



Multisensory integration

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Outline

1. Theoretical foundations
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3. Multisensory integration and neuroplasticity
4. Synesthesia

Theoretical foundations

“Multisensory integration refers to the process by which **inputs from two or more senses** are **combined** to form a product that is **distinct** from, and thus **cannot be easily 'deconstructed'** to reconstitute the components from which it is created.” (Stein et al., 2014)



Uta Noppeney

<https://www.ru.nl/en/people/noppeney-u>

“While all of our senses continuously provide the brain with **uncertain information** about our environment, they are **specialized** for different sorts of information and environmental conditions. For instance, **vision** provides us with **precise spatial information** under **optimal lighting** conditions, but it is impaired in darkness and blind to sources behind us. Conversely, **audition** tends to be inferior to vision in its spatial precision during the daytime, yet it can **exceed vision** in **darkness** and provide spatial information about sources outside our current field of view.”

“These considerations highlight the extraordinary benefits that we gain from **collaborative interactions** across all our **senses**, combining their **complementary strengths** and mitigating their individual limitations. **Multisensory integration is one of the brain’s key strategies to reduce its uncertainty and resolve ambiguities about the current state of the world.** It is thus critical for effective interactions with our environment in everyday life.” (Noppeney, 2020)



Combining inputs

seeing the animal's tail &
hearing the rustling of foliage
=> **faster** and **more accurate** to
detect a potential threat

Increasing robustness and precision




back turned => **no visual input**,
but **hearing** to sources (i.e. source localization)
outside of field of view is **more precise**

Human echolocation



<https://www.youtube.com/watch?v=xATlyq3uZM4>

Mouth-clicks used by blind expert human echolocators – signal description and model based signal synthesis

Lore Thaler  , Galen M. Reich , Xinyu Zhang, Dinghe Wang, Graeme E. Smith, Zeng Tao, Raja Syamsul Azmir Bin. Raja Abdullah, Mikhail Cherniakov, Christopher J. Baker, Daniel Kish, Michail Antoniou

Published: August 31, 2017 • <https://doi.org/10.1371/journal.pcbi.1005670>

Abstract

Echolocation is the ability to use sound-echoes to infer spatial information about the environment. Some **blind people** have developed extraordinary proficiency in echolocation using **mouth-clicks**. The first step of human biosonar is the transmission (mouth click) and subsequent reception of the resultant sound through the ear. Existing head-related transfer function (HRTF) data bases provide descriptions of reception of the resultant sound. For the current report, **we collected a large database of click emissions with three blind people expertly trained in echolocation**, which allowed us to perform unprecedented analyses. Specifically, the current report provides the first ever **description of the spatial distribution (i.e. beam pattern) of human expert echolocation transmissions, as well as spectro-temporal descriptions** at a level of detail not available before. Our data show that **transmission levels are fairly constant within a 60° cone emanating from the mouth, but levels drop gradually at further angles**, more than for speech. In terms of spectro-temporal features, our data show that emissions are consistently very brief (~3ms duration) with peak frequencies 2-4kHz, but with energy also at 10kHz. This differs from previous reports of durations 3-15ms and peak frequencies 2-8kHz, which were based on less detailed measurements. Based on our measurements we propose to model transmissions as sum of monotonies modulated by a decaying exponential, with angular attenuation by a modified cardioid. We provide model parameters for each echolocator. These results are a step towards developing computational models of human biosonar. For example, in bats, spatial and spectro-temporal features of emissions have been used to derive and test model based hypotheses about behaviour. The data we present here suggest similar research opportunities within the context of human echolocation. Relatedly, the data are a basis to develop synthetic models of human echolocation that could be virtual (i.e. simulated) or real (i.e. loudspeaker, microphones), and which will help understanding **the link between physical principles and human behaviour**.

<https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1005670>

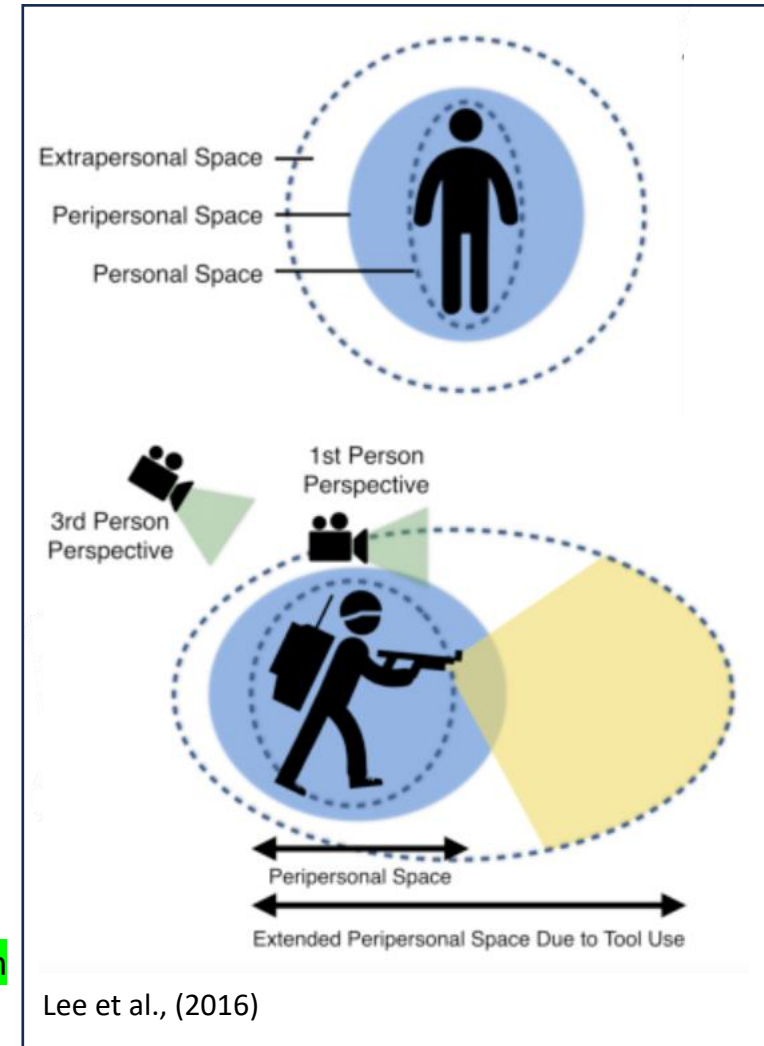
Enhanced audio-tactile multisensory interaction in a peripersonal task after echolocation

Alessia Tonelli,¹ Claudio Campus,¹ Andrea Serino,^{2,3} and Monica Gori¹

Abstract

Peripersonal space (PPS) is created by a multisensory interaction between different sensory modalities and can be modified by experience. In this article, we investigated whether an auditory training, inside the peripersonal space area, can modify the PPS around the head in sighted participants. The auditory training was based on echolocation. We measured the participant's reaction times to a tactile stimulation on the neck, while task-irrelevant looming auditory stimuli were presented. Sounds more strongly affect tactile processing when located within a limited distance from the body. We measured spatially dependent audio-tactile interaction as a proxy of PPS representation before and after an echolocation training. We found a significant speeding effect on tactile RTs after echolocation, specifically when sounds were around the location where the echolocation task was performed. This effect could not be attributed to a task repetition effect nor to a shift of spatial attention, as no changes of PPS were found in two control groups of participants, who performed the PPS task after either a break or a temporal auditory task (with stimuli located at the same position of echolocation task). These findings show that echolocation affects multisensory processing inside PPS representation, likely to better represent the space where external stimuli have to be localized.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6394550/>



Theoretical background

“An important property of **PPS representation** is that it **dynamically modifies through experience**, i.e., by short and long-term **tool-use**, social interaction and potential movements.”

“In this study, **we investigated whether** a novel form of exploring and interacting with the environment through sounds (**echolocation**) **shapes PPS representation**. Echolocation is based on the ability to measure the time delay between a sound and any echoes reflected by the environment. Specifically, using self-generated sounds, expert echolocators are able to navigate and detect an object present in the environment. Therefore, **echolocation can be conceived as a form of tool-use** able to modify the PPS. Echolocation can be used to “reach” sectors of space which are normally out of reach without visual information, thanks to the interpretation of the echoes produced by sound reflections on the objects.”

“To this aim, we **evaluated** the **PPS** around the head **before and after** an **echolocation** detection task.”

Procedure: determining individual PPS

“All participants started the experiment **blindfolded**. First, we **evaluated the PPS** for all participants (Fig. 1a), to **assess the location of their PPS boundary** before any training. Then participants were divided into three groups: **ECHO**, **TIME**, and **REST** group.”

“To **quantify the PPS** [...] participants had to respond as **fast** as possible to a **tactile stimulus** applied to their body, while task-irrelevant sounds were presented, giving the impression of a looming sound. Previous results showed that **sounds speeded up the detection of tactile stimuli** specifically when presented at a certain distance from the participants (and not farther from them). Such distance can be measured as a **proxy of the extent of the participant’s PPS**.”

Tonelli et al., (2019)

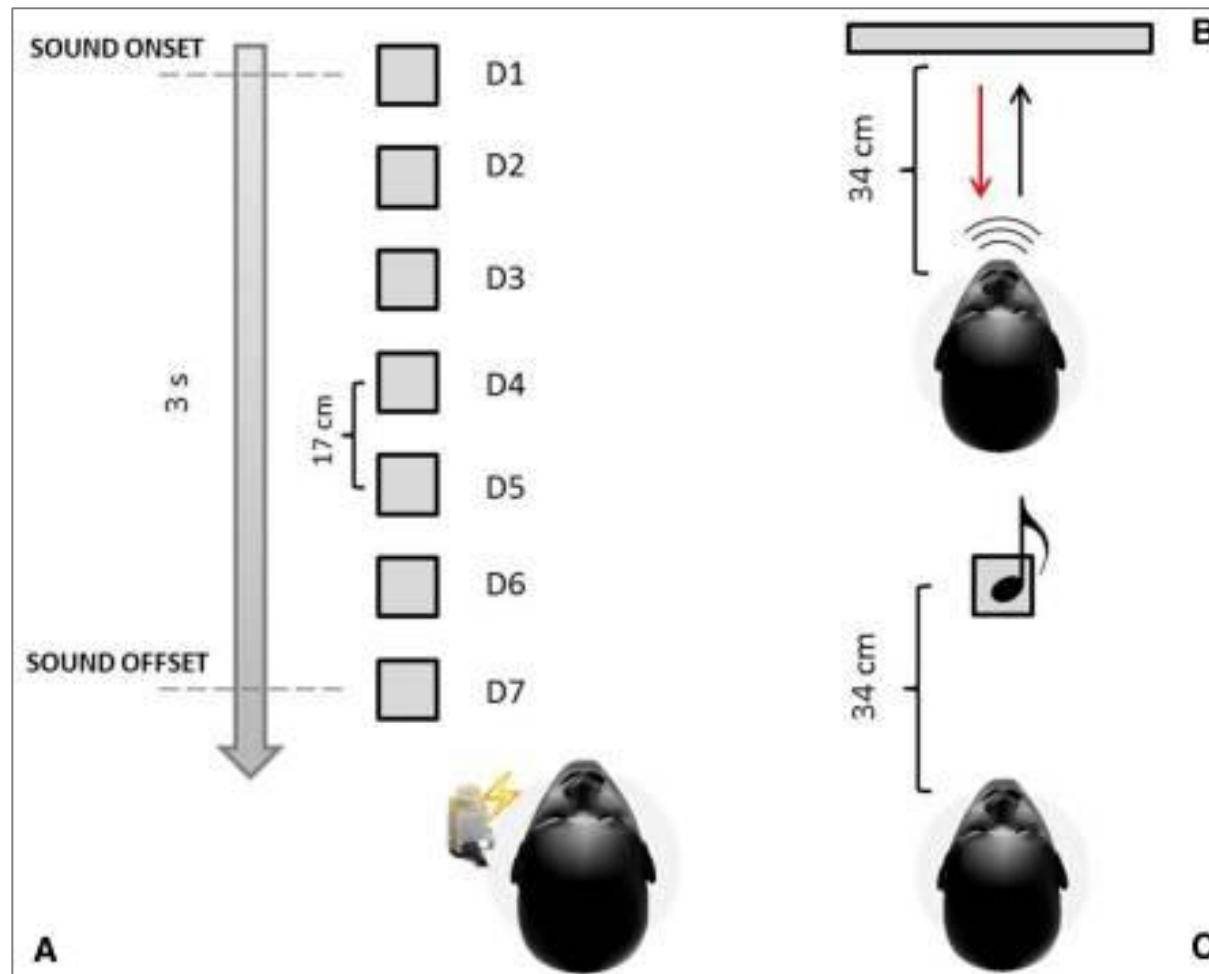
Procedure: the echolocation detection task

“A **rectangular bar** made of poly-methyl methacrylate (40 × 30 cm) was used as a **target stimulus for the echolocation training**. The bar was located in front of the participant at the head level.”

“The first group—ECHO group—(N = 14; 7 females) performed an **echolocation detection task** after the evaluation of the PPS. [...] Participants **had no knowledge of echolocation technique**, therefore, before the beginning of the task, they received instructions on how to produce the echolocation signals with their mouth [...]. **The echolocation sound was naturally produced, using no external device**. While the **experimenter moved the target**, participants wore headphones played mixed music. Once the experimenter placed the target, the participant received a patch on the shoulder as a signal to remove the headphones and start the trial.

Participants had to judge whether the bar was in front of them or not, producing mouth clicks and estimating their echoes (Fig. 1b).”

Procedure: overview



Tonelli et al., (2019)

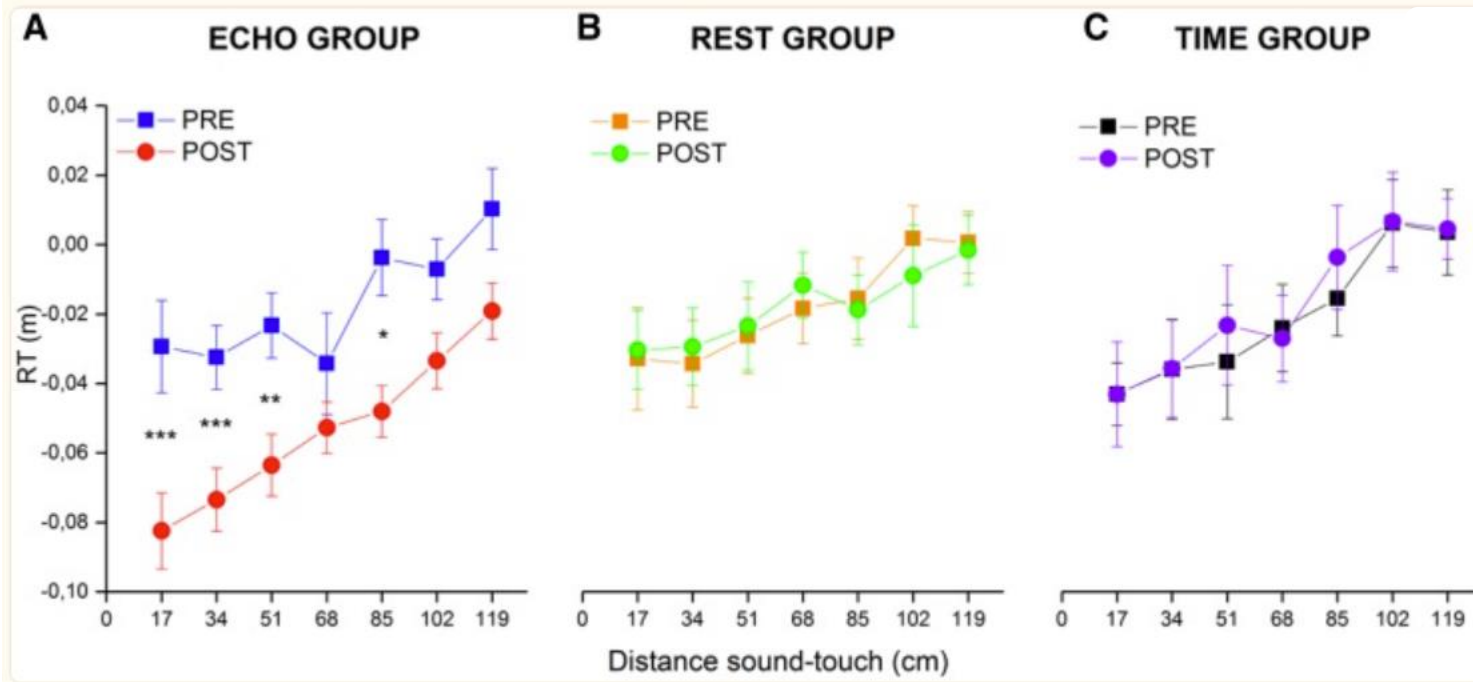
Fig 1. Experimental set-ups.

a The set-up for the PPS task is shown. There were seven speakers generating sound sources at a different distance from the body. The first sound source was placed 17 cm apart from the left side of the head of each participant. The sound moved across the speakers as approaching the participant's head (grey arrow). The vibro-tactile device was placed on the left side of the neck. The tactile stimulus was delivered when the sound was placed at one of the seven possible depicted distances 17, 34, 51, 68, 85, 102, 119).

b The set-up for the echolocation detection task is shown. We used a bar located at 34 cm ahead the participant. The black and the red arrows represent, respectively, the path of the self-generated click and the echo reflected by the bar.

c The set-up of the temporal bisection task is shown.

Results



The **averaged bimodal RTs** (normalized for the unimodal RTs) for each group is shown as a function of the **seven distances** sampled during the PPS task. Data for the **ECHO** group before (in blue) and after (in red) the echolocation training. Data for the **TIME** group before (in green) and after (in orange) the time bisection task. Data for the **REST** group before (in magenta) and after (in cyan) 15 min of break.

*Significant difference with $p < 0.05$.

***Significant difference with $p < 0.001$.

The error bars represent the standard error.

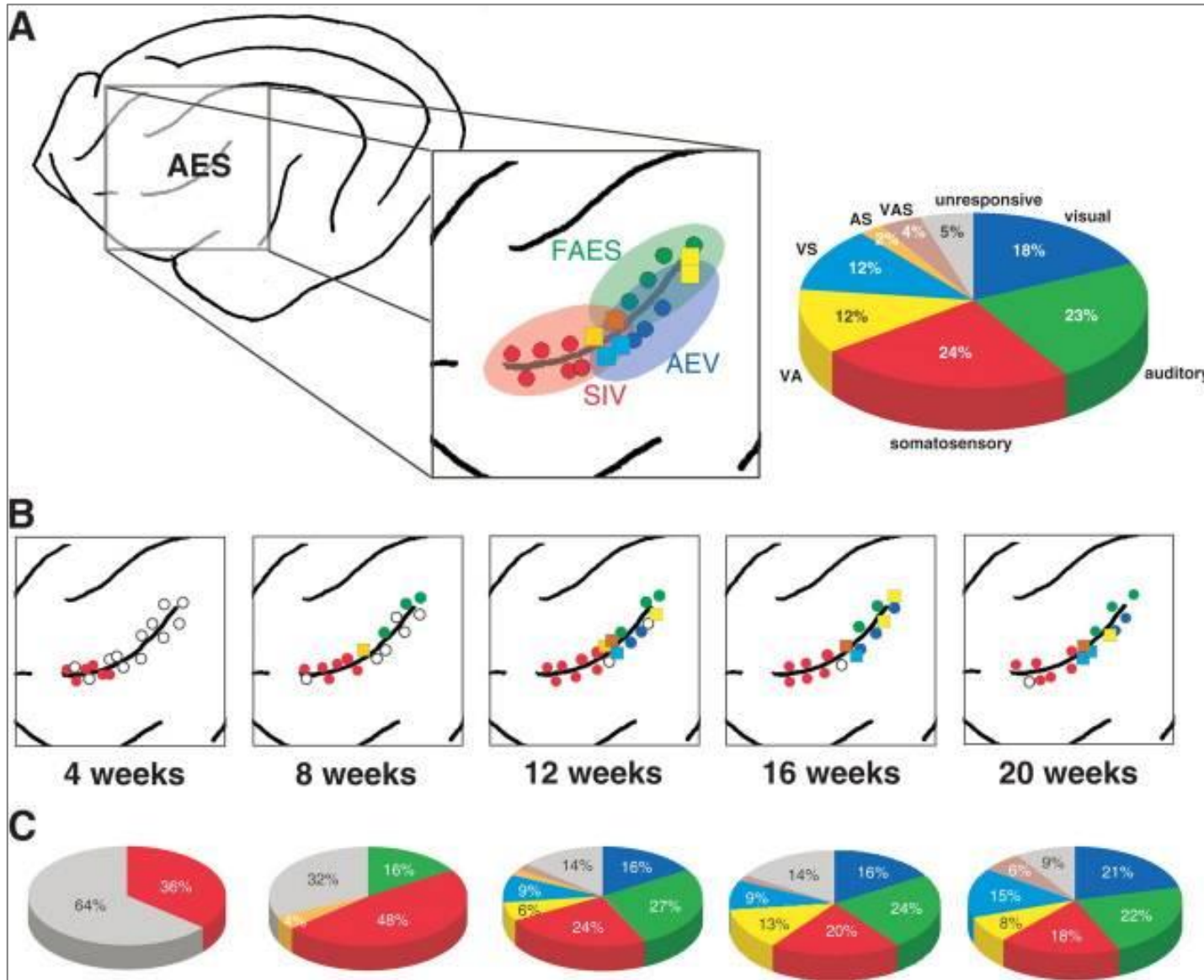
Conclusion

“In the present study, we showed that performing echolocation training with stimuli in the near space, affected multisensory interaction within the PPS.”

The superior colliculus

Multisensory integration is **not predetermined** => experience-driven.

“[...] **multisensory development** does not require that each individual sense reaches its maturational end point [...]. Rather, multisensory development and **unisensory development** are **interconnected** but **parallel** processes.” (Stein et al., 2014)



multisensory neurons

neurons that respond to stimuli from more than one sensory modality

The developmental chronology of sensory and multisensory responses in **anterior ectosylvian sulcus (AES) cortex**.

A, Schematic drawing of the lateral surface of the **cat cortex** showing the **location of the AES in the adult**. Inset shows the modality distributions of neurons within the **three major subdivisions of AES: somatosensory division (SIV), presumptive auditory (FAES), and presumptive visual (AEV)**. **Colored circles** represent penetrations in which only **unisensory neurons** [...] were found. [...] **Pie graph** shows the **modality distributions in the adult** and is pooled for the three animals.

B, Emergence of sensory-responsive neuron types as a function of **postnatal age**. [...]

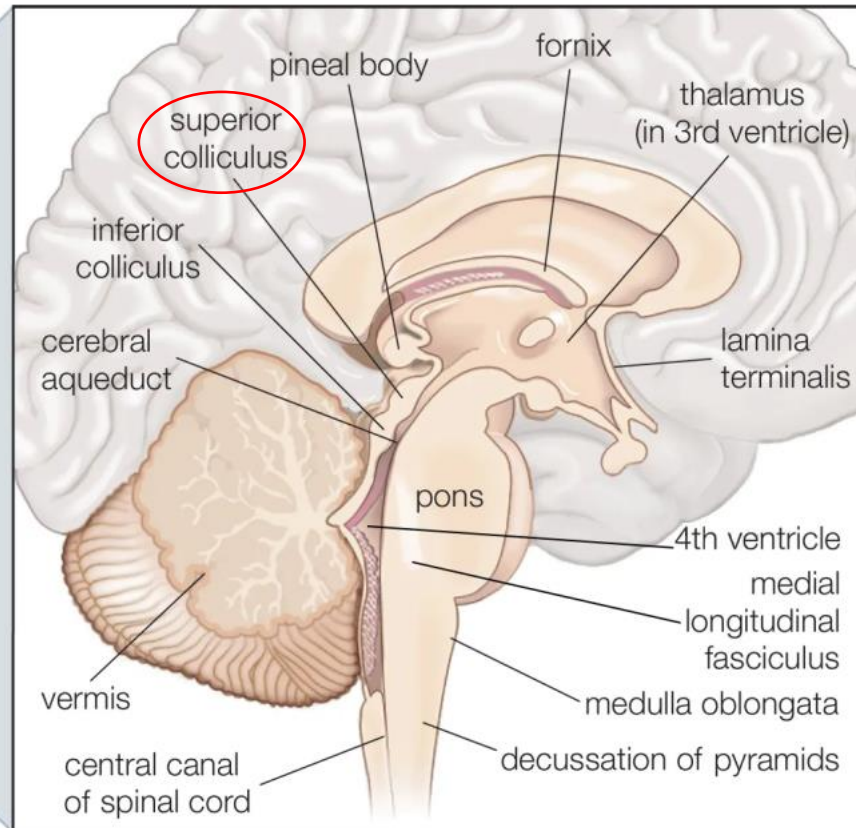
C, **Modality distributions in AES at the sampled ages**. [...]

Wallace et al. (2006); <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6674880/>

unisensory: **red**, somatosensory; **green**, auditory; **blue**, visual

multisensory: **light blue**, auditory–somatosensory (AS); **yellow**, visual–auditory (VA); **orange**, visual–somatosensory (VS); **brown**, visual–auditory–somatosensory (VAS)

4th ventricle and cerebellum in situ



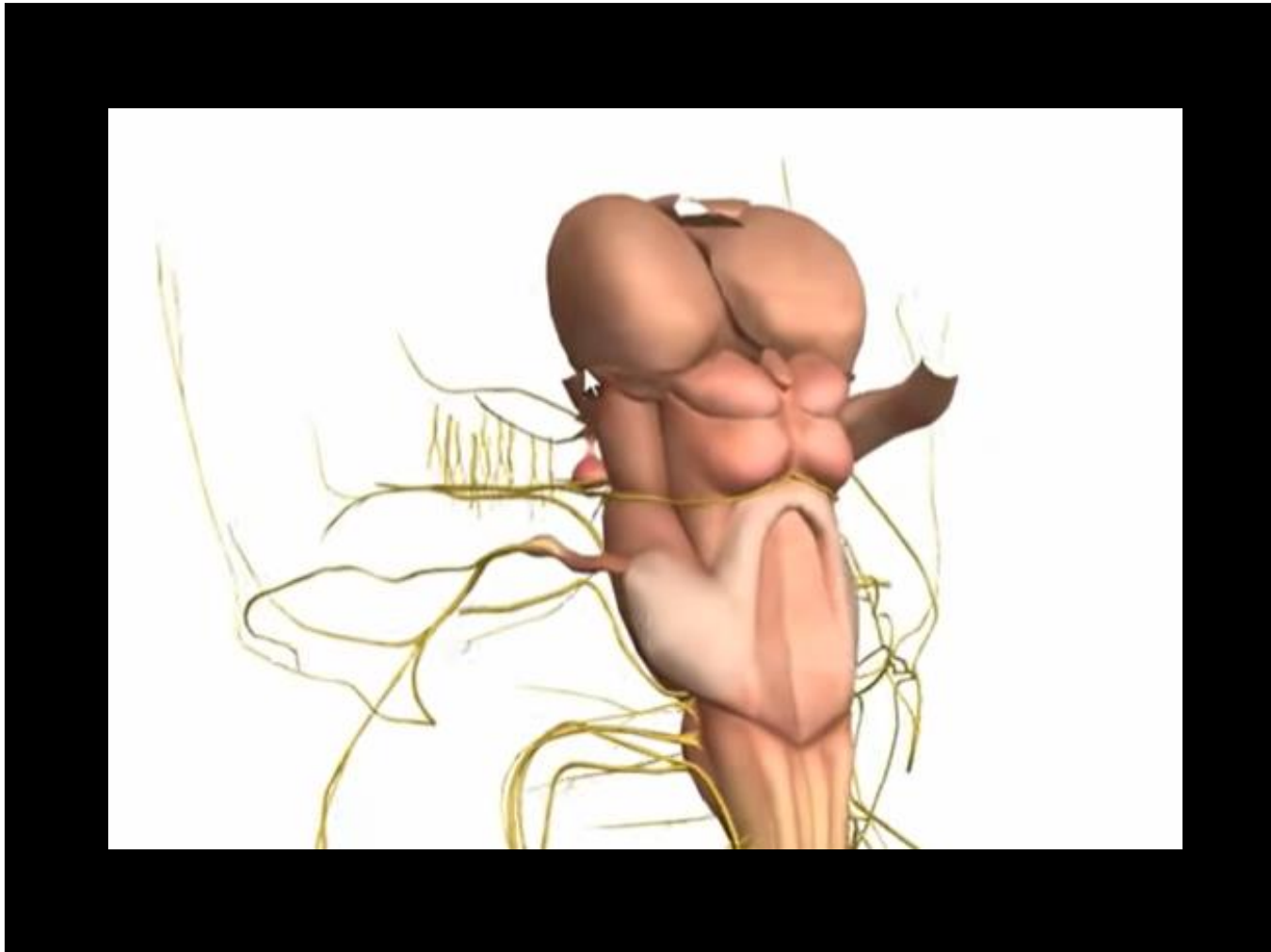
© 2012 Encyclopædia Britannica, Inc.

<https://www.britannica.com/science/midbrain#ref1114747>

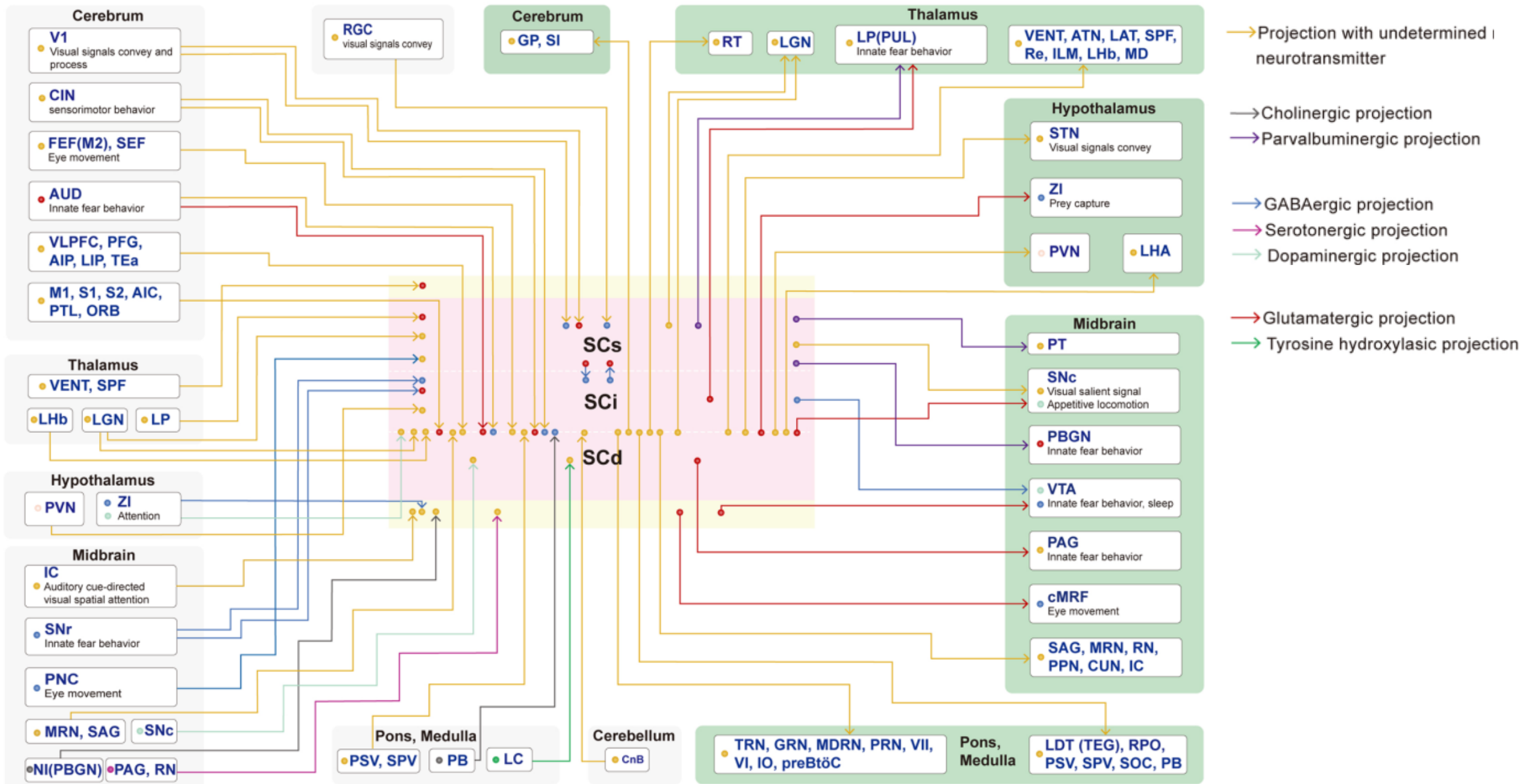
- receives **visual** information from the **retina** via the optic nerve and tract;
- receives **auditory** input from the **inferior colliculus** to coordinate a movement response;
- receives inputs from the **prefrontal cortex** involved in the regulation of **attention** and **distractibility**;
- responds to **tactile** stimuli;

- projects to the **oculomotor, trochlear, and abducens** nuclei => controls the six extraocular muscles;
- stimulates the contralateral deep **neck muscles** during a **gaze shift**; these muscles are ipsilateral to the visual field being stimulated and function to **turn the head and eyes towards the stimulus**.

3D visualization of midbrain structures



<https://anatomyzone.com/neuroanatomy/structure-of-the-nervous-system/basic-parts-of-the-brain/>



Multisensory integration and neuroplasticity

Initiating the development of multisensory integration by manipulating sensory experience

Liping Yu¹, Benjamin A Rowland, Barry E Stein

Abstract

The multisensory integration capabilities of superior colliculus neurons emerge gradually during early postnatal life as a consequence of experience with cross-modal stimuli. Without such experience neurons become responsive to multiple sensory modalities but are unable to integrate their inputs.

The present study demonstrates that neurons retain sensitivity to cross-modal experience well past the normal developmental period for acquiring multisensory integration capabilities. Experience surprisingly late in life was found to rapidly initiate the development of multisensory integration, even more rapidly than expected based on its normal developmental time course. Furthermore, the requisite experience was acquired by the anesthetized brain and in the absence of any of the stimulus-response contingencies generally associated with learning. The key experiential factor was repeated exposure to the relevant stimuli, and this required that the multiple receptive fields of a multisensory neuron encompassed the cross-modal exposure site. Simple exposure to the individual components of a cross-modal stimulus was ineffective in this regard. Furthermore, once a neuron acquired multisensory integration capabilities at the exposure site, it generalized this experience to other locations, albeit with lowered effectiveness. These observations suggest that the prolonged period during which multisensory integration normally appears is due to developmental factors in neural circuitry in addition to those required for incorporating the statistics of cross-modal events; that neurons learn a multisensory principle based on the specifics of experience and can then apply it to other stimulus conditions; and that the incorporation of this multisensory information does not depend on an alert brain.

<https://pubmed.ncbi.nlm.nih.gov/20371810/>

neuroplasticity

the ability of the nervous system to **change its activity** in response to intrinsic or extrinsic stimuli by **reorganizing its structure, functions, or connections**

Clinically, it is the process of **brain changes after injury**, such as a stroke or traumatic brain injury (TBI). These changes can either be **beneficial** (restoration of function after injury), **neutral** (no change), or **negative** (can have pathological consequences).

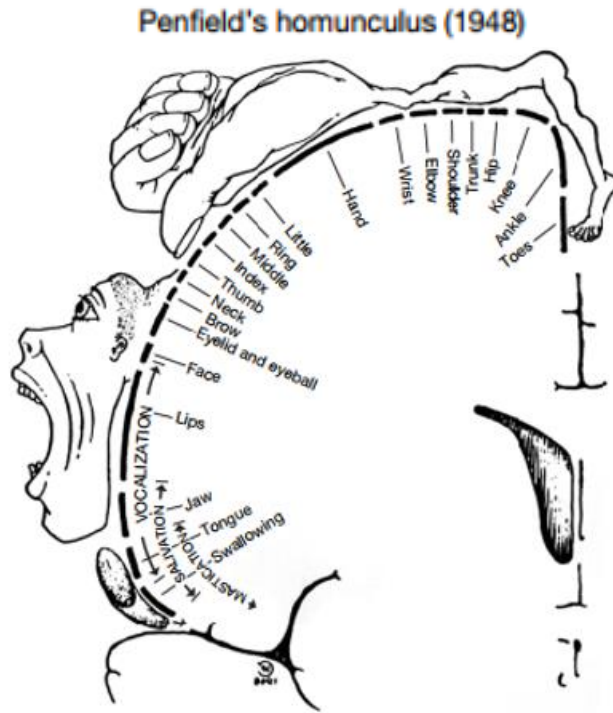
(for more please see: <http://tinyurl.com/3h67t5vt>)

The “homunculus” is plastic

> J Neurosci. 2000 May 15;20(10):3884-99. doi: 10.1523/JNEUROSCI.20-10-03884.2000.

Progressive transneuronal changes in the brainstem and thalamus after long-term dorsal rhizotomies in adult macaque monkeys

T M Woods ¹, C G Cusick, T P Pons, E Taub, E G Jones



Gordon et al., (2023)

This study deals with a potential brainstem and thalamic substrate for the **extensive reorganization of somatosensory cortical maps that occurs after chronic, large-scale loss of peripheral input**. Transneuronal atrophy occurred in neurons of the dorsal column (DCN) and ventral posterior lateral thalamic (VPL) nuclei in **monkeys** subjected to cervical and upper thoracic dorsal rhizotomies for 13–21 years and that had shown extensive representational plasticity in somatosensory cortex and thalamus in other experiments. Volumes of DCN and VPL, number and sizes of neurons, and neuronal packing density were measured by unbiased stereological techniques. When compared with the opposite, unaffected, side, the ipsilateral cuneate nucleus (CN), external cuneate nucleus (ECN), and contralateral VPL showed reductions in volume: 44–51% in CN, 37–48% in ECN, and 32–38% in VPL. In the affected nuclei, neurons were progressively shrunken with increasing survival

time, and their packing density increased, but there was relatively little loss of neurons (10–16%). There was evidence for loss of axons of atrophic CN cells in the medial lemniscus and in the thalamus, with accompanying severe disorganization of the parts of the ventral posterior nuclei representing the normally innervated face and the deafferented upper limb. Secondary transneuronal atrophy in VPL, associated with retraction of axons of CN neurons undergoing primary transneuronal atrophy, is likely to be associated with similar withdrawal of axons from the cerebral cortex and should be a powerful influence on reorganization of somatotopic maps in the somatosensory cortex.

Key words: plasticity; dorsal rhizotomy; transneuronal atrophy; dorsal column nuclei; ventral posterior lateral nucleus; stereology

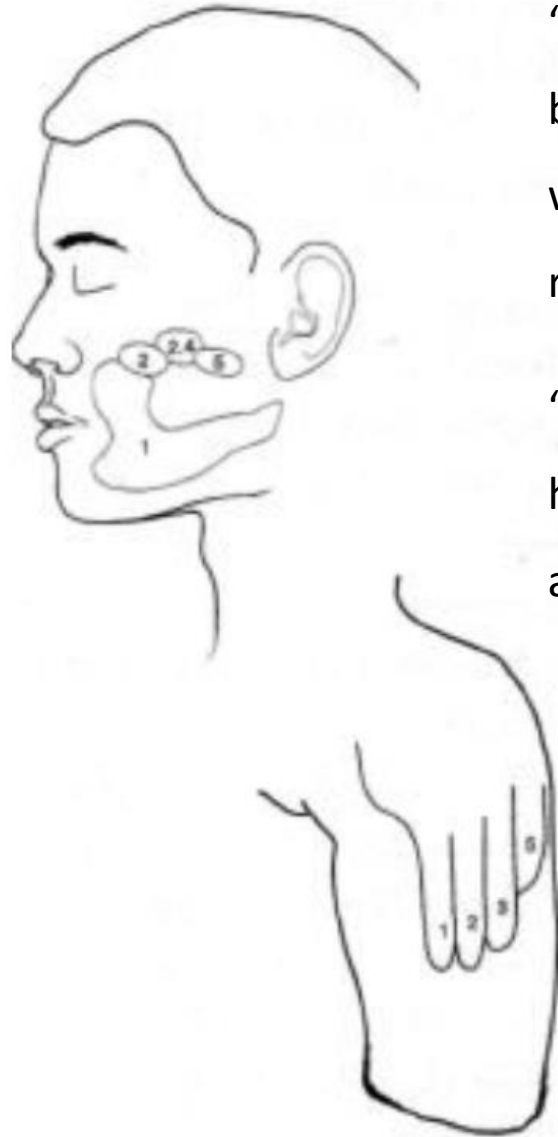
<https://pubmed.ncbi.nlm.nih.gov/10804228/>

dorsal rhizotomy = severing of all the nerve fibers carrying sensory information from one arm into the spinal cord

Over ten years later => stimulating the denervated hand elicited **no activity in the “hand” area, but it did in the monkey’s “face” area.**

“The implications of this finding are astonishing: It means that you can change the map; you can alter the brain circuitry of an adult animal, and connections can be modified over distances spanning a centimeter or more.”

Phantom limb



"[...] Tom **lost his left arm just above the elbow**. [...] Tom could still **feel its ghostly presence** below the elbow. He could wiggle each "finger," "reach out" and "grab" objects that were within arm's reach. [...] Since Tom had been **left-handed, his phantom would reach** for the receiver whenever the telephone rang."

"[...] I placed a **blindfold** over his eyes because I didn't want him to see where I was touching him. Then I took an ordinary Q-tip and started **stroking** various parts of his **body surface**, asking him to tell me **where** he felt the sensations."

I swabbed his cheek. "What do you feel?"

"You are touching my cheek."

"Anything else?"

"Hey, you know it's funny," said Tom. "**You're touching my missing thumb**, my phantom thumb."

I moved the Q-tip to his upper lip. "How about here?"

"You're touching my index finger. And my upper lip."

Phantom limb



“I soon **found a complete map of Tom's phantom hand—on his face!** I realized that what I was seeing was perhaps a direct perceptual correlate of the remapping that **Tim Pons** had seen in his monkeys. For there is no other way of explaining why touching an area so far away from the stump—namely, the face—should generate sensations in the phantom hand; **the secret lies in the peculiar mapping of body parts in the brain**, with the face lying right beside the hand.”

“But I also found a **second**, beautifully laid out “**map**” of his missing hand— tucked onto his **left upper arm** a few inches above the line of amputation.”

“Why were there **two maps** instead of just one? If you look again at the **Penfield map**, you'll see that the hand area in the brain is flanked below by the face area and above by the upper arm and shoulder area.”

Neurological Review

March 2000

Phantom Limbs and Neural Plasticity

Vilayanur S. Ramachandran, MD, PhD; Diane Rogers-Ramachandran, PhD

» [Author Affiliations](#) | [Article Information](#)

Arch Neurol. 2000;57(3):317-320. doi:10.1001/archneur.57.3.317

“We tested 18 patients with either **arm amputation** or **brachial avulsion**, and found that 8 patients systematically referred **sensation from the face to the phantom limb**. In many of them, there was a **topographically organized map of the hand on the lower face region** (Figure 2) and the referred sensations were **modality specific**. For example, hot, cold, vibration, rubbing, metal, or massage are felt as hot, cold, vibration, rubbing, metal, and massage at precisely localized points on the phantom limb.”



Figure 2. Points on the face of a patient that elicit precisely localized, modality-specific referral in the phantom limb 4 weeks after amputation of the left arm below the elbow. **Sensations were felt simultaneously on the face and phantom limb.**

<https://jamanetwork.com/journals/jamaneurology/fullarticle/776122>

A brachial plexus avulsion occurs when the root of the nerve is completely separated from the spinal cord. This injury is usually caused by trauma, such as a car or motorcycle accident. More severe than ruptures, avulsions often cause severe pain. Because it is difficult and usually impossible to reattach the root to the spinal cord, avulsions can lead to permanent weakness, paralysis and loss of feeling. (<http://tinyurl.com/3vm2rvb2>)

Phantom limb pain and mirror box therapy



Vilayanur Subramanian Ramachandran



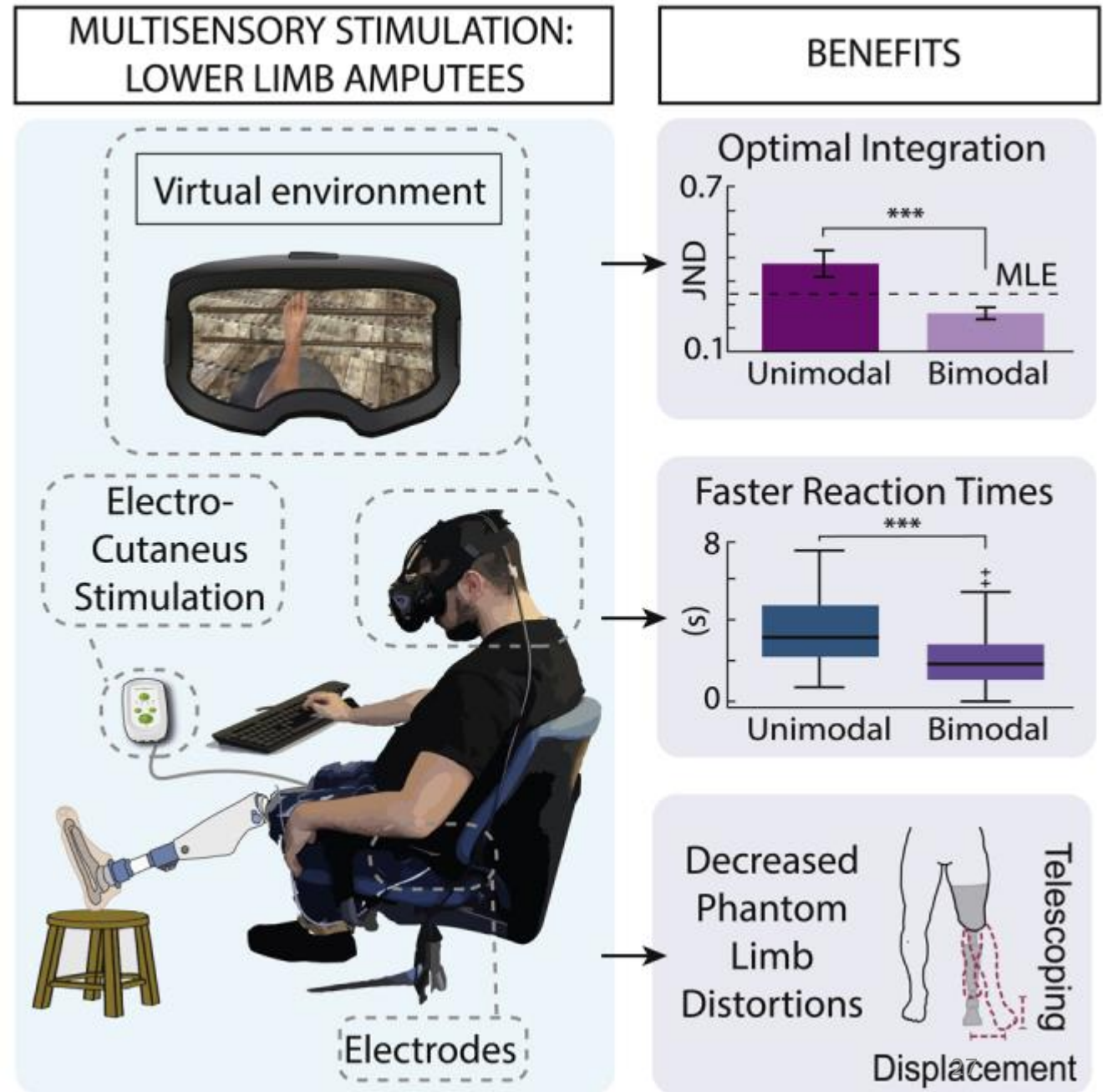
https://www.youtube.com/watch?v=gc3CmS8_vUI

Phantom limb and virtual reality therapy

Explanation of the procedures and results by the authors



Risso et al., (2022), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8980810/>



Phantom limb pain: a case of maladaptive CNS plasticity?

<https://www.nature.com/articles/nrn1991>

[Herta Flor](#) , [Lone Nikolajsen](#) & [Troels Staehelin Jensen](#)

[Nature Reviews Neuroscience](#) 7, 873–881 (2006) | [Cite this article](#)

“It has been reported that **topographical referred phantom sensations** occur in **only a small percentage of amputees**, whereas **phantom limb pain is common**; this suggests that **referred phantom sensation and phantom pain might be related to different central processes**. [...] Imaging studies have reported that upper extremity amputees actually show a **shift of the mouth into the hand representation** in the SI cortex. [...] **The larger the shift** of the mouth representation into the zone that formerly represented the arm, **the more pronounced the phantom limb pain.**”



Functional MRI data from seven patients **with phantom limb pain**, seven **amputees without pain** and seven **healthy controls** during a **lip pursing task**. Activation in primary somatosensory and motor cortices is **unaltered in amputees without pain** and is **similar to that of healthy controls**. In the **amputees with phantom limb pain** the **cortical representation of the mouth extends into the region of the hand and arm**.

(Based on Lotze et al., (2001), <https://pubmed.ncbi.nlm.nih.gov/11673327/>)

Synesthesia



What Synesthesia Can Tell Us About Connections in the Brain

<https://www.youtube.com/watch?v=IBm4fvCwcGM>

synesthesia

the ability to perceive an **internally generated sensation in one sensory modality** triggered by a stimulus coming from **another sensory modality**

Grapheme-color synesthesia

=> most widely studied;

=> perceiving written and heard letters in different colors.

Synesthetic experience is **idiosyncratic**

=> the same inducer always triggers the same concurrent for one synesthete.

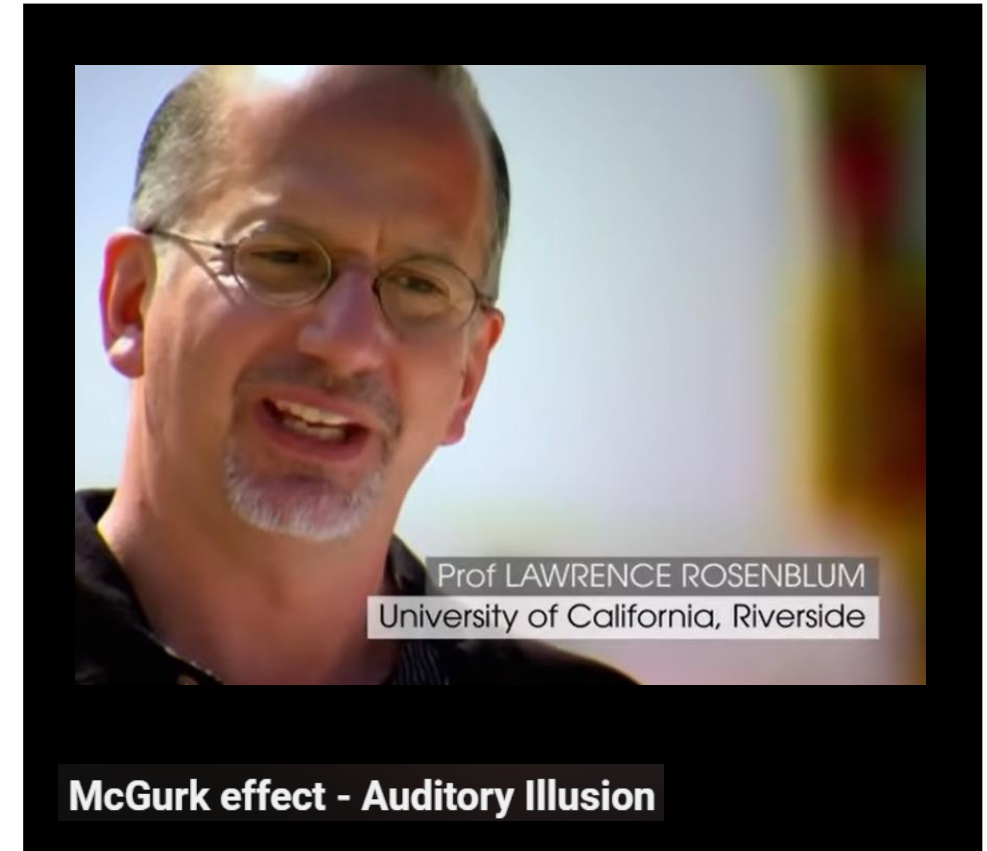
› J Neuropsychol. 2014 Mar;8(1):94-106. doi: 10.1111/jnp.12006. Epub 2012 Dec 20.

Reduced audiovisual integration in synesthesia-- evidence from bimodal speech perception

Christopher Sinke ¹, Janina Neufeld, Markus Zedler, Hinderk M Emrich, Stefan Bleich, Thomas F Münte, Gregor R Szykik

Recent research suggests synesthesia as a result of a hypersensitive multimodal binding mechanism. To address the question whether multimodal integration is altered in synesthetes in general, grapheme-colour and auditory-visual synesthetes were investigated using speech-related stimulation in two behavioural experiments. First, we used the McGurk illusion to test the strength and number of illusory perceptions in synesthesia. In a second step, we analysed the gain in speech perception coming from seen articulatory movements under acoustically noisy conditions. We used disyllabic nouns as stimulation and varied signal-to-noise ratio of the auditory stream presented concurrently to a matching video of the speaker. We hypothesized that if synesthesia is due to a general hyperbinding mechanism this group of subjects should be more susceptible to McGurk illusions and profit more from the visual information during audiovisual speech perception. The results indicate that there are differences between synesthetes and controls concerning multisensory integration – but in the opposite direction as hypothesized. Synesthetes showed a reduced number of illusions and had a reduced gain in comprehension by viewing matching articulatory movements in comparison to control subjects. Our results indicate that rather than having a hypersensitive binding mechanism, synesthetes show weaker integration of vision and audition.

<https://pubmed.ncbi.nlm.nih.gov/23279836/>



<https://www.youtube.com/watch?v=2k8fHR9jKVM>

Further resources

2023: A Review of the Year in Neuroscience



<https://medium.com/the-spike/2023-a-review-of-the-year-in-neuroscience-ece56b1dcc89>

Further reading

Review > Prog Brain Res. 2011;191:145-63. doi: 10.1016/B978-0-444-53752-2.00007-2.

Organization and plasticity in multisensory integration: early and late experience affects its governing principles

Barry E Stein ¹, Benjamin A Rowland

Abstract

Neurons in the midbrain superior colliculus (SC) have the ability to integrate information from different senses to profoundly increase their sensitivity to external events. This not only enhances an organism's ability to detect and localize these events, but to program appropriate motor responses to them. The survival value of this process of multisensory integration is self-evident, and its physiological and behavioral manifestations have been studied extensively in adult and developing cats and monkeys. These studies have revealed, that contrary to expectations based on some developmental theories this process is not present in the newborn's brain. The data show that is acquired only gradually during postnatal life as a consequence of at least two factors: the maturation of cooperative interactions between association cortex and the SC, and extensive experience with cross-modal cues. Using these factors, the brain is able to craft the underlying neural circuits and the fundamental principles that govern multisensory integration so that they are adapted to the ecological circumstances in which they will be used.

<https://pubmed.ncbi.nlm.nih.gov/21741550/>

