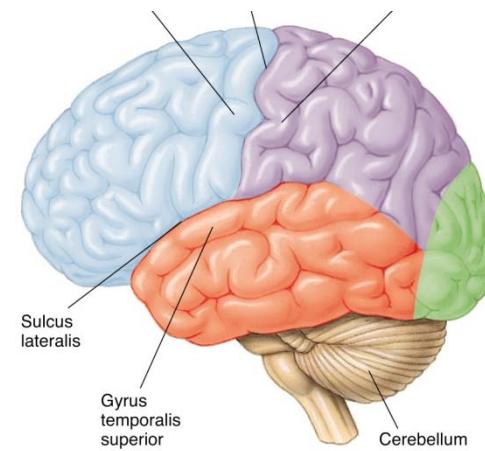


- 😊 Neuronale Entwicklung
- 😊 Auswirkung von Erfahrung auf die neuronale Entwicklung
- 😊 Neuroplastische Reaktionen des adulten ZNS
- 😊 Neuroplastizität nach kognitivem Training

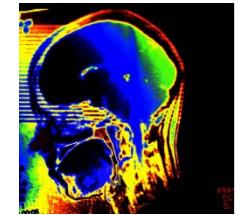
Auswirkung von Erfahrung auf topographische Karten des sensorischen und des motorischen Kortex



- Retinotopie
- Tonotopie
- Hommunkulus im somatosensorischen und motorischen Kortex



Auswirkung von Erfahrung auf topographische Karten des sensorischen Kortex



- Retinotope Organisation der Hörrinde nach visuellem Input!
- Augenprismen bei Schleiereulen verändern auditive Wahrnehmung.
- Frühe musikalische Ausbildung beeinflusst die Organisation des Hörkortex

Mechanismen ?

- Neurale Aktivität -> Expression von Genen zur Synthese von Zelladhäsionsolekülen
-> Ausschüttung von Neurotrophin

Neuronale Reorganisation im somatosensorischen System

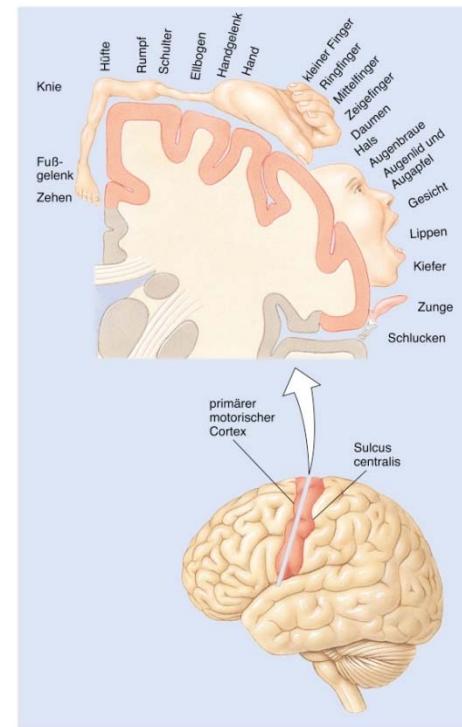
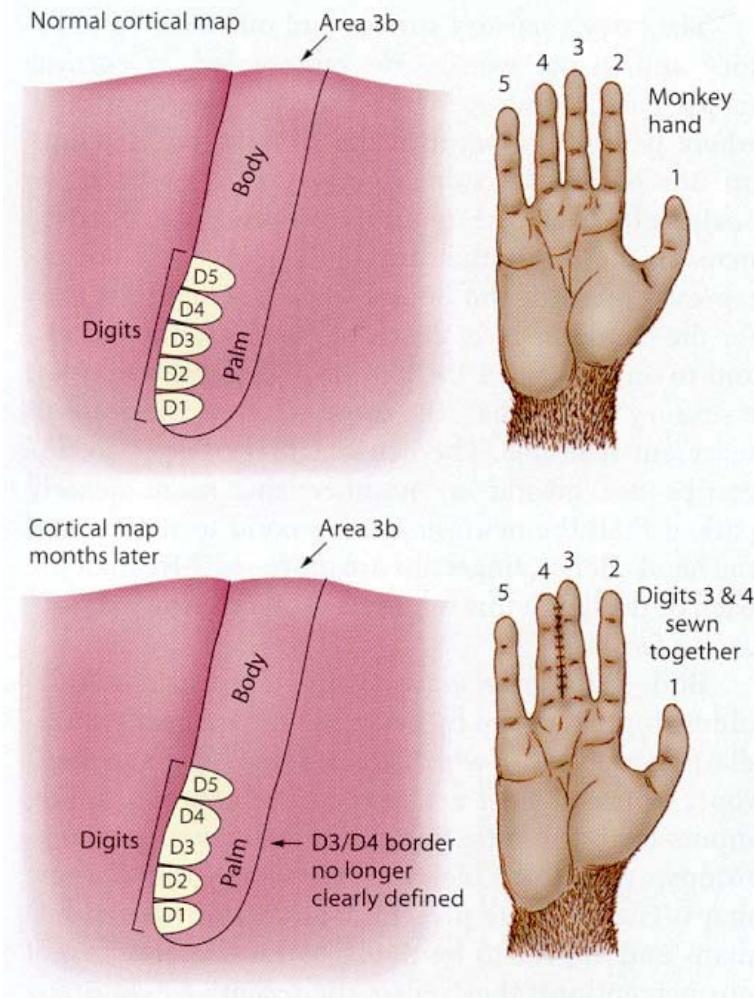
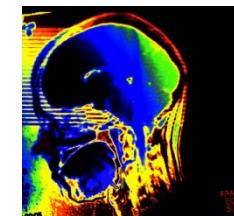


Figure 15.24 Reorganization of sensory maps in the primate cortex. At the top left is a mapping of the somatosensory hand area in a normal monkey cortex. The individual digit representations can be revealed using single unit recording. If the two fingers of one hand are sewn together, months later the cortical maps change such that the sharp border once present between the sewn fingers is now blurred. Adapted from Kandel et al. (1991).

Neuronale Reorganisation im Hörkortex

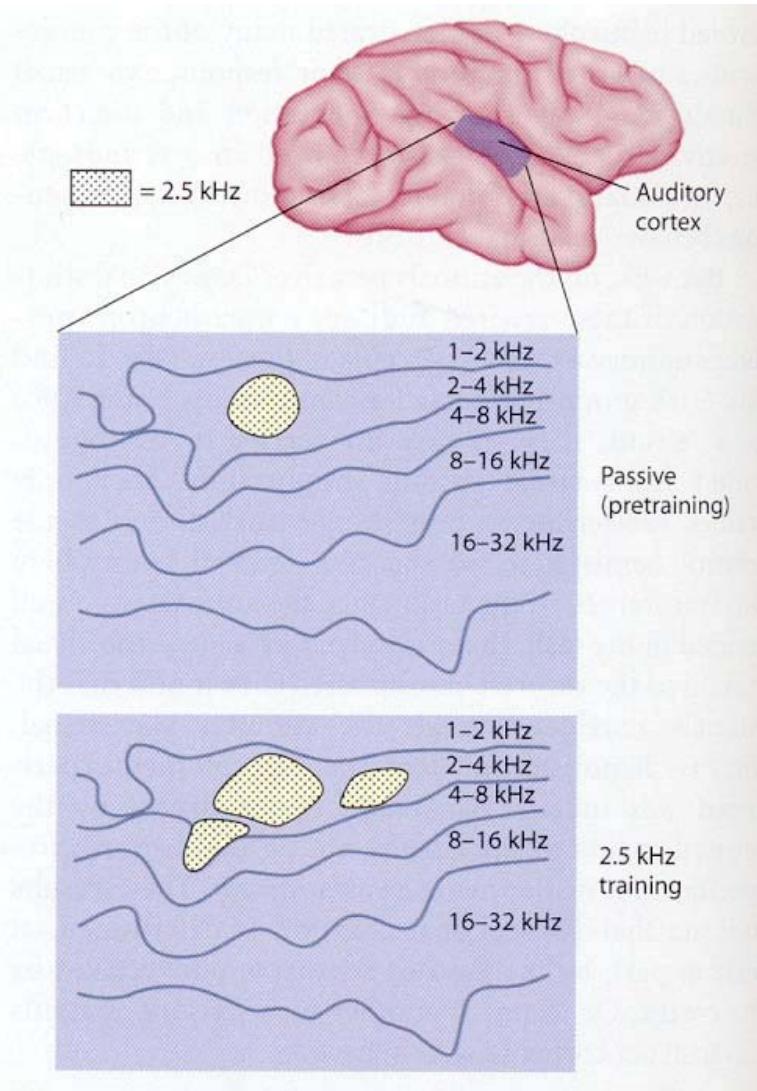
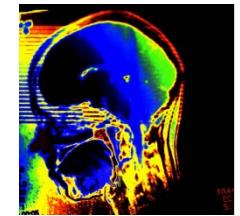


Figure 15.25 Changes in auditory frequency mapping following training. Gregg Recanzone and colleagues (1993) showed that training animals to discriminate specific tone frequencies leads to an enlargement of the cortical regions mapping the trained frequency.

Neuronale Reorganisation in sensorischen Systemen

- Nach Läsion eines Teils der Retina besetzen Neurone des vis Kortex die ursprünglich RF im verletzten Areal hatten neue RF rund um die Läsion (bereits nach Minuten).

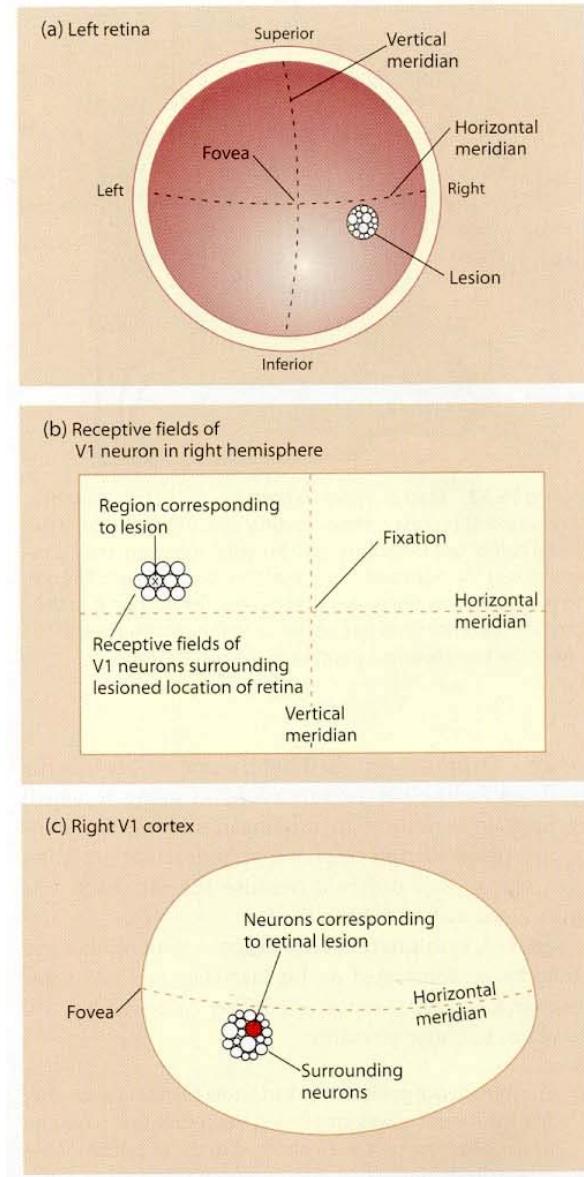
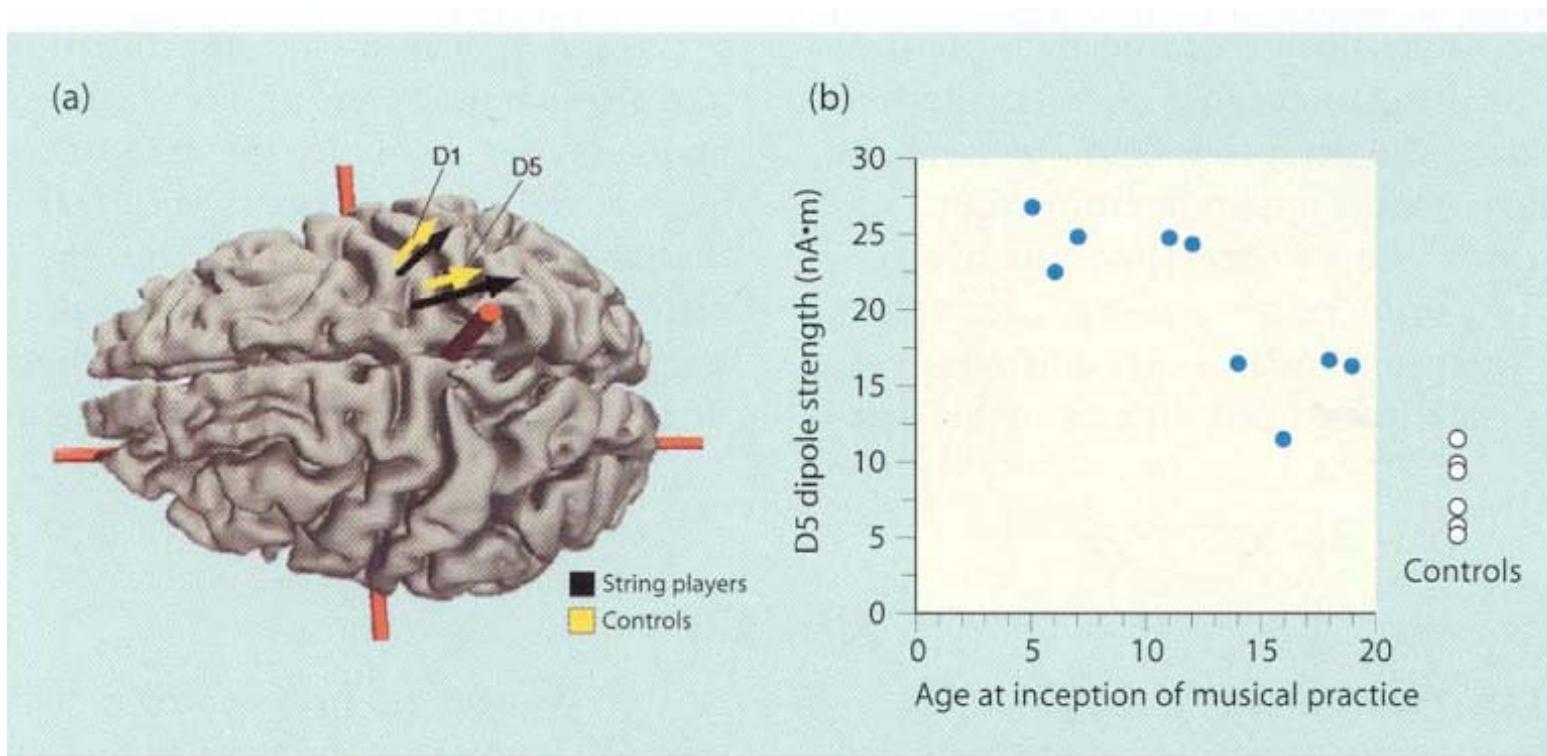


Figure 15.26 Reorganization of cortical visual receptive fields in response to retinal damage. **(a)** A representation of the retina shows the area of the lesion and the fovea. **(b)** The lesion in the lower right portion of the retina produces a scotoma (blindspot in the visual field); the lesioned region is indicated by an x. **(c)** The sizes of the receptive field of neurons in the visual cortex change when the fields are adjacent to those corresponding to the retinal lesions. This process is called *filling in*. It occurs over time and mitigates the negative impact of the lesions by allowing nearby neurons to assume some of the processing responsibilities of the neurons that lost their inputs owing to the retinal lesion.

Neuronale Reorganisation in sensorischen Systemen: Fingerrepräsentation bei Musikern (Saiteninstrumente)



D1: Daumen; D5 Kleiner Finger

Elbert et al (1995)

Neuronale Reorganisation in sensorischen Systemen

Durchtrennung der sensorischen Neurone eines Arms durch Amputation:
Tastempfindungen in der amputierten Hand bei Berührung des Gesichts.

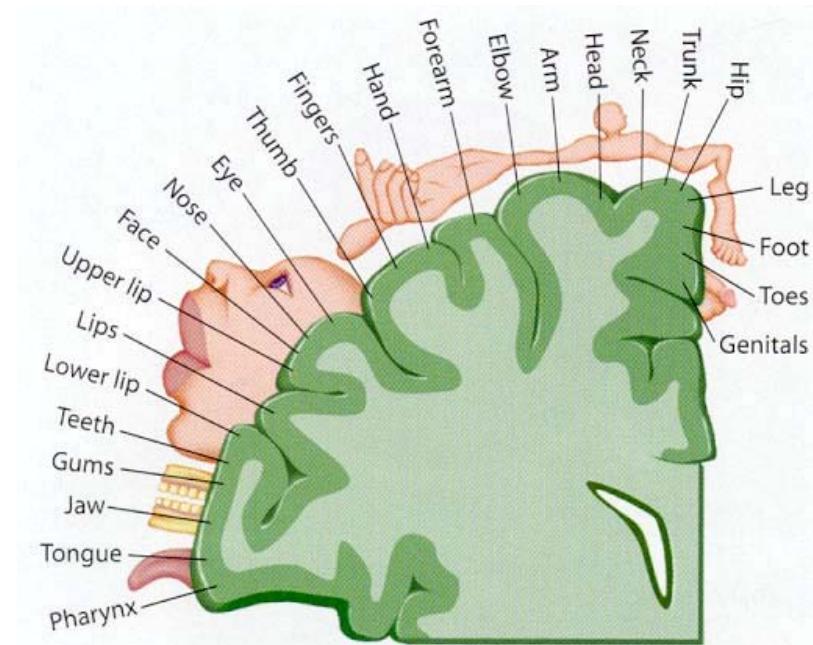


Figure 15.27 Map of a human homunculus in somatosensory cortex. This cross section (coronal section) shows only the dorsal half of one hemisphere. The medial surface of the hemisphere is at the right and the lateral surface, at the left. The cortex is indicated by the darker green color. The section is at the anterior-posterior level just posterior to the central sulcus, within the somatosensory cortex of the parietal lobe.

Neuronale Reorganisation in sensorischen Systemen



Durchtrennung der sensorischen Neurone eines Arms durch Amputation:
Tastempfindungen in der amputierten Hand bei Berührung des Gesichts.
=> Wahrnehmung eines Phantomgliedes!

- Referred Sensations

Kortikale Gesichtsrepräsentation breitet sich in das vormalige Armsareal des somatosensorischen Kortex aus.

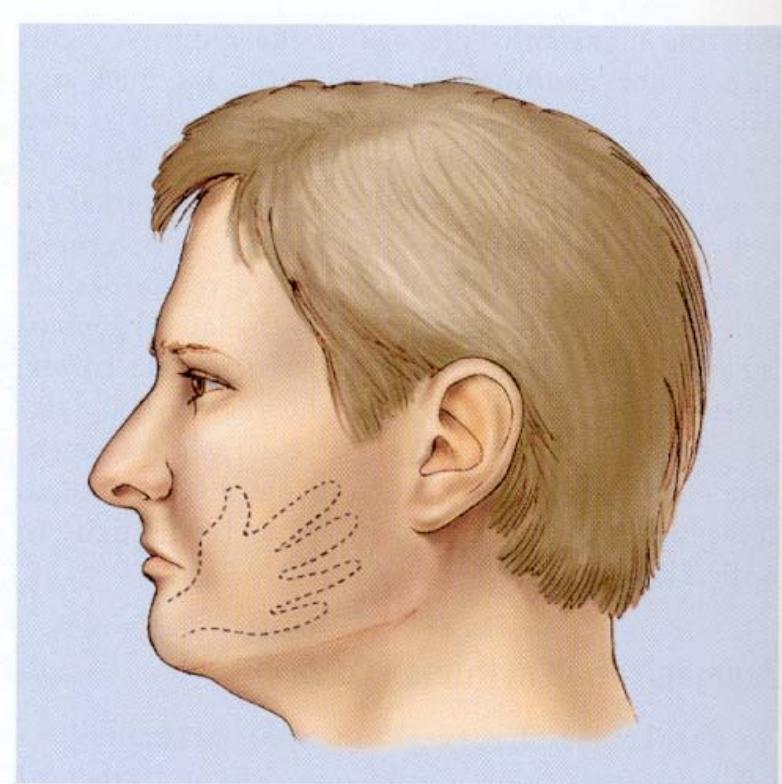
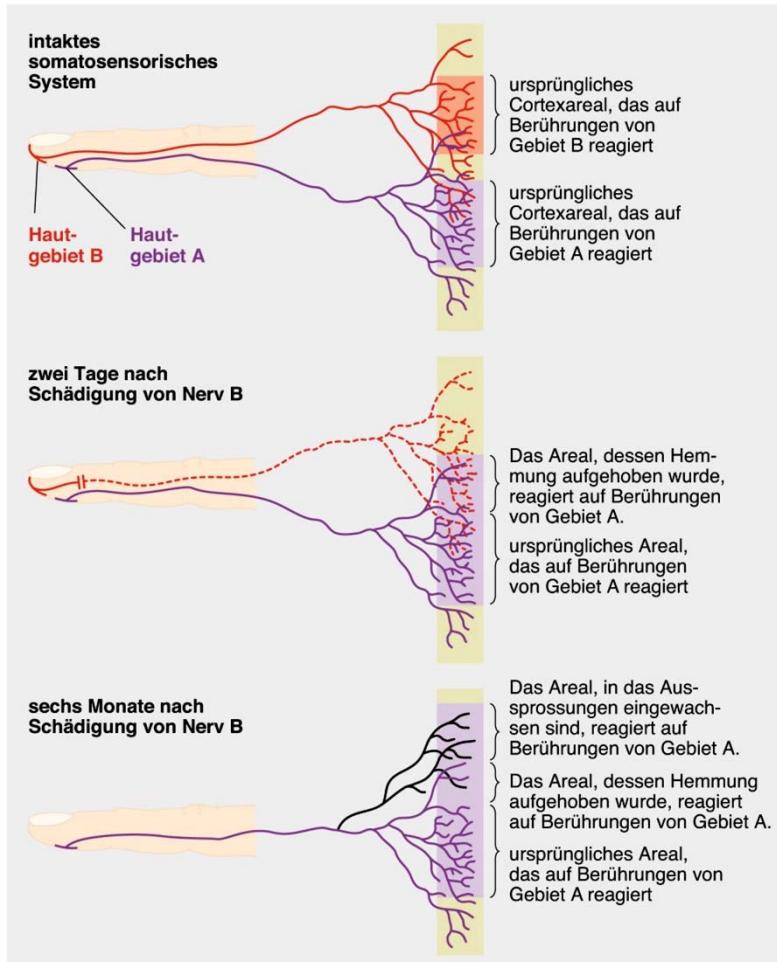
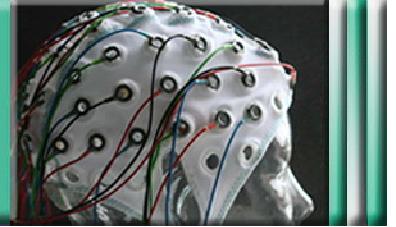


Figure 15.28 The drawing shows the hand representation sketched on the face of the amputee studied by Professor Ramachandran. The hand map on the face was obtained as described in Figures 15.1 and 15.2. Do you now have an idea as to why this might occur? See text for discussion.

Ramachandran et al. (1993)



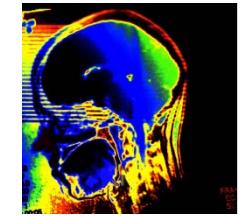
Das Zwei-Stadien-Modell der neuronalen Reorganisation



- 1) Verstärkung bereits bestehender Verbindungen über den Wegfall von Hemmung
- 2) Bildung von neuen Verbindungen über kollaterale Aussprossungen



Inhalt

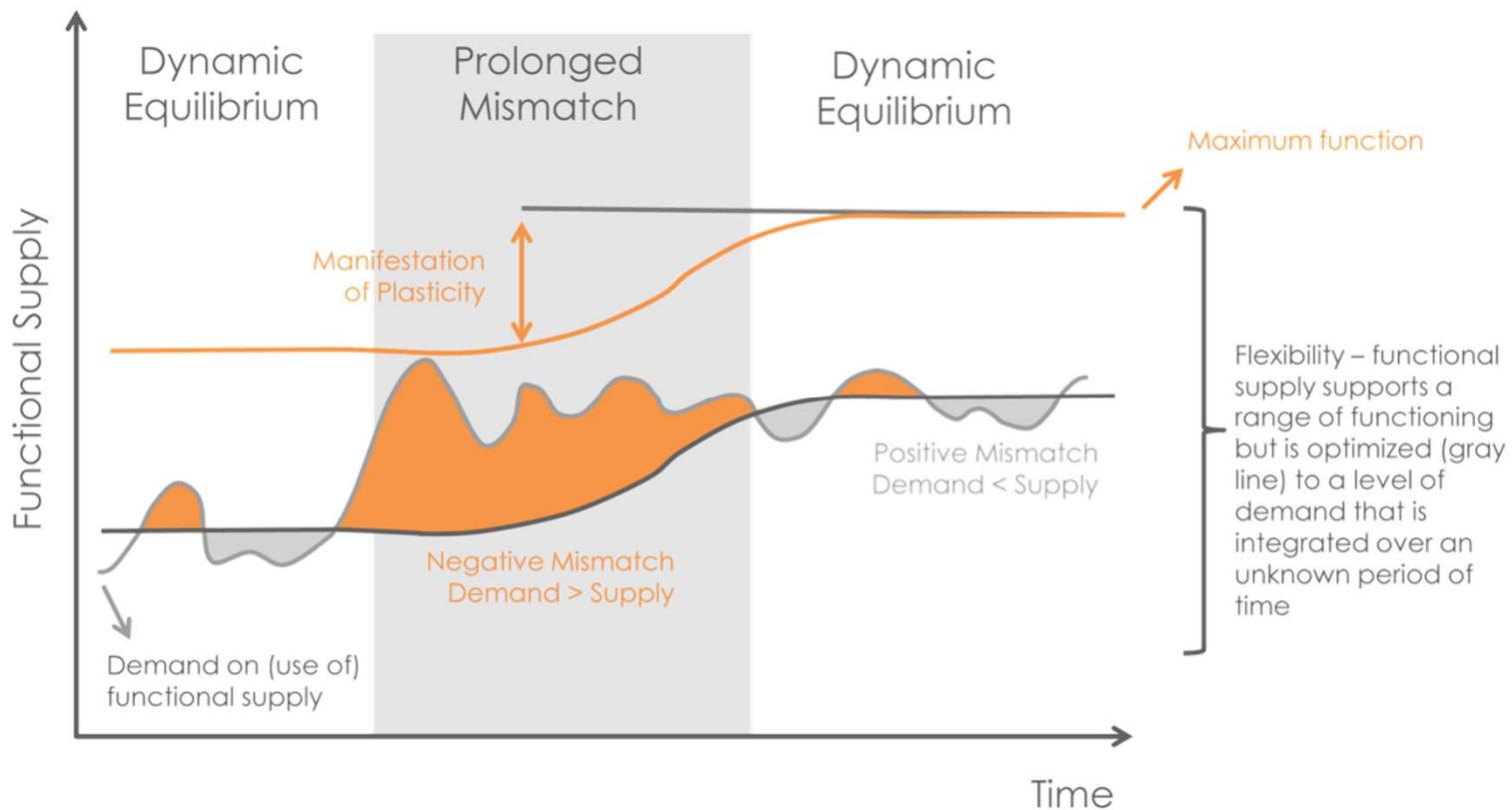


- 😊 Neuronale Entwicklung
- 😊 Auswirkung von Erfahrung auf die neuronale Entwicklung
- 😊 Neuroplastische Reaktionen des adulten ZNS
- 😊 Neuroplastizität nach kognitivem Training

Neuronale Reorganisation durch Training kognitiver Prozesse?



Ein theoretischer Rahmen zur Analyse neuronaler Plastizität: Missverhältnis aus Angebot (supply) und Nachfrage (demands)



Lövdén et al. (2010)



- N = 24
- 3 monatiges Jonglieren
- 3 Brain Scans
- 3. Scan, 3 Monate nach Training
- Voxel-basierte Morphometrie

Draganski et al. (2004)

Erhöhte Nachfrage führt zu Zunahmen der grauen Substanz im Bewegungswahrnehmungsareal V5

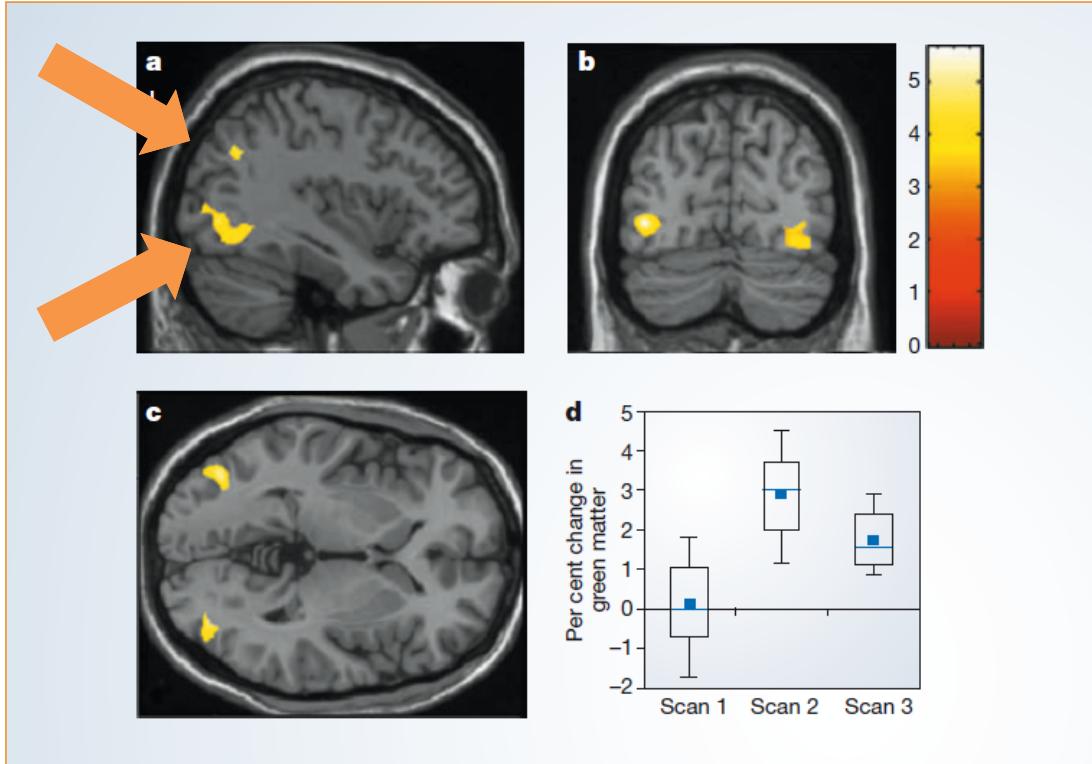


Figure 1 Transient changes in brain structure induced while learning to juggle. **a–c**, Statistical parametric maps showing the areas with transient structural changes in grey matter for the jugglers group compared with non-juggler controls. **a**, Sagittal view; **b**, coronal view; **c**, axial view. The increase in grey matter is shown superimposed on a normalized T1 image. The left side (L) of the brain is indicated. A significant expansion in grey matter was found between the first and second scans in the mid-temporal area (hMT/V5) bilaterally (left: $x = -43$; $y = -75$; $z = -2$, with $Z = 4.70$; right: $x = 33$; $y = -82$; $z = -4$, with $Z = 4.09$) and in the left posterior intraparietal sulcus ($x = -40$; $y = -66$; $z = 43$ with $Z = 4.57$), which had decreased by the time of the third scan. Colour scale indicates Z scores, which correlate with the significance of the change. **d**, Relative grey-matter change in the peak voxel in the left hMT for all jugglers over the three time points. The box plot shows the standard deviation, range and the mean for each time point.



Costs of reorganisation: Taxi drivers revisited

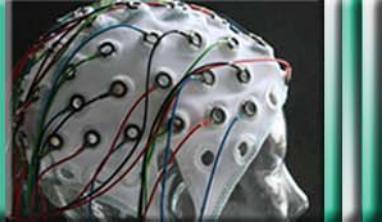


TABLE 1.

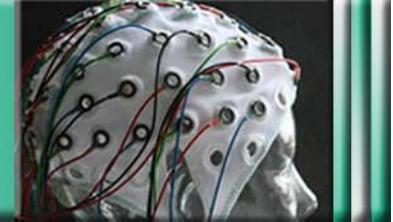
Participant Characteristics

	London taxi drivers	London bus drivers
Mean age (yr)	39.33 (4.49)	35.88 (5.79)
Mean full-time driving experience in London (yr)	10.94 (5.25)	7.71 (6.47)
Mean age at leaving school (yr)	16.50 (0.90)	16.53 (1.00)
Mean laterality index (handedness)	69.72 (43.40)	57.12 (51.15)
Mean scaled score on matrix reasoning	11.61 (1.76)	11.59 (2.26)

SDs in parentheses. Group comparisons revealed no significant differences on any of these background characteristics (see text).

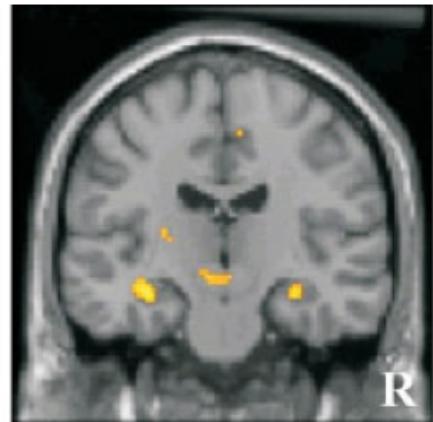


Costs of reorganisation: Taxi drivers revisited



Taxi > Bus

Posterior Hc



Taxi < Bus

Anterior Hc

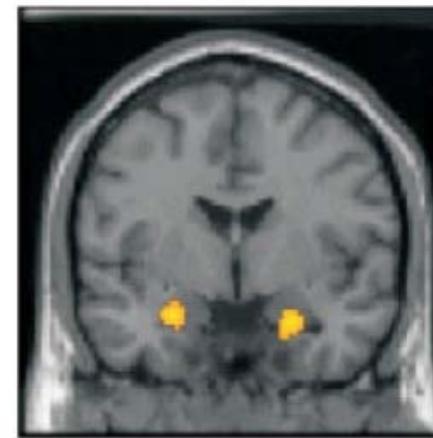


TABLE 3.

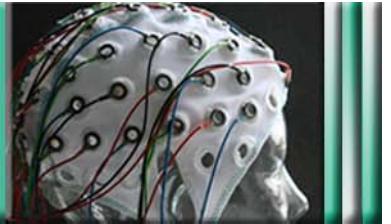
Mean Scores on Stress and Anxiety Measures

	London taxi drivers	London bus drivers
Perceived stress sale	16.39 (7.96)	15.59 (5.68)
Life stress rating	5.50 (2.72)	4.29 (1.75)
Job stress rating	4.94 (2.55)	4.29 (1.96)
State trait anxiety inventory state	29.50 (7.99)	26.41 (9.46)
State trait anxiety inventory trait	38.11 (12.31)	34.35 (9.91)

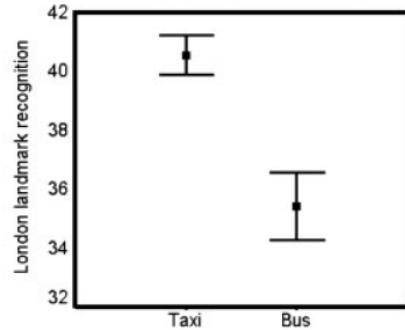
SDs in parentheses. Group comparisons revealed no significant differences on any of these measures (see text).



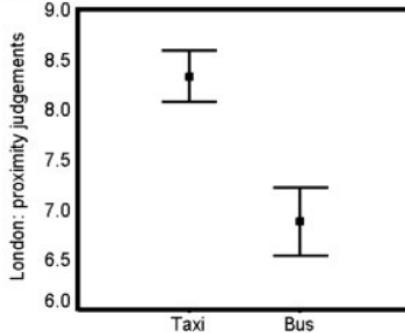
Costs of reorganisation: Taxi drivers revisited



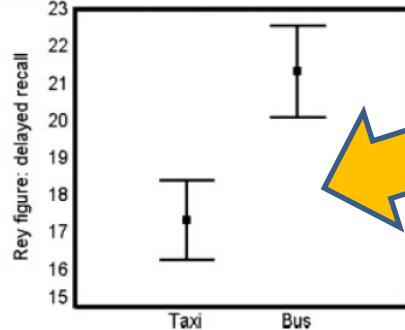
A



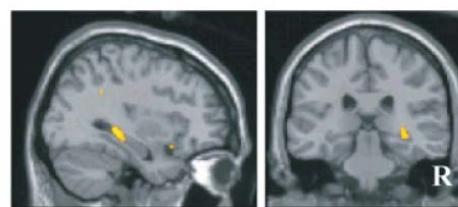
B



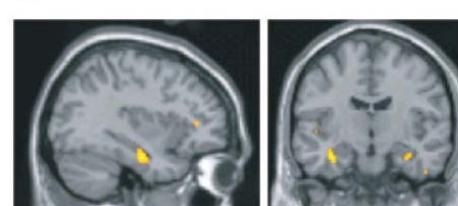
C



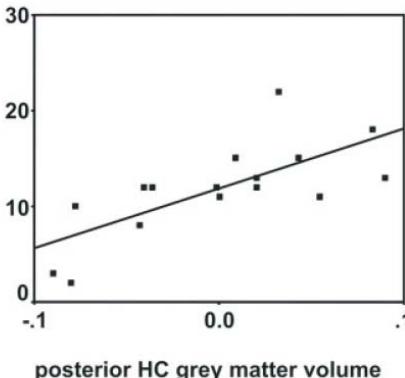
A



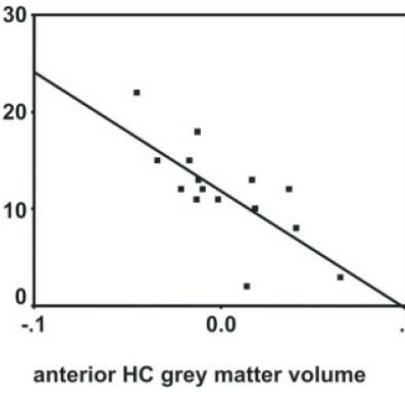
B



years experience taxi driving



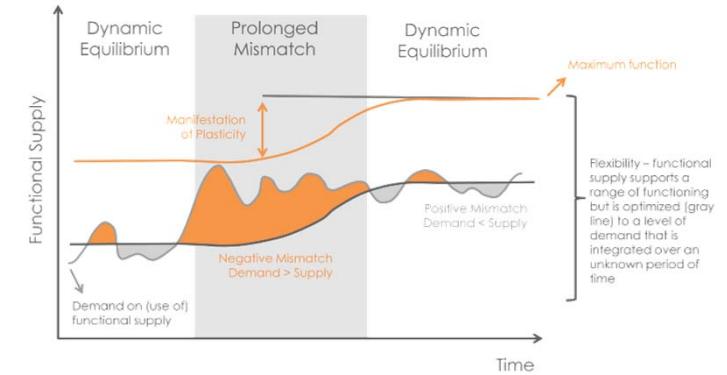
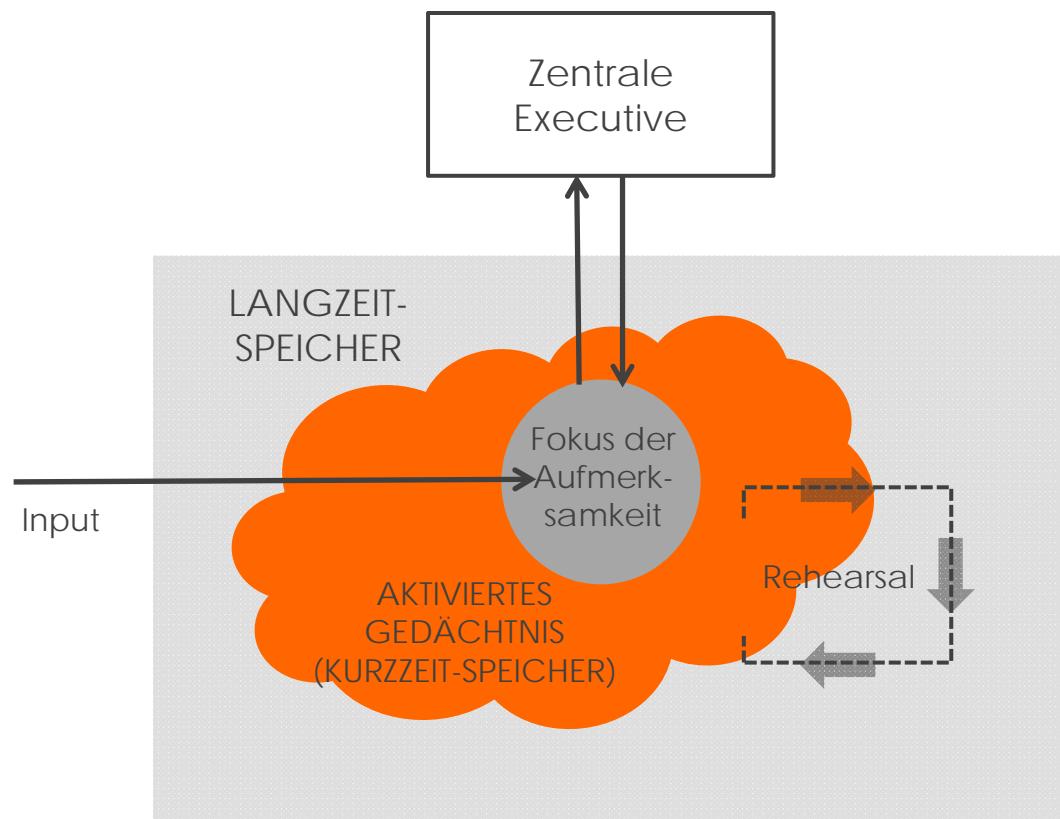
years experience taxi driving



Maguire et al. (2006)

Arbeitsgedächtnistraining: Supply / Demand Mismatch ?

Embedded Processes Model (Cowan, 1999)



Arbeitsgedächtnistraining

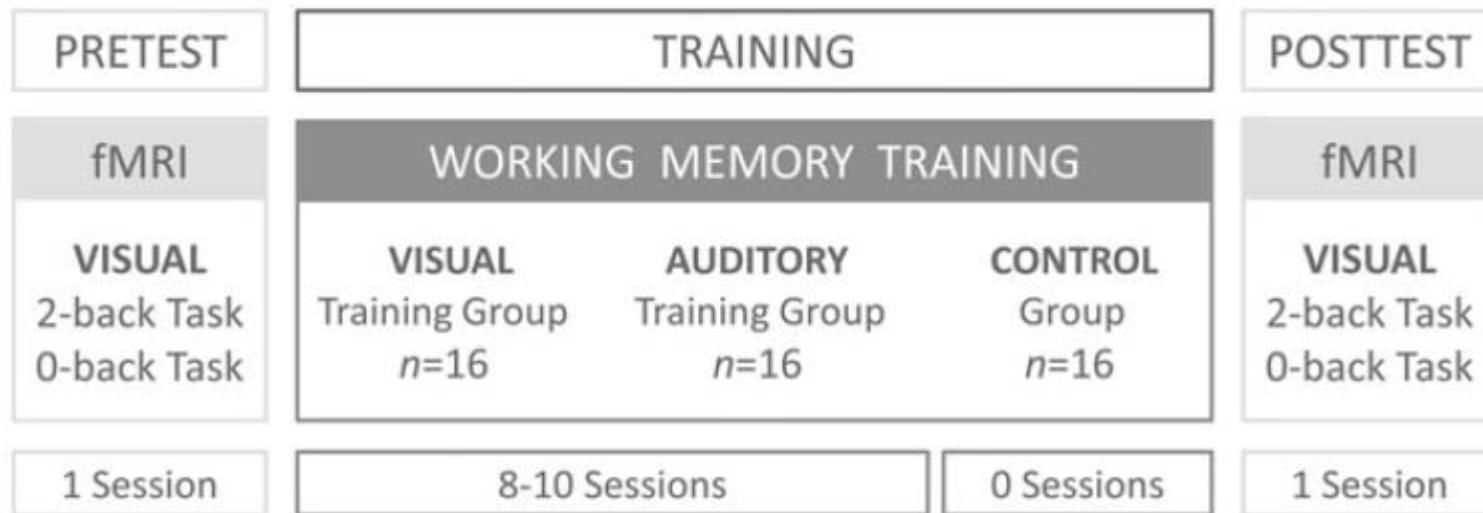
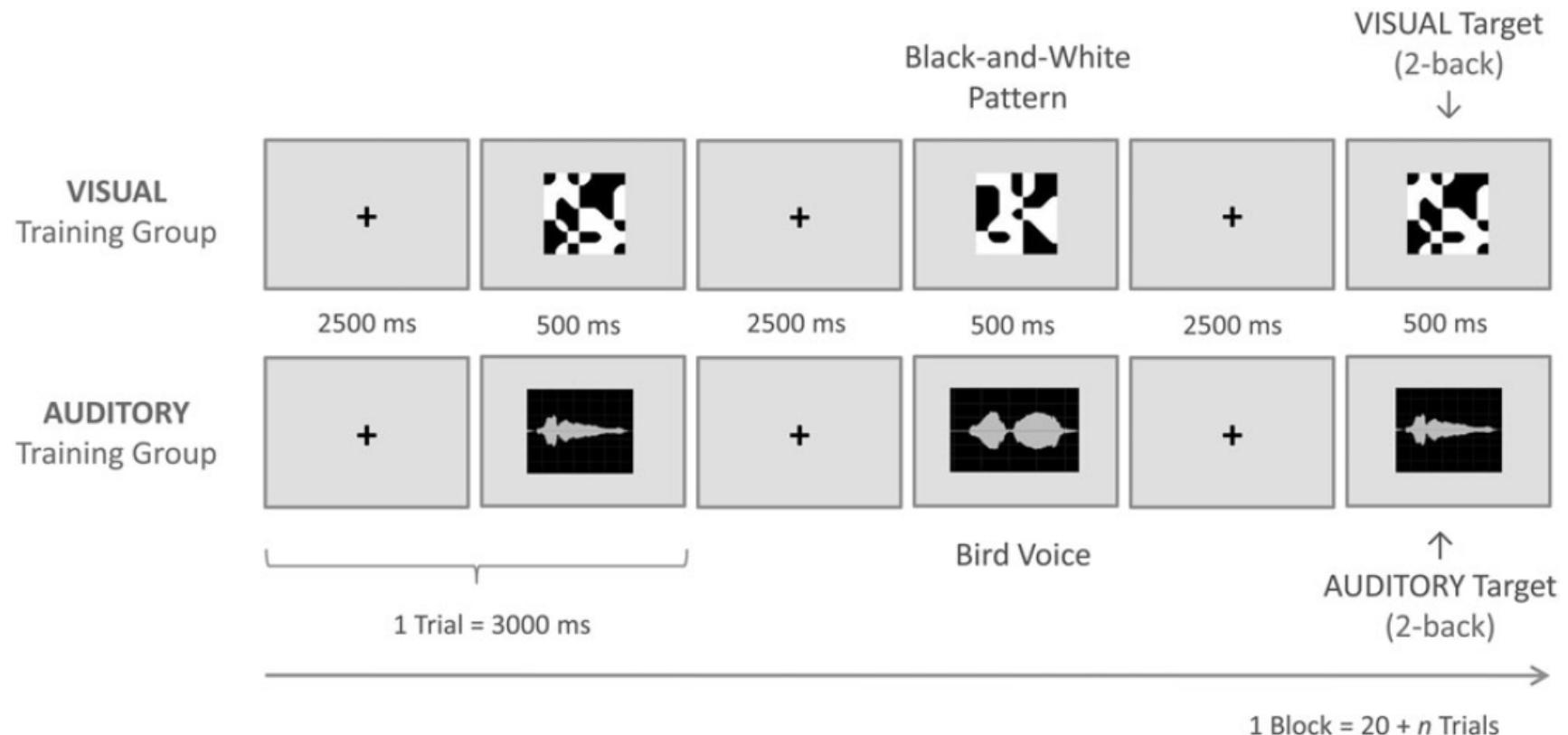


Figure 1. Schematic description of the experimental design. All 3 groups performed the same visual 2-back task and a 0-back control task in the pretest and posttest fMRI session. During the training interval, the visual training group was trained on an adaptive *n*-back task using visual stimuli, the auditory training group was trained on the same task using auditory stimuli, whereas the control group did not receive any training.

Schneiders et al. 2011

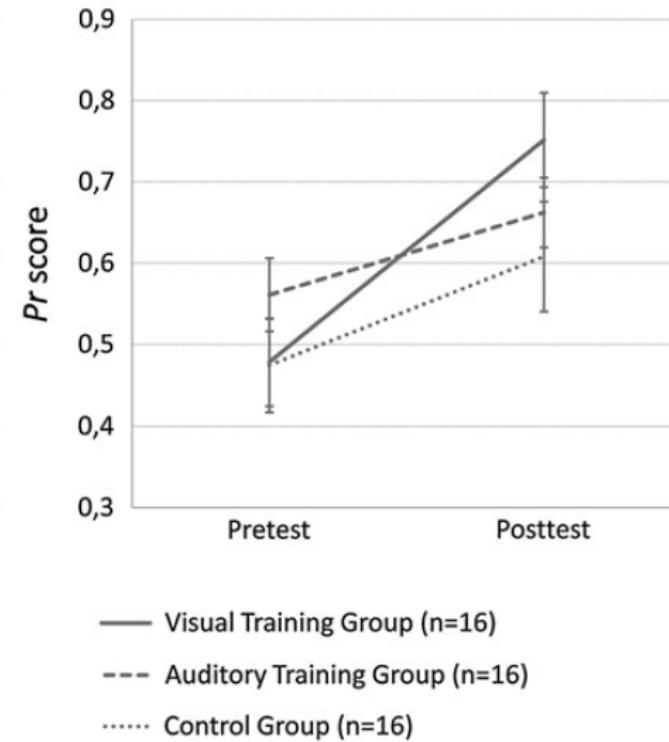
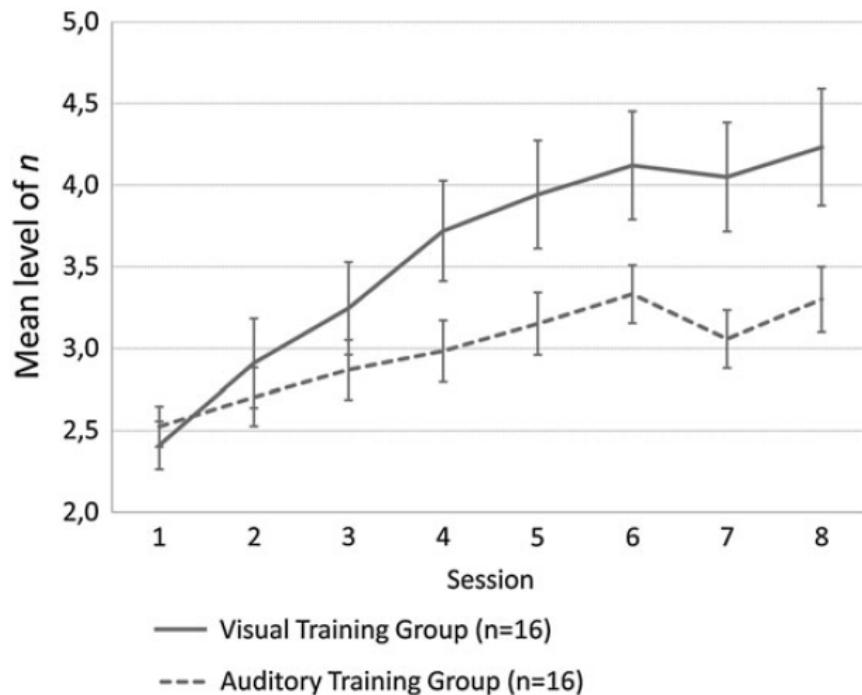
Arbeitsgedächtnistraining



Arbeitsgedächtnistraining

- ? Intramodale Effekte: visuelles Training -> visuelle 2-back Aufgabe
- ? Intermodale Effekte: Training (vis & aud) vs Kontrollgruppe

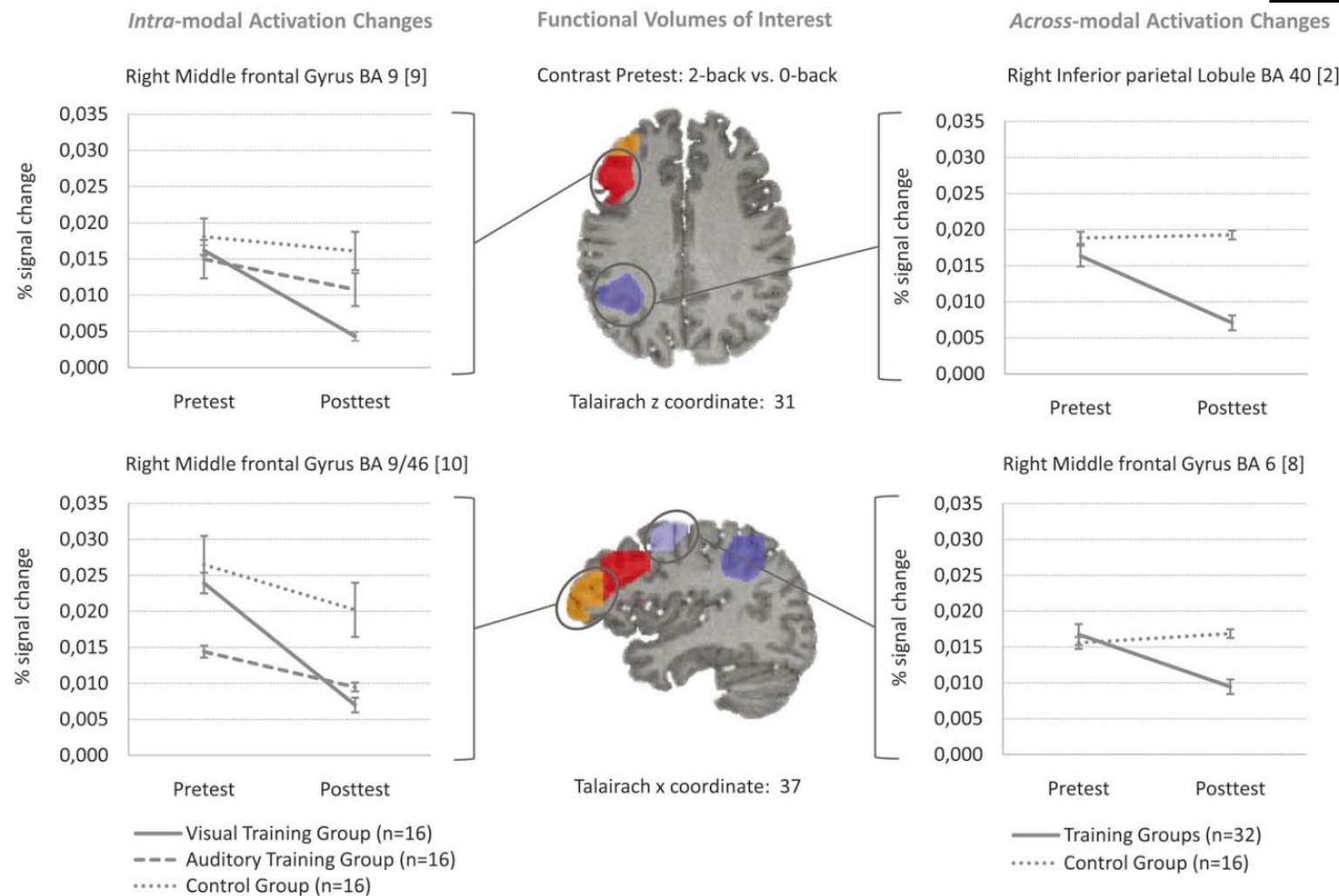
Arbeitsgedächtnistraining



Schneiders et al. 2011

53

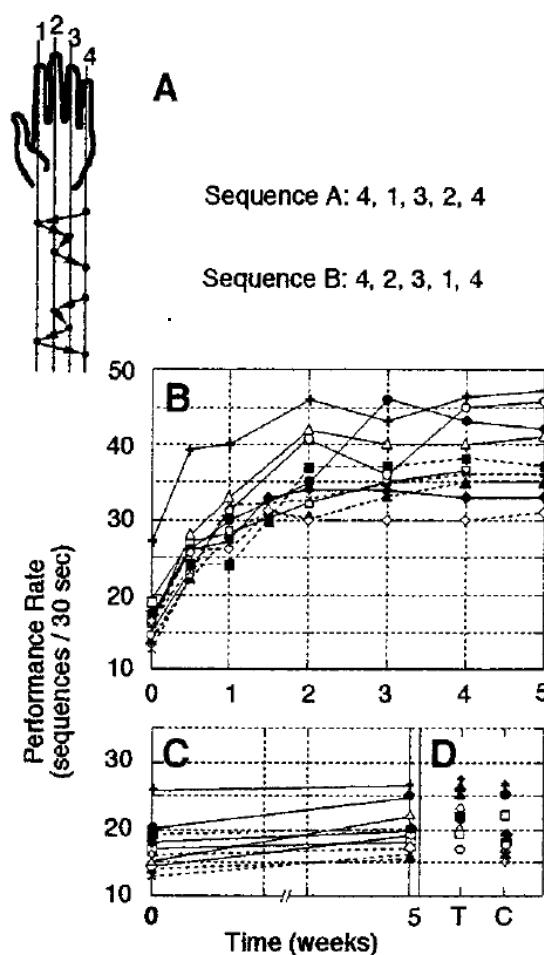
Arbeitsgedächtnistraining



Arbeitsgedächtnistraining

- **Intramodale Effekte:** visuelles Training -> visuelle 2-back Aufgabe.
BA 46/9: Höhere Effizienz beim Speichern von und Zugreifen auf visuelles AG:
- **Intermodale Effekte:** Training (vis & aud) vs Kontrollgruppe.
BA 6: Modalitätsübergreifend höhere Effizienz beim Prozessieren sequentieller Ereignisse

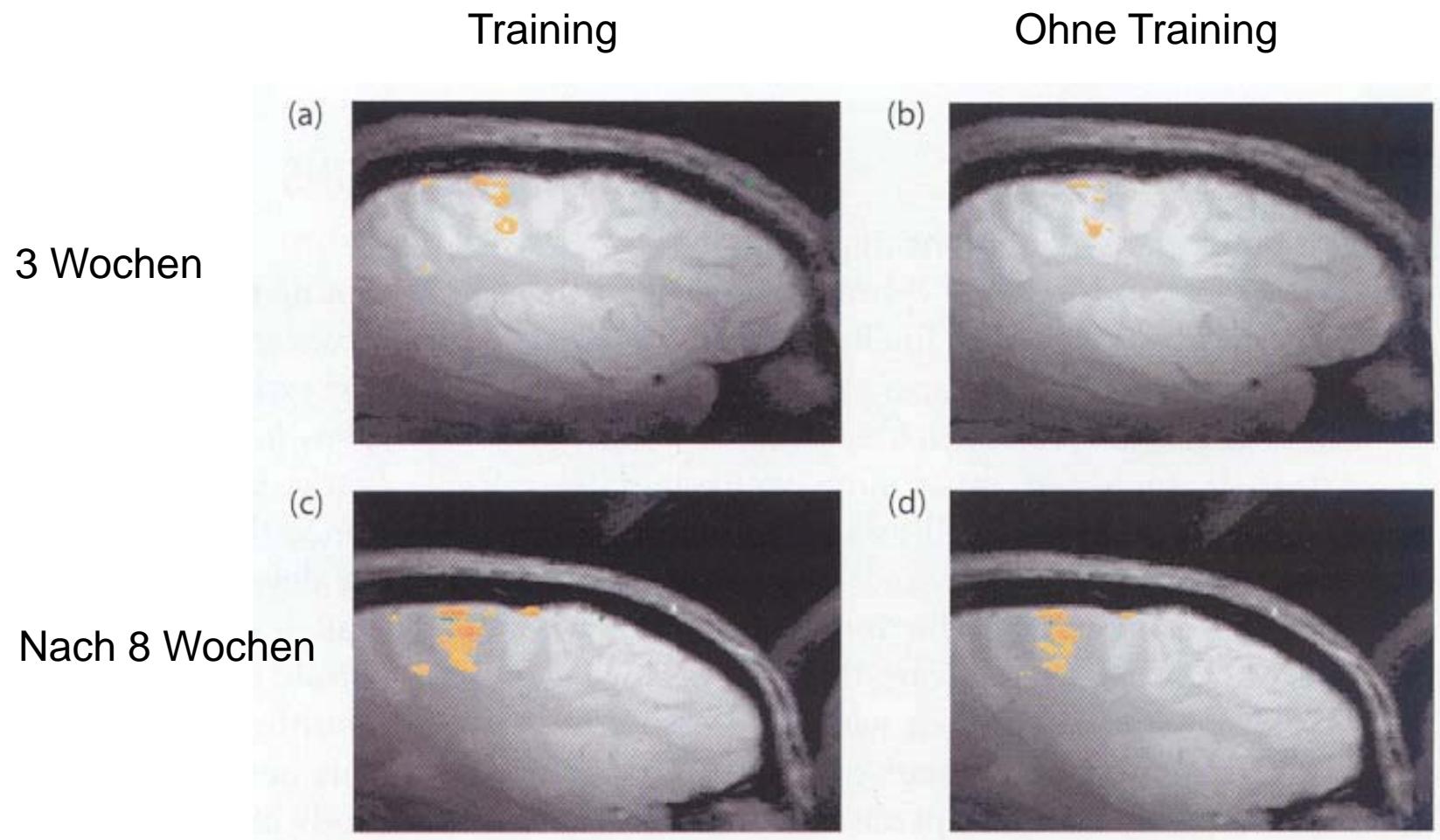
Neuronale Reorganisation in sensorischen Systemen: Veränderte Handrepräsentation durch Fingertraining



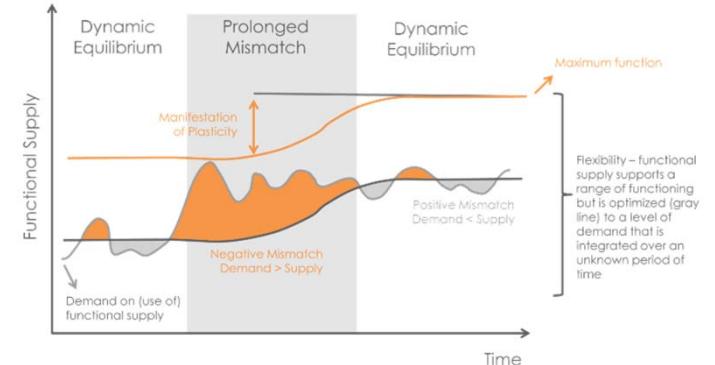
Karni et al. 1998

56

Neuronale Reorganisation in sensorischen Systemen: Veränderte Handrepräsentation durch Fingertraining



Zwei Manifestationen neuronaler Plastizität nach kognitivem Training



- Redistribution



- Aktivierungsabnahmen als Funktion des Trainings (z.B. Arbeitsgedächtnis)
- Aufmerksamkeit und Kontrolle agieren als Baugerüst (Scaffolding)

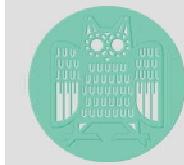
- Reorganisation



- Sensorische und motorische Aufgaben
- Veränderte kognitive Verarbeitung/ Mechanismen nach Training (Fingertraining)
- Synaptogense

? Ausmaß / Dauer des Trainings.

? Interaktions- und Konnektivität zwischen Arealen.



PERSPECTIVES

OPINION

Neurogenesis in the adult brain: death of a dogma

Charles G. Gross

For over 100 years a central assumption in the field of neuroscience has been that new neurons are not added to the adult mammalian brain. This perspective examines the origins of this dogma, its perseverance in the face of contradictory evidence, and its final collapse. The acceptance of adult neurogenesis may be part of a contemporary paradigm shift in our view of the plasticity and stability of the adult brain.

Until very recently, a central dogma of neuroscience has been that new neurons are not added to the adult mammalian brain. For more than 100 years it has been assumed that neurogenesis, or the production of new neurons, occurs only during development and stops before puberty^{1–3}. Indeed, there are few views of the brain that have persisted for so long with so little successful challenge.

This perspective examines the origins of this dogma and discusses how it has persisted even in the face of new techniques that were able to disprove it, how it finally narrowed and is now in disarray. This decline in belief in the stability of the neuronal population seems to be part of a more general paradigm shift⁴ that recognizes the plasticity of the adult brain and its structural modulation by experience.

The dogma up to mid-century

By the end of the nineteenth century, the idea that the brain of the adult mammal remains structurally constant was already universally held by the main figures of the time, including Koelliker⁵, His⁶ and Cajal^{1,7}. What were the

origins of this view? Koelliker, His and others had described in detail the development of the central nervous system of humans and other mammals. They found that the structure of the brain remained fixed from soon after birth. Because the elaborate architecture of the brain remained constant in appearance, the idea that neurons were continually added to it was, understandably, inconceivable. Similarly, Ramón y Cajal and others had also described the different phases in the development of the neuron, terminating with the multipolar structure characteristic of the adult. As neither mitotic figures nor these developmental stages had been seen in the adult brain, the possibility of continuing neuronal addition to the adult brain was rarely, if ever, seriously entertained.

In the first half of the twentieth century, there were occasional reports of postnatal neurogenesis in mammals. For example, Schaper^{8,9} claimed there were "indifferent" cells that were widely distributed in the brain from teleost to human, even into adult life, and that these indifferent cells could become either neurons or glia; and Levi¹⁰ reported mitosis in small, but not large, neurons in brain-injured guinea pigs. At about the same time, Hamilton¹¹ saw mitosis in four-day-old rats; and Allen¹² found mitotic figures in the cerebrum of the rat until at least 120 days after birth. Moreover, Sugita¹³ counted an increased number of cortical neurons in the rat over the first 20 postnatal days; and Bryans¹⁴, using colchicine to freeze mitosis, detected cell division in the brains of rats that were at least one year old. In several of these studies, mitotic fig-

ures were found lining the walls of the lateral ventricle, in the subependymal layer (now termed the subventricular zone) of adult rats. Consequently, the possibility that the new cells arising in the subependymal layer might migrate into the cerebrum to form mature neurons was raised^{11,13,14}.

However, in these and similar studies, it was unclear whether the cells undergoing mitosis subsequently became glia or neurons. As Ramón y Cajal¹ put it in a critique of the earlier of these studies:

"Unfortunately, however, none of the methods used by these investigators are capable of distinguishing absolutely a multiplying neuroglia cell from a small mitotic neuron."

These scattered reports, raising the possibility of adult mammalian neurogenesis, tended to be ignored by textbooks and were rarely cited. Presumably this was because of the weight of authority opposed to the idea and the inadequacy of the available methods both for detecting cell division and for distinguishing glia from small neurons.

Tritiated thymidine

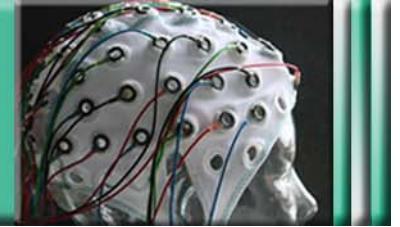
An important advance in the study of neurogenesis came in the late 1950s with the introduction of [³H]-thymidine autoradiography. [³H]-thymidine is incorporated into the DNA of dividing cells. Therefore, the progeny of cells that had just divided could be labelled, and their time and place of birth determined (FIG.1a). Initially, this new method was applied almost exclusively to the study of the developing rodent, particularly by Richard Sidman and his students¹⁵. Their emphasis on using this method to study pre- and perinatal development, rather than looking across the life span of the animal, reflected the persistence of the belief that neurogenesis did not occur in the adult mammal.

In 1961, [³H]-thymidine autoradiography was used for the first time to study proliferation in the adult brain by Smart¹⁶. Whereas he found cells that arose from the subependymal layer and migrated into the adjacent brain to become neurons and glia in three-day-old

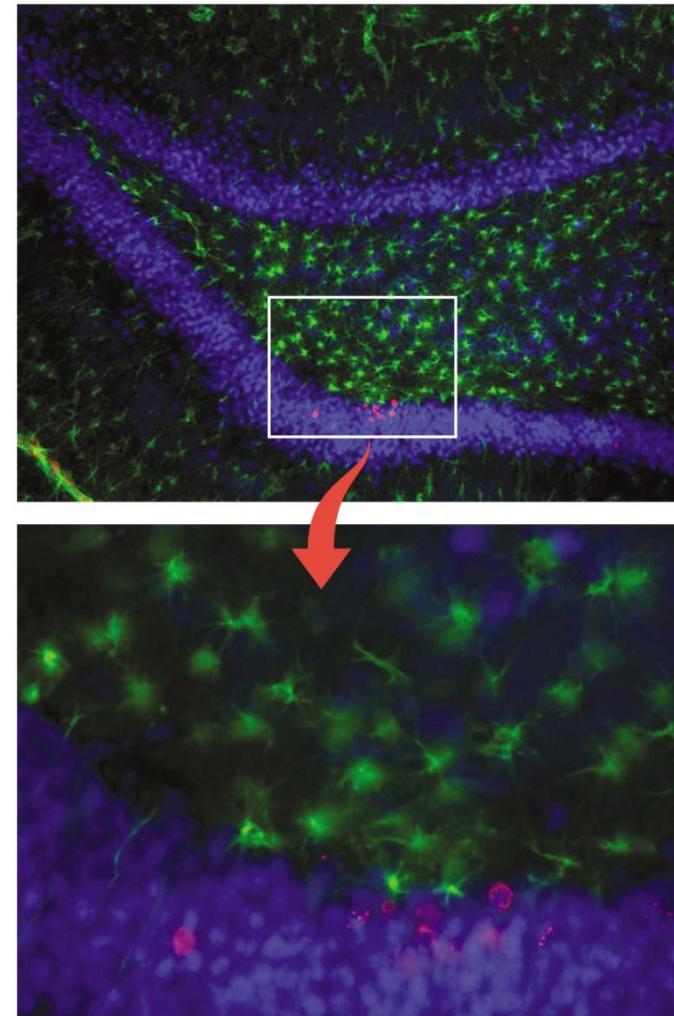




Neurogenese im adulten Gehirn

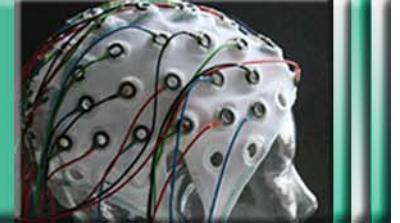


- Zunahme von Neuronen in singrelevanten Gehirnstrukturen bei Singvögeln vor der Paarungssaison.
- Neurogenese im Bulbus olfaktorius und im Hippocampus erwachsener Tiere.
- Adulte neuronale Stammzellen im Ependym wandern zum Bulbus olfaktorius.
- 60% mehr Hc Neurone bei Ratten in stimulierender Umgebung. (?)



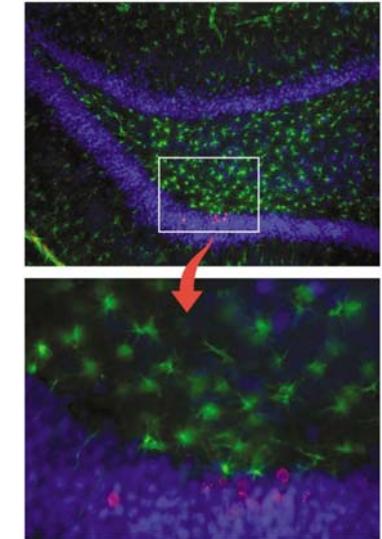


Neurogenese im adulten Gehirn



... ist relevant für Lern- und Gedächtnisvorgänge.

- Neurogenese in gedächtnisrelevanten Arealen.
- Lernbeeinträchtigen nach reduzierter Proliferation im Hc.
- Bedingungen die Hc Proliferation erhöhen verbessern Lernleistung.
- Besserer Erinnerungen in „alten“ (nicht neugebildeten) Schaltkreisen.
- Hc Neurone existieren nur so lange wie Gedächtnisse im Hc repräsentiert sind.



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Danke für Ihre
Aufmerksamkeit!