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Origins of task-specific sensory-independent organization in the visual and auditory brain: neuroscience evidence, open questions and clinical implications

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Evidence of task-specific sensory-independent (TSSI) plasticity from blind and deaf populations has led to a better understanding of brain organization. However, the principles determining the origins of this plasticity remain unclear. We review recent data suggesting that a combination of the connectivity bias and sensitivity to task-distinctive features might account for TSSI plasticity in the sensory cortices as a whole, from the higher-order occipital/temporal cortices to the primary sensory cortices. We discuss current theories and evidence, open questions and related predictions. Finally, given the rapid progress in visual and auditory restoration techniques, we address the crucial need to develop effective rehabilitation approaches for sensory recovery.

Addresses

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neuroscience. A consistent body of data from blind and deaf populations has shown that sensory cortices deprived of their natural sensory input still primarily process the same type of perceptual/computational/categorical information, although it is conveyed by an atypical sensory input (e.g., audition; touch), and in many cases this same task-specific sensory-independent (TSSI) organization can be observed also in the general (healthy sighted or hearing) population [1–7]. Studies using sensory substitution devices (SSDs) which have mainly been conducted with the congenitally blind population, have found that TSSI plasticity can emerge after a relatively short training period designed to teach a different sensory modality (e.g., audition) to interpret some type of information typically processed by vision [8–10,11^{**},12^{**}]. Visual-to-auditory SSDs topographically convert visual images into auditory ‘soundscapes’, which can be interpreted fairly rapidly by users [10]. Studies involving SSD-training have been conducted in adulthood, thus ultimately suggesting the absence of a critical/sensitive period subtending the pairing of a given sensory input (either typical or atypical) with a given task-specific brain region. Thus, if task-specific sensory-independent (TSSI) brain organization is not driven by sensory inputs, what drives its maintenance? Here we analyze results on the basis of the use of two forms of sensory restoration to investigate this crucial issue: sensory substitution devices (SSDs) and cochlear (and to a lesser extent visual) prostheses.

New evidence from our group concerning reading and number processing in the ventral occipito-temporal cortex suggests that a combination of two principles may drive the emergence of its task-specific sensory-independent (TSSI) organization [13^{**}]. The first is known as the biased connectivity principle (BCp), which posits that task-specific recruitment draws on pre-existing cortical connections linking the ventral occipito-temporal cortex TSSI regions to the rest of the networks processing information for a specific computational task (see also [2,10,11^{**},12^{**},14,15]). The second is the shape-feature sensitivity principle (SFSp), which states that task-specific recruitment can emerge from the intrinsic circuitry of the ventral occipito-temporal pathway which may be tuned to the extraction of the specific but invariant shape-features of an object (when a shape is defined as representing the proximity of the component parts of an

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The origin of task-specific-sensory-independent plasticity

In the last decade or so, task-specific sensory-independent (TSSI) brain organization has rapidly become a firmly established notion in the field of cognitive

object [13**]). In other words, this extraction is expected to occur independently of translation, rotation, size, distance or other variations in the object, and moreover, independently of the sensory modality through which the object-related information is conveyed [13**]. Recent data from our lab and others have supported this claim by documenting both TSSI recruitment in the ventral occipito-temporal cortex regions along with preserved network connectivity organization [11**,12**,13**,16] in blind participants. This was shown using resting-state functional connectivity magnetic imaging, which exploits the assumption that correlations in the activity of different brain regions during resting-state (i.e., without an explicit task) reflect functionally relevant correlations in neuronal firing [17,18]. For instance, we showed that in congenitally blind participants, the visual number form area was recruited in a TSSI-manner after a relatively short SSD training on number identification, and that this recruitment was accompanied by preserved cortical connections between this region and other crucial areas involved in the representation of quantities in the sighted population [11**,19,20]. In contrast, in the same group, the visual word-form area showed preserved connections to fundamental areas for language processing ([21,22]; see Figure 1a; see also [10]).

Crucially, additional recent data suggest that the combination of these two principles might account for task-specific sensory-independent (TSSI) plasticity in the deprived occipital cortices in a much more general way. That is, even beyond the ventral occipito-temporal cortex, extending to other occipital regions, such as the lateral occipito-temporal cortex [23], MT+ [24] and the extrastriate body area [12**] which are all located more laterally than the ventral occipito-temporal cortex. For instance, similar to the results obtained in the ventral occipito-temporal cortex [10,11**], we observed in a group of blind participants TSSI recruitment of the extrastriate body area elicited by the perception of SSD-presented body shapes, accompanied by preserved functional connectivity between this region and other areas considered to be integral part of the body-image network in the sighted population, such as the posterior superior temporal sulcus and the temporal–parietal junction ([12**]; see Figure 1a). A recent study showed that the retention of category preference and functional connectivity yield overlapping results in vast areas of the visual cortex of the blind [25**]. Furthermore this study showed that this combination of shape-feature sensitivity principle (SFSp) and biased connectivity principle (BCp) in the blind population also correlated with polymodal activations in the brains of sighted controls, thus additionally supporting the suggestion that both these principles guide visual cortex organization even without visual experience. We further propose that in order for the combination of BCp and SFSp to account for TSSI plasticity in the sensory cortices as a whole, shape-feature sensitivity

principle (SFSp) needs to be generalized to include the emergence of task-specificity in auditory regions (e.g., in deaf humans for sign language; [4,26]), and in auditory and visual regions activated by tasks that do not involve any shape information (e.g., in MT; [24,27], in deaf animals and in blind humans for visual [5] and auditory localization [3]). We term this extended SFSp the ‘task-distinctive feature sensitivity principle’ (TDFSp).

This expanded proposal still leaves several critical questions open (see Box 1). Here we discuss two especially important ones: the generalization of these two principles to the organization of the early sensory cortices, and more practically, the implications of these principles for sensory restoration — could including them in rehabilitative programs help maximize sensory recovery?

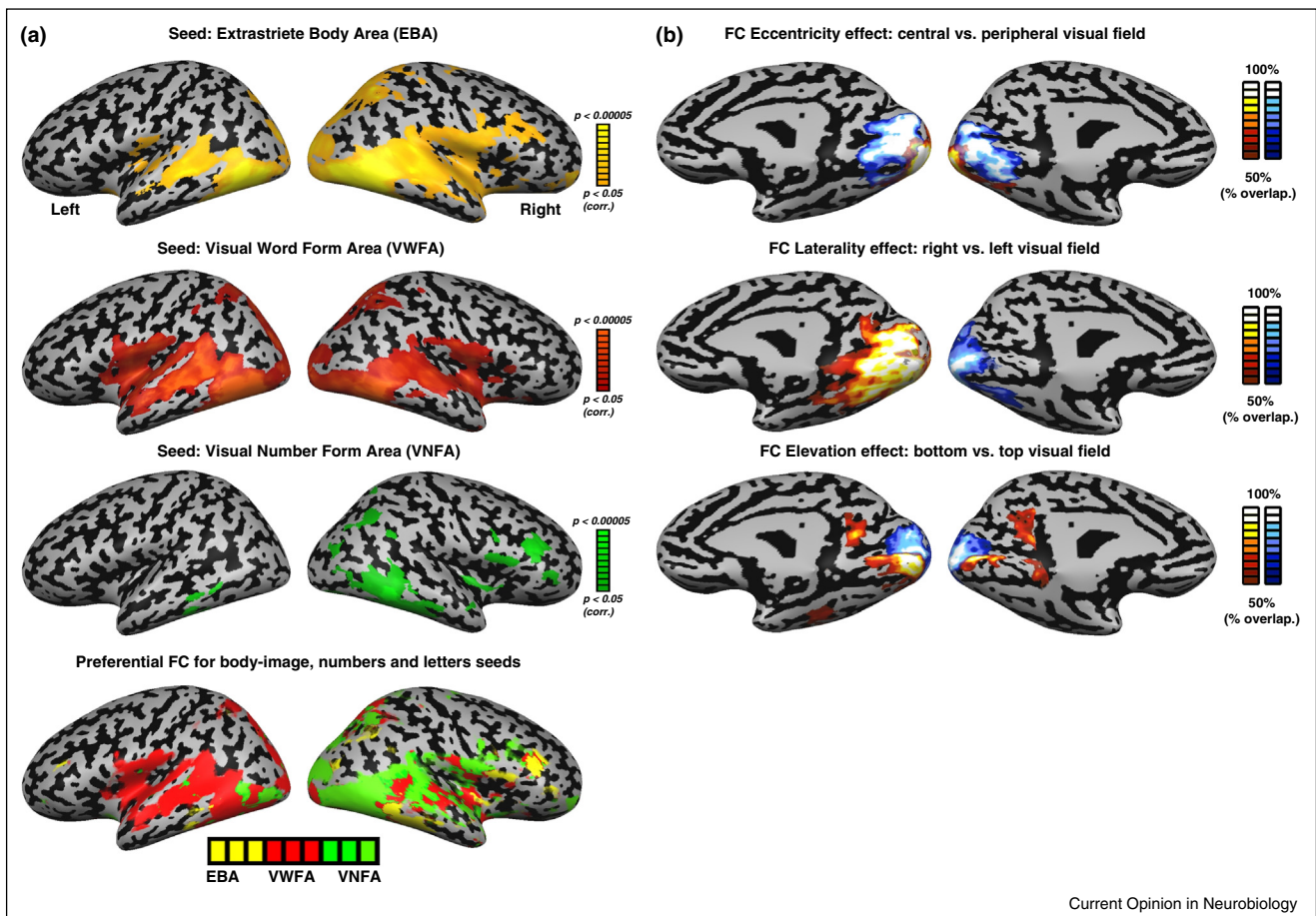
Reorganization of deprived primary sensory cortices

Till date, the extent to which a combination of biased connectivity principle (BCp) and task-distinctive feature sensitivity principle (TDFSp) can explain also the reorganization occurring within the deprived *early* sensory cortices remains unclear, but such uncertainty ultimately undermines current interpretations of TSSI brain organization.

There is no conclusive evidence regarding which TSSI computational tasks these cortices should maintain if deprived of their natural input from birth. Hence it is currently impossible to determine whether the TDFSp extends to these cortices. A few studies on early blind populations have reported recruitment of the deprived primary visual cortex (V1) by low-level spatially related features [28,29]. However, such reports are rare and weaker compared to the accumulating evidence of ‘task-switching’ in V1 toward higher cognitive functions in the case of language or memory tasks [30–33], in tasks requiring focused attention [34] or executive control [35]. These results are thought to diverge dramatically from the predictions of TSSI brain organization, because such functions do not typically recruit early visual areas in sighted individuals (but see [36*]).

Nonetheless, data collected in the deaf population seems to extend the task-distinctive feature sensitivity principle (TDFSp) to the primary sensory cortex as well. Recent studies consistently report vibrotactile recruitment of the primary auditory cortex (A1) in deaf humans [37–39]. There is no conclusive data as to whether such recruitment is low-level and follows the functional organization of the hearing auditory cortices (i.e., TSSI recruitment). However, the high functional similarity between the computations underlying both types of stimulation (oscillatory pressure patterns translated into frequency

Figure 1



(a) Resting-state functional connectivity (FC) MRI in congenitally blind adults. A lateral view of an inflated cortex overlaid with the connectivity maps. Results of random-effects group analysis (corrected for multiple comparisons) of functional connectivity maps using an EBA seed (top panel — readapted from Striem-Amit and Amedi [12**]), visual word-form area seed (second panel — readapted from Striem-Amit *et al.* [10]), and visual number form area seed (third panel — readapted from Abboud *et al.* [11**]). In the bottom panel a preferential FC map for the three computational tasks (winner — takes-all approach) is depicted. **(b)** Resting-state functional connectivity (FC) MRI-retinotopic organization in congenitally fully blind adults. Results of FC analyses showing preserved retinotopic organization in congenitally blind adults for the three main retinotopic mapping axes: eccentricity (center–periphery; top panel), laterality (left–right; middle panel), and elevation (upper–lower; bottom panel). Data readapted from Striem-Amit *et al.* [45**].

percepts [40]) lends weight to this conclusion. Within a given frequency range, the very same oscillatory pattern can be perceived simultaneously by the peripheral receptors of both sensory modalities (i.e., the basilar membrane of the cochlea and the skin; e.g. [40,41]), suggesting that even deaf people can perceive certain sounds through touch naturally. In fact, through vibrotactile stimulations, deaf individuals can perceive music [42], differentiate timbres [43] and different pitches of voices [44]. These reports in turn suggest that such abilities may depend, in a task-specific manner, on cortical integration of activity across different channels of mechanoreceptors, both auditory and tactile. Future studies should assess the properties of vibrotactile recruitment in the *deaf* A1 more systematically and test whether a similar recruitment is

observed in the *blind* V1 for atypical sensory stimuli sharing functional similarities with visual preferences.

At the same time, studies should also investigate to what extent the biased connectivity principle (BCp) is present within deprived primary sensory cortices. Recent evidence from our lab in congenitally blind adults supports this conclusion by showing retained functional connectivity (FC) patterns mimicking retinotopic organization, a hallmark of the visual cortex structural architecture [45**]. These retained FC patterns were observed for all three main retinotopic mapping axes: eccentricity (center–periphery), laterality (left–right), and elevation (upper–lower), throughout the early and high-level ventral and dorsal streams (see Figure 1b; see also [46,47]). This functional

Box 1 Outstanding open questions and predictions concerning the notion of task-specific sensory-independent (TSSI) organization as emerging from the combination of biased connectivity principle (BCp) and task-distinctive feature sensitivity principle (TDFSp)

1. Would the preserved V1 resting-state functional connectivity result in functional-specific recruitment of the deprived visual cortex as predicted by the task-distinctive feature sensitivity principle (TDFSp)? For instance one hypothesis is that auditory/tactile localization tasks recruit V1 in a retinotopic manner, such that central auditory/tactile localization would recruit central retinotopic areas, peripheral auditory/tactile localization would recruit peripheral areas, etc.
2. Or would TDFSp not entirely generalize to V1 plasticity, given results documenting both retention and divergence in V1 organization in the blind compared to the sighted? For example, one could expect that reading, a task performed foveally by the sighted, would show central-visual-field preferences in the blind [85] when reading Braille, although Braille reading does not elicit V1 activation in the sighted.
3. What are the implications for visual rehabilitation outcomes of the mixed findings documenting both retained and divergent plasticity in deprived V1? To what extent will V1 retained functional connectivity organization be beneficial for sight restoration? And will V1 divergent functional connectivity limit sight restoration efforts?
4. Could divergent V1 activations emerge in the sighted population for the same types of non-visual stimuli, with or without 'unmasking' following short term visual deprivation [1]? If so, this latter result could explain the so-called task-switching toward high-level cognitive functions repeatedly reported in blind populations and reconcile the blind results with the TDFSp predictions.
5. Do biased connectivity principle (BCp) and TDFSp exist from birth or do they need to be established during critical/sensitive periods of development? These questions may already be addressed, in that neuroimaging investigations, although very challenging, are starting to be feasible even in fetuses [86,87].
6. In terms of importance and temporal precedence, does BCp or TDFSp determine task-specific sensory-independent (TSSI) recruitment? If large-scale functional networks connectivity precedes selective tuning to specific shapes and task-distinctive features, the visual word-form area functional connectivity patterns, for example, would exist in blind children before learning Braille and in illiterate blind adults, and perhaps also predict their prospective reading abilities.
7. What is the relative contribution of BCp versus TDFSp in mediating the reorganization occurring within the deprived high-order and *early* sensory cortices? Can different occipital areas be influenced differently by BCp and TDFSp? In higher-order sensory regions, reorganization could be mostly mediated by the BCp, whereas the opposite could be true in early sensory cortices.
8. To what extent does the combination of the BCp and the TDFSp explain the emergence of plasticity in the late blind? Data suggest that at least for certain tasks late-blind plasticity does not follow the predictions of these two principles [14]. Is this true as well for category-selective regions in the occipito-temporal cortex?

connectivity (FC) architecture was also observed in people whose eyes did not fully develop in utero (i.e., without any possible visual experience). Thus this architecture appears to be hard-wired and dependent on genetic blueprints, rather than on experience-dependent or even activity-dependent mechanisms [45**]. Further supportive findings were reported by other groups for the retained fine-detailed FC within V1 [45**], and for retained visual

callosal anatomical connectivity [46]. However, consistent with previous studies [3,24,33,48–52] we showed that this retained organization coexisted with some level of divergent organization in FC in the blind [44]. These latter connections varied in accordance with retinotopic division. The *blind* central V1 showed increased FC to the left frontal language areas and their peripheral V1 showed increased FC to the parieto-frontal attention networks. This might indicate distinctive V1 localizations for the two functional roles generally attributed to the *blind* V1; namely, higher-order cognitive functions such as language processing [33,53,54] and non-visual spatial (and also non-spatial) attention [3,14,55,56]. Future studies should further clarify the functional meaning of the findings indicating both the retention and divergence of early visual cortices FC organization, test such connections in tonotopic areas of the deaf population and test their effects on sight/hearing restoration outcomes (see Box 1).

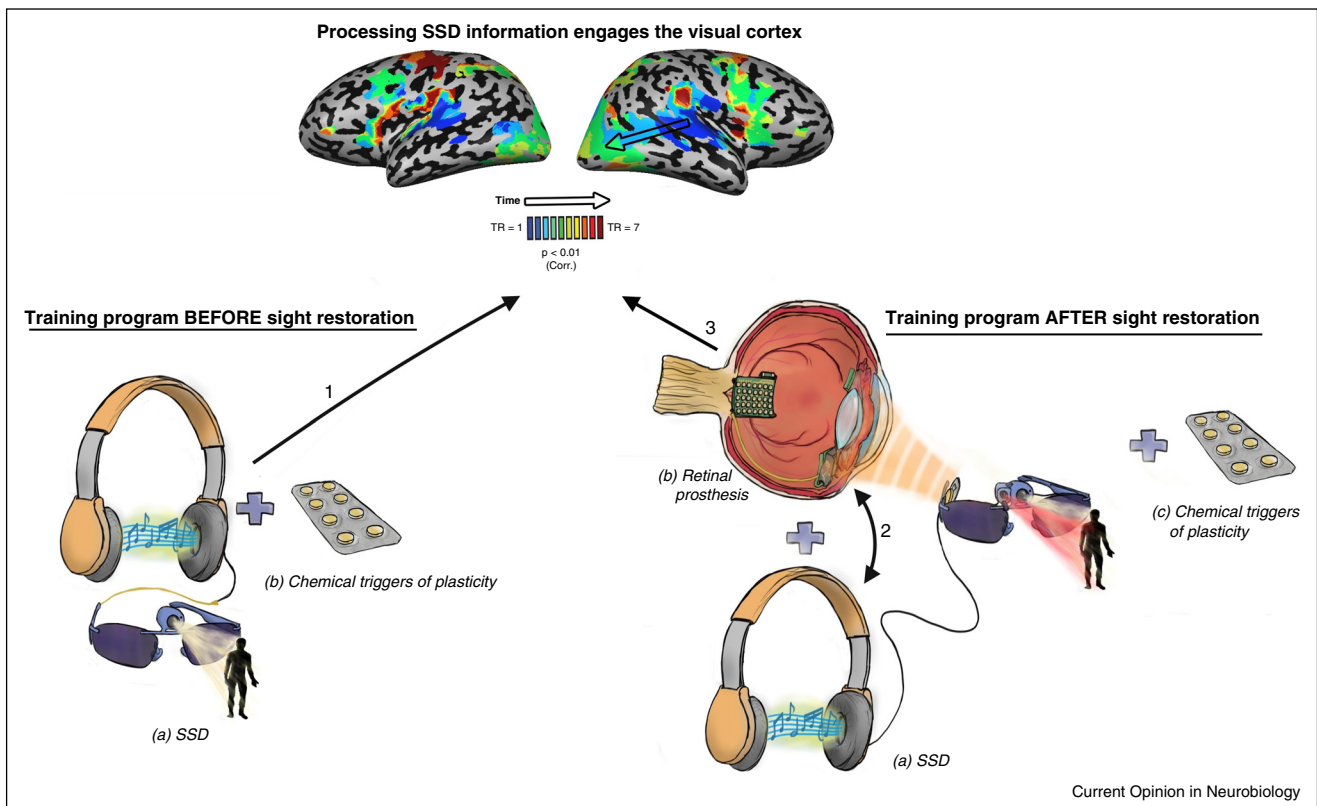
New frontiers for sight restoration

Given the rapid advances in biotechnology in the last decades, it may soon be possible to restore visual input in a variety of ways including retinal implants with increasing levels of resolution (paralleling the more widespread cochlear implants for auditory restoration), stem cell transplants and molecular manipulations [57]. Thus, there is a real need to formulate sight restoration approaches and be able to predict their success from the available evidence, especially since the behavioral outcome of such approaches were quite disappointing so far [57].

A certain number of indications can be gleaned from the few cases of patients who have regained their sight during adulthood [58–60,61*,62]. While their restored visual abilities are far from optimal, these patients are mainly deficient in high-level visual tasks such as feature binding, object-background segregation, 3D shapes and face processing [59,61*,63,64]. Since these are precisely the visual abilities that can be learned using sensory substitution devices (SSDs) [10,65], one logical step is the systematic implementation of multisensory training programs, where SSD input is paired with the restored visual modality to boost the recovery of specific computational tasks ([65] see Figure 2).

The efficacy of multisensory training has never been systematically tested for sight restoration. However, there is initial encouraging evidence from cochlear implantation. Cochlear implants are now a firmly established procedure for auditory recovery [66]. The classic approach favors rehabilitation programs in audition alone [67]. Recent evidence, though, documents the higher efficacy of multisensory training programs (e.g., audio-visual) compared to unisensory ones (i.e., auditory only) for recovering specific cognitive/computational tasks. For instance, exposure to audio-visual language rehabilitative

Figure 2



Multisensory training program for sight restoration. This figure shows a visual-to auditory SSD used to teach processing of visual body shapes (and the corresponding brain activations) as an example. The same approach could be implemented using visual-to-tactile SSD as well as many other cognitive/computational tasks. Similarly, the figure depicts a retinal prosthesis as an example of a sight restoration system. *Left*: Before sight restoration surgery, patients can be trained with sensory-substitution devices (SSDs) to teach the brain to process (typically visual) specific tasks through a sensory modality (e.g., audition) that has never performed such a task, thus activating TSSI regions and their related network (top). *Right*: After medical sight restoration, patients can pair the newly reacquired and developing visual input with a familiar sensory input (e.g., auditory SSD input). Medical visual restoration systems and SSDs could be used together to facilitate, strengthen, and complete the visual experience. This pairing may eventually facilitate the adaptability of the visual cortex to process its typical sensory input (top). In the near future, chemical agents that remove molecular breaks in plasticity (chemical triggers of plasticity) may be available to human patients, who can start the treatment a few weeks/months before surgery and after the intervention. This would help set the deprived visual cortex back to its juvenile state, and thus increase its plasticity resources and overcome deficits in the development of the visual system due to early visual deprivation.

training (speech-reading therapy, pairing sign language with spoken language) substantially improves auditory linguistic recovery compared to auditory-only training in cochlear-implant patients [67–69]. Furthermore, a recent study showed that learning sign language boosts auditory linguistic recovery in early-implanted deaf children [70]. Thus, the development of a cognitive skill (e.g., language) even if achieved through an atypical modality, seems to facilitate rather than impede the recovery of this skill in the restored sensory input [67]. The occurrence of task-specific sensory-independent (TSSI) development during childhood is thought to be crucial for efficient multisensory training in sensory restoration programs [67,69]: recently it was claimed that two distinct critical/sensitive periods regulate and predict the success of sensory recovery. One, which we term *task-specific critical/*

sensitive period is related to TSSI components such as, the development of the language-network regardless of the modality used to convey linguistic inputs (sounds or sign-language). The second, which we term *modality-specific critical/sensitive period* is related to the maturation of the specific sensory pathways, for instance the development of connectivity enabling processing of auditory sensory inputs [67,69].

A recent study on deaf ferrets nevertheless challenges the importance of this latter type of critical/sensitive period [71**] and has huge implications for multisensory restoration training. Isaiah and colleagues [71**] showed that in early-deaf ferrets who were fitted with cochlear implants in adulthood, namely after the closure of modality-specific critical/sensitive periods [72,73], an audio-visual

focused training was more effective than an auditory one for recovering auditory localization abilities. This result suggests that binding inputs from different sensory modalities, and especially the combination of a familiar modality (e.g., vision) with a novel, developing one (e.g., audition), might be a powerful way to restore efficient and task-specific sensory recovery, even in case of late interventions.

Thus, now more than ever before, the implementation of multisensory training programs using sensory substitution devices (SSDs) holds promise for sight recovery as well. Candidates for sight restoration might use SSDs before the intervention, and learn for example to perceive SSD-presented body-shapes (i.e., an otherwise typically visual skill), ultimately recruiting the extrastriate body area and its related network of processing [12**]. Then, after medical sight restoration, the SSD stimulation can be paired with visual input, mediating two types of benefits. The familiar SSD input can help better understand the newly restored visual input. For example, presenting a body-shape both through SSD and through vision simultaneously may help the patient perceive fine details of the image or bind visual features into a coherent shape. Moreover, such pairing may facilitate a neural network's adaptability to efficiently process its typical sensory input. For instance, in the case of body-shapes, data have shown that in the blind population SSD-presented body shapes recruit extrastriate body area and that this region is functionally connected to other regions typically involved in body-shape processing [12**]. Therefore, pairing SSD and visually presented body-shapes may aid the visual cortex to sensory tune toward specific visual inputs (see Figure 2). A similar logic can be applied to reading and numbers in the visual word-form area and the visual number-form area, as well as many other tasks and even for more low-level computations [65].

However, this optimistic view and rehabilitation protocol proposed above may not suffice, given evidence of deficient low-level visual information in sight restored adult patients [62,74,75]. This suggests that at least to a certain extent, modality-specific critical/sensitive periods still impact the overall success of sight recovery (see also [76*]). Thus, an additional step to improve low-level visual abilities, and ultimately aid rehabilitation, seems needed. Intriguingly, recent evidence with animals indicate that chemical interventions can release molecular 'breaks' of plasticity (involving the balance between inhibition and excitation) and trigger the reopening of modality-specific critical/sensitive periods, thus ultimately resetting juvenile brain plasticity and increasing sensitivity to external inputs ([77**,78,79,80**,81], see [72]). Treatment on the basis of this approach is being piloted for amblyopia [82,83*,84], where endogenous permissive neuromodulators are modified to induce plasticity in adults who have had monocular visual deprivation (see

also [80**]). Should this approach prove useful, it may be expanded to people recovering from binocular deprivation, e.g., blindness. In this case, the maintenance of the macro-structural organization of V1 [45**,46,85], along with rejuvenating its ability to wire and refine its connections once visual input is restored, may facilitate a vision efficient takeover of the reafferented visual cortex. One groundbreaking possibility to improve sensory restoration outcomes might be to pair SSD-based multisensory training with the reopening of critical/sensitive periods of development (see Figure 2). Although these action paths are only tentative at best and still need systematic testing, their potential convergence may herald a new era in the medical ability to restore lost senses, and to overcome multiple developmental brain challenges.

Conflict of interests statement

Nothing declared.

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References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Pascual-Leone A, Hamilton R: **The metamodal organization of the brain.** *Prog Brain Res* 2001, **134**:427-445.
2. Mahon BZ, Caramazza A: **What drives the organization of object knowledge in the brain?** *Trends Cogn Sci* 2011, **15**:97-103.
3. Collignon O, Vandewalle G, Voss P, Albouy G, Charbonneau G, Lassonde M, Lepore F: **Functional specialization for auditory-spatial processing in the occipital cortex of congenitally blind humans.** *Proc Natl Acad Sci U S A* 2011, **108**:4435-4440.
4. MacSweeney M, Woll B, Campbell R, McGuire PK, David AS, Williams SC, Suckling J, Calvert GA, Brammer MJ: **Neural systems underlying British sign language and audio-visual English processing in native users.** *Brain* 2002, **125**:1583-1593.
5. Lomber SG, Meredith MA, Kral A: **Cross-modal plasticity in specific auditory cortices underlies visual compensations in the deaf.** *Nat Neurosci* 2010, **13**:1421-1427.
6. Ricciardi E, Handjaras G, Pietrini P: **The blind brain: how (lack of) vision shapes the morphological and functional architecture of the human brain.** *Exp Biol Med* 2014, **239**:1414-1420 <http://dx.doi.org/10.1177/1535370214538740>.
7. Renier L, De Volder AG, Rauschecker JP: **Cortical plasticity and preserved function in early blindness.** *Neurosci Biobehav Rev* 2014, **41**:53-63.
8. Amedi A, Stern WM, Camprodon JA, Bermpohl F, Merabet L, Rotman S, Hémond C, Meijer P, Pascual-Leone A: **Shape conveyed by visual-to-auditory sensory substitution activates the lateral occipital complex.** *Nat Neurosci* 2007, **10**:687-689.
9. Collignon O, Lassonde M, Lepore F, Bastien D, Veraart C: **Functional cerebral reorganization for auditory spatial**

- processing and auditory substitution of vision in early blind subjects.** *Cereb Cortex* 2007, **17**:457-465.
10. Striem-Amit E, Cohen L, Dehaene S, Amedi A: **Reading with sounds: sensory substitution selectively activates the visual word form area in the blind.** *Neuron* 2012, **76**:640-652.
 11. Abboud S, Maidenbaum S, Dehaene S, Amedi A: **A number-form area in the blind.** *Nat Commun* 2015:6.
Demonstrates that in the same group of blind adults their visual number form area is recruited in a number identification task using a sensory substitution device, and that this area is functionally connected to other areas that generally respond to quantities in the sighted population. In contrast, their Visual World Form Area is functionally connected to crucial areas for language processing in the sighted population.
 12. Striem-Amit E, Amedi A: **Visual cortex extrastriate body-selective area activation in congenitally blind people seeing by using sounds.** *Curr Biol* 2014, **24**:687-692.
Demonstrates that in the same group of blind adults their extrastriate body area is recruited when perceiving body shapes presented through a sensory substitution device, and that this area is functionally connected to other crucial areas of the body image network in the sighted population.
 13. Hannagan T, Amedi A, Cohen L, Dehaene-Lambertz G, Dehaene S: **Origins of the specialization for letters and numbers in ventral occipitotemporal cortex.** *Trends Cognit Sci* 2015.
Reviews evidence in visual deprivation, developmental, and animal studies on the organization of the ventral occipito-temporal cortex (vOTC) and proposes that the emergence of its organization can be explained through a combination of the biased connectivity and the shape sensitivity principles.
 14. Collignon O, Dormal G, Albouy G, Vandewalle G, Voss P, Phillips C, Lepore F: **Impact of blindness onset on the functional organization and the connectivity of the occipital cortex.** *Brain* 2013, **136**:2769-2783.
 15. Johnson MH: **Interactive specialization: a domain-general framework for human functional brain development?** *Dev Cognit Neurosci* 2011, **1**:7-21.
 16. He C, Peelen MV, Han Z, Lin N, Caramazza A, Bi Y: **Selectivity for large nonmanipulable objects in scene-selective visual cortex does not require visual experience.** *Neuroimage* 2013, **79**:1-9.
 17. Fox MD, Raichle ME: **Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging.** *Nat Rev Neurosci* 2007, **8**:700-711.
 18. Damoiseaux JS, Greicius MD: **Greater than the sum of its parts: a review of studies combining structural connectivity and resting-state functional connectivity.** *Brain Struct Funct* 2009, **213**:525-533.
 19. Eger E, Sterzer P, Russ MO, Giraud A-L, Kleinschmidt A: **A supramodal number representation in human intraparietal cortex.** *Neuron* 2003, **37**:719-726.
 20. Nieder A, Dehaene S: **Representation of number in the brain.** *Annu Rev Neurosci* 2009, **32**:185-208.
 21. Price CJ: **A review and synthesis of the first 20 years of PET and fMRI studies of heard speech, spoken language and reading.** *Neuroimage* 2012, **62**:816-847.
 22. Vigneau M, Beaucois V, Herve P-Y, Duffau H, Crivello F, Houde O, Mazoyer B, Tzourio-Mazoyer N: **Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing.** *Neuroimage* 2006, **30**:1414-1432.
 23. Peelen MV, Bracci S, Lu X, He C, Caramazza A, Bi Y: **Tool selectivity in left occipitotemporal cortex develops without vision.** *J Cognit Neurosci* 2013:1-10.
 24. Sani L, Ricciardi E, Gentili C, Vanello N, Haxby JV, Pietrini P: **Effects of visual experience on the human MT+ functional connectivity networks: an fMRI study of motion perception in sighted and congenitally blind individuals.** *Front Syst Neurosci* 2010, **4**:159.
 25. Bi Y, Wang X, Peelen MV, Han Z, He C, Caramazza A: **How visual is the visual cortex? Comparing connectional and functional fingerprints between congenitally blind and sighted individuals.** *J Neurosci* 2015, **35**:12545-12559.
- Demonstrates that there is close agreement between category functional task-based preferences and resting-state functional connectivity in extensive areas of the visual cortex of the blind.
26. Emmorey K, Mehta S, Grabowski TJ: **The neural correlates of sign versus word production.** *Neuroimage* 2007, **36**:202-208.
 27. Saenz M, Lewis LB, Huth AG, Fine I, Koch C: **Visual motion area MT+/V5 responds to auditory motion in human sight-recovery subjects.** *J Neurosci* 2008, **28**:5141-5148.
 28. Ptito M, Fumal A, de Noordhout AM, Schoenen J, Gjedde A, Kupers R: **TMS of the occipital cortex induces tactile sensations in the fingers of blind Braille readers.** *Exp Brain Res* 2008, **184**:193-200.
 29. Thaler L, Arnott SR, Goodale MA: **Neural correlates of natural human echolocation in early and late blind echolocation experts.** *PLoS ONE* 2011, **6**:e20162.
 30. Sadato N, Pascual-Leone A, Grafman J, Ibanez V, Deiber MP, Dold G, Hallett M: **Activation of the primary visual cortex by Braille reading in blind subjects.** *Nature* 1996, **380**:526-528.
 31. Amedi A, Raz N, Pianka P, Malach R, Zohary E: **Early 'visual' cortex activation correlates with superior verbal memory performance in the blind.** *Nat Neurosci* 2003, **6**:758-766.
 32. Burton H, Diamond JB, McDermott KB: **Dissociating cortical regions activated by semantic and phonological tasks: a fMRI study in blind and sighted people.** *J Neurophysiol* 2003, **90**:1965-1982 Epub 2003 Jun 1964.
 33. Bedny M, Pascual-Leone A, Dodell-Feder D, Fedorenko E, Saxe R: **Language processing in the occipital cortex of congenitally blind adults.** *Proc Natl Acad Sci U S A* 2011, **108**:4429-4434.
 34. Weaver KE, Stevens AA: **Attention and sensory interactions within the occipital cortex in the early blind: an fMRI study.** *J Cogn Neurosci* 2007, **19**:315-330.
 35. Strnad L, Peelen MV, Bedny M, Caramazza A: **Multivoxel pattern analysis reveals auditory motion information in MT+ of both congenitally blind and sighted individuals.** *PLOS ONE* 2013, **8**:e63198.
 36. Vetter P, Smith FW, Muckli L: **Decoding sound and imagery content in early visual cortex.** *Curr Biol* 2014, **24**:1256-1262.
Demonstrates that in blindfolded participants category-specific information from both complex natural sounds and imagery can be read out from early visual cortex activity. It posits that this information is abstract rather than pictorial in nature because it generalizes to other sounds belonging to the same category.
 37. Auer ET Jr, Bernstein LE, Sungkarat W, Singh M: **Vibrotactile activation of the auditory cortices in deaf versus hearing adults.** *Neuroreport* 2007, **18**:645.
 38. Karns CM, Dow MW, Neville HJ: **Altered cross-modal processing in the primary auditory cortex of congenitally deaf adults: a visual-somatosensory fMRI study with a double-flash illusion.** *J Neurosci* 2012, **32**:9626-9638.
 39. Levänen S, Jousmäki V, Hari R: **Vibration-induced auditory-cortex activation in a congenitally deaf adult.** *Curr Biol* 1998, **8**:869-872.
 40. Soto-Faraco S, Deco G: **Multisensory contributions to the perception of vibrotactile events.** *Behav Brain Res* 2009, **196**:145-154.
 41. Von Bekesy G: **Similarities between hearing and skin sensations.** *Psychol Rev* 1959, **66**:1.
 42. Good A, Reed MJ, Russo FA: **Compensatory plasticity in the deaf brain: effects on perception of music.** *Brain Sci* 2014, **4**:560-574.
 43. Russo FA, Ammirante P, Fels DI: **Vibrotactile discrimination of musical timbre.** *J Exp Psychol: Hum Percept Perform* 2012, **38**:822.
 44. Ammirante P, Russo FA, Good A: **Fels DI: feeling voices.** *PLoS ONE* 2013, **8**:e53585.
 45. Striem-Amit E, Ovadia-Caro S, Caramazza A, Margulies DS, Villringer A, Amedi A: **Functional connectivity of visual cortex in**

- the blind follows retinotopic organization principles.** *Brain* 2015, **138**:1679-1695.
Demonstrates that in congenitally blind adults, large-scale retinotopic organization is preserved. This retained organization appears to be hard-wired and dependent on genetic blueprints because it was also present in individuals whose eyes did not develop *in utero*.
46. Butt OH, Benson NC, Datta R, Aguirre GK: **The fine-scale functional correlation of striate cortex in sighted and blind people.** *J Neurosci* 2013, **33**:16209-16219.
 47. Bock AS, Saenz M, Tungaraza R, Boynton GM, Bridge H, Fine I: **Visual callosal topography in the absence of retinal input.** *Neuroimage* 2013, **81**:325-334.
 48. Liu Y, Yu C, Liang M, Li J, Tian L, Zhou Y, Qin W, Li K, Jiang T: **Whole brain functional connectivity in the early blind.** *Brain* 2007, **130**:2085-2096.
 49. Watkins KE, Cowey A, Alexander I, Filippini N, Kennedy JM, Smith SM, Ragge N, Bridge H: **Language networks in anophthalmia: maintained hierarchy of processing in 'visual' cortex.** *Brain* 2012.
 50. Burton H, Snyder AZ, Raichle ME: **Resting state functional connectivity in early blind humans.** *Front Syst Neurosci* 2014, **8**:51.
 51. Bock AS, Fine I: **Anatomical and functional plasticity in early blind individuals and the mixture of experts architecture.** *Front Hum Neurosci* 2014, **8**:971.
 52. Deen B, Saxe R, Bedny M: **Occipital cortex of blind individuals is functionally coupled with executive control areas of frontal cortex.** *J Cognit Neurosci* 2015:1-15.
 53. Burton H: **Visual cortex activity in early and late blind people.** *J Neurosci* 2003, **23**:4005-4011.
 54. Amedi A, Floel A, Knecht S, Zohary E, Cohen LG: **Transcranial magnetic stimulation of the occipital pole interferes with verbal processing in blind subjects.** *Nat Neurosci* 2004, **7**:1266-1270.
 55. Gougoux F, Zatorre RJ, Lassonde M, Voss P, Lepore F: **A functional neuroimaging study of sound localization: visual cortex activity predicts performance in early-blind individuals.** *PLoS Biol* 2005, **3**:e27.
 56. Garg A, Schwartz D, Stevens AA: **Orienting auditory spatial attention engages frontal eye fields and medial occipital cortex in congenitally blind humans.** *Neuropsychologia* 2007, **45**:2307-2321.
 57. Zrenner E, Birch D: **Restoring vision to the blind: the new age of implanted visual prostheses. Restoring vision to the blind.** *Transl Vis Sci Technol* 2014, **3**:3.
 58. Gregory RL, Wallace JG: **Recovery from early blindness: a case study.** In *Experimental Psychology Society, Monograph Supplement*. 2Heffers1963.
 59. Fine I, Wade AR, Brewer AA, May MG, Goodman DF, Boynton GM, Wandell BA, MacLeod DI: **Long-term deprivation affects visual perception and cortex.** *Nat Neurosci* 2003, **6**:915-916.
 60. Levin N, Dumoulin SO, Winawer J, Dougherty RF, Wandell BA: **Cortical maps and white matter tracts following long period of visual deprivation and retinal image restoration.** *Neuron* 2010, **65**:21-31.
 61. Huber E, Webster JM, Brewer AA, MacLeod DIA, Wandell BA, Boynton GM, Wade AR, Fine I: **A lack of experience-dependent plasticity after more than a decade of recovered sight.** *Psychol Sci* 2015.
Reports the lack of category-selectivity in the ventral visual cortex of M.M. together with a remarkably normal category-selectivity in his lateral occipital cortex. These imaging results extend previous behavioral results reported on the same patient. Overall, this work shows that the recovery of high level visual functions is problematic when sight is restored in adulthood.
 62. Dormal G, Lepore F, Harissi-Dagher M, Albouy G, Bertone A, Rossion B, Collignon O: **Tracking the evolution of crossmodal plasticity and visual functions before and after sight-restoration.** *J Neurophysiol* 2014.
 63. Le Grand R, Mondloch CJ, Maurer D, Brent HP: **Impairment in holistic face processing following early visual deprivation.** *Psychol Sci* 2004, **15**:762-768.
 64. Le Grand R, Mondloch CJ, Maurer D, Brent HP: **Neoperception early visual experience and face processing.** *Nature* 2001, **410**:890.
 65. Reich R, Amedi A: **'Visual' parsing can be taught quickly without visual experience during critical periods.** *Sci Rep* 2015. (in press).
 66. Gaylor JM, Raman G, Chung M, Lee J, Rao M, Lau J, Poe DS: **Cochlear implantation in adults: a systematic review and meta-analysis.** *JAMA Otolaryngol — Head Neck Surg* 2013, **139**:265-272.
 67. Lyness CR, Woll B, Campbell R, Cardin V: **How does visual language affect crossmodal plasticity and cochlear implant success?** *Neurosci Biobehav Rev* 2013.
 68. Strelnikov K, Rouger J, Demonet J-F, Lagleyre S, Fraysse B, Deguine O, Barone P: **Visual activity predicts auditory recovery from deafness after adult cochlear implantation.** *Brain* 2013, **136**:3682-3695.
 69. Heimler B, Weisz N, Collignon O: **Revisiting the adaptive and maladaptive effects of crossmodal plasticity.** *Neuroscience* 2014.
 70. Hassanzadeh S: **Outcomes of cochlear implantation in deaf children of deaf parents: comparative study.** *J Laryngol Otol* 2012, **126**:989.
 71. Isaiah A, Vongpaisal T, King AJ, Hartley DE: **Multisensory training improves auditory spatial processing following bilateral cochlear implantation.** *J Neurosci* 2014, **34**:11119-11130.
Demonstrates that early-deaf ferrets implanted in adulthood exhibited better recovery of auditory localization abilities through multisensory rather than unisensory training.
 72. Kral A: **Auditory critical periods: a review from system's perspective.** *Neuroscience* 2013, **247**:117-133.
 73. Sharma A, Campbell J, Cardon G: **Developmental and cross-modal plasticity in deafness: Evidence from the P1 and N1 event related potentials in cochlear implanted children.** *Int J Psychophysiol* 2014.
 74. Lewis TL, Maurer D: **Multiple sensitive periods in human visual development: evidence from visually deprived children.** *Dev Psychobiol* 2005, **46**:163-183.
 75. Maurer D, Ellemberg D, Lewis TL: **Repeated measurements of contrast sensitivity reveal limits to visual plasticity after early binocular deprivation in humans.** *Neuropsychologia* 2006, **44**:2104-2112.
 76. Ishikawa AW, Komatsu Y, Yoshimura Y: **Experience-dependent emergence of fine-scale networks in visual cortex.** *J Neurosci* 2014, **34**:12576-12586.
Investigates the effects of early visual experience on the development of fine-scale networks and individual synaptic connections in rat visual cortical slices, using two kinds of deprivation, binocular deprivation and dark rearing. It demonstrates that diffuse light stimulation is sufficient for the maturation of individual synapses but that pattern-vision is necessary for the development of fine-scale networks, thus highlighting the crucial role of early visual experience in shaping the intrinsic connections of visual cortex.
 77. Deidda G, Allegra M, Cerri C, Naskar S, Bony G, Zunino G, Bozzi Y, Caleo M, Cancedda L: **Early depolarizing GABA controls critical-period plasticity in the rat visual cortex.** *Nat Neurosci* 2014.
Demonstrates that brief interference with depolarizing GABA during early development prolongs critical-period plasticity in the visual cortical circuits of rats without affecting the overall development of the visual system.
 78. Duffy KR, Mitchell DE: **Darkness alters maturation of visual cortex and promotes fast recovery from monocular deprivation.** *Curr Biol* 2013, **23**:382-386.
 79. Morishita H, Hensch TK: **Critical period revisited: impact on vision.** *Curr Opin Neurobiol* 2008, **18**:101-107.
 80. Lunghi C, Emir UE, Morrone MC, Bridge H: **Short-term monocular deprivation alters GABA in the adult human visual cortex.** *Curr Biol* 2015, **25**:1496-1501.

Reports a decrease of the resting GABA concentration in V1 of adult humans after monocular deprivation. This decrease is highly correlated with the deprived eye perceptual boost as measured by binocular rivalry as well as with the deprived eye dominance measured in terms of GABA concentration during monocular stimulation.

81. Bavelier D, Levi DM, Li RW, Dan Y, Hensch TK: **Removing brakes on adult brain plasticity: from molecular to behavioral interventions.** *J Neurosci* 2010, **30**:14964-14971.
82. Davis MF, Velez DXF, Guevarra RP, Yang MC, Habeeb M, Carathedathu MC, Gandhi SP: **Inhibitory neuron transplantation into adult visual cortex creates a new critical period that rescues impaired vision.** *Neuron* 2015.
83. Sengpiel F: **Plasticity of the visual cortex and treatment of amblyopia.** *Curr Biol* 2014, **24**:R936-R940.

Reviews recent evidence from animal studies showing that visual cortex plasticity can be restored or enhanced later in life by attempting to remove

molecular breaks in plasticity. It uses this evidence to propose new approaches for the treatment of amblyopia.

84. Vetencourt JFM, Sale A, Viegi A, Baroncelli L, De Pasquale R, O'Leary OF, Castrén E, Maffei L: **The antidepressant fluoxetine restores plasticity in the adult visual cortex.** *Science* 2008, **320**:385-388.
85. Bock A, Saenz M, Bridge H, Fine I: **Gross topographic organization in the corpus callosum is preserved despite abnormal visual input.** *J Vis* 2014:1462. VSS August 2014.
86. Hasson U, Levy I, Behrmann M, Hendler T, Malach R: **Eccentricity bias as an organizing principle for human high-order object areas.** *Neuron* 2002, **34**:479-490.
87. Schopf V, Kaspryan G, Brugger PC, Prayer D: **Watching the fetal brain at 'rest'.** *Int J Dev Neurosci* 2012, **30**:11-17.