

“Low road” to rehabilitation: a perspective on subliminal sensory neuroprosthetics

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Abstract: Fear can propagate parallelly through both cortical and subcortical pathways. It can instigate memory consolidation habitually and might allow internal simulation of movements independent of the cortical structures. This perspective suggests delivery of subliminal, aversive and kinematic audiovisual stimuli via neuroprosthetics in patients with neocortical dysfunctions. We suggest possible scenarios by which these stimuli might bypass damaged neocortical structures and possibly assisting in motor relearning. Anticipated neurophysiological mechanisms and methodological scenarios have been discussed in this perspective. This approach introduces novel perspectives into neuropsychology as to how subcortical pathways might be used to induce motor relearning.

Keywords: motor learning, fear perception, internal simulation, sonification, cortical dysfunctions

Background

The structural organization of a human brain is like a mushroom growing inside out, suggesting the ancient prevalence of innermost subcortical structures such as brain stem, amygdala to superficial neocortical structure such as prefrontal cortex. Evolution has bestowed different functional roles on these neural centers based on their development; for instance, the innermost structures usually mediate basic survival functions, such as breathing and fear (threat) processing, whereas the outermost structures manage sophisticated abilities such as decision-making and self-control and more.¹ Being a basic survival function, fear is mainly mediated within the innermost, subcortical structures of the brain.^{1–3} However, due to the evolutionary course, neocortical structures have also formed parallel connections for processing fear, possibly to allow a more cognitive and context-driven processing of the stimuli.^{3–5} LeDoux⁴ labeled such parallel processing of fear by subcortical pathways as “low road processing” and cortical pathways as “high road processing”. However, these pathways operate on distinct terms. On one hand, the “low road” pathways process stimuli in a “quick and dirty” manner while utilizing subcortical pathways, and independent of consciousness.^{6,7} This pathway prioritizes physical safety and acts as a fail-safe mechanism while ignoring any social or environmental context whatsoever. On the other hand, the “high road” pathways allow a rather slower resource-dependent cognitive processing of stimuli via higher cortical structures and prioritize contextual information associated with social, psychological and environmental factors. For instance, longer propagation latency has been reported when fear processing takes place through higher cortical structures, possibly suggesting costs for higher level processing,⁸ whereas processing with “low road pathways” has been reported to be considerably shorter, ie, as low as 30–120 ms.⁹

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Neuroanatomical studies reveal that processing of stimuli through “low road” allows the propagation of fear stimuli in amygdala by the way of superior colliculi and pulvinar nuclei of thalamus,^{4,10} a short pathway, whereas in the high road pathway, for visual information, the stimuli would pass from the retinal ganglion cells to lateral geniculate nucleus, visual cortex (V1, V2 and V4) and inferior temporal cortex, and then end up in amygdala. Under the conditions of threat, mediation of stimuli first to the “low road” pathway is gated by amygdala,⁸ for both visual^{11,12} and auditory streams.^{13,14} It might be because of its higher sensitivity to process low spatial frequency information,^{15,16} thereby initiating action even to a “close enough” stimulus.⁶ For instance, Carter and Frith⁵ proposed that parallel processing by high and low roads¹⁷ allows mediating balance between cortex and the amygdala by allowing both contextualized and fail-safe responses to a threat, respectively.

Several cortical and subcortical structures take part in processing fear-related stimuli. For instance, hypothalamus, amygdala, superior colliculi, lateral geniculate nuclei, thalamus (pulvinar nuclei), locus coeruleus and periaqueductal gray are the main subcortical structures involved in mediating fear,^{10,18} whereas (medial-lateral) prefrontal, orbitofrontal, visual, parietal cortices, anterior cingulate cortex and hippocampus and bilateral anterior insulate cortex are the main cortical structures.^{8,18} Moreover, the functioning of “low road” subcortical pathways is suggested to be independent of higher cortical processing. For instance, diffusion tensor imaging has demonstrated projections between superior colliculi and amygdala via the pulvinar.¹⁹ Furthermore, Morris et al²⁰ in their neuroimaging study reported perception of aversive visual stimuli in a patient with effective blind sight (extensive lesion in occipital cortex).^{21,22}

Additionally, “low road” pathways possess specialized interconnections with the motor control centers of the brain, independent of cortical control, primarily to initiate fight or flight response to a threat. Grezes et al²³ using diffusion tensor magnetic resonance imaging and probabilistic tractography demonstrated interconnectivity of amygdala to descending corticospinal tracts, lateral and medial precentral, motor cingulate, primary motor cortices and postcentral gyrus. Gokdemir et al²⁴ further reported fear potentiation of both corticospinal and reticulospinal pathways in humans, post auditory and visual fear conditioning. Moreover, a strong role of these primitive subcortical pathways has also been reported for the perception of biological motion.^{25,26} Furl et al²⁷ in an fMRI analysis revealed enhanced fear sensitivity in dorsal and ventral temporal motion-sensitive areas corresponding to superior temporal sulcus, hMT+/V5, inferior frontal gyrus,

fusiform cortex (fusiform face area) and the action observation system.²⁸ The authors further added that amygdala might also control encoding and prediction of aversive incidence based on the elements of stimuli. Moreover, Bastiaansen et al²⁹ added that such interconnections of amygdala with these motor centers might be helpful in triggering for mirroring of emotions.

Likewise, this subcortical pathway (especially amygdala²) mediates a unique learning and memory mechanism. This mechanism has been reported to play a key role in predicting threat-based events before recognition of sensory stimuli.^{2,30} Here, amygdala has also been reported to facilitate learning in a rapid,³¹ habitual^{1,31–34} and resilient manner.³⁵ Possibly, by modulating the activity and connectivity of prefrontal cortex,^{36,37} Schwabe et al³⁸ suggested that threat-induced stress can selectively gate memory consolidation in favor of thalamus-dependent habitual learning^{2,39} as compared to hippocampus.^{33,35} Shiromani et al³¹ too affirmed that the altered strength of synaptic signaling in amygdala is the major reason for habitual consolidation of memory. The authors stated that relatively weak conditioned stimuli (activating postsynaptic *N*-methyl D-aspartate receptors) gets strengthened by co-occurrence of unconditioned stimuli (triggering calcium influx), thereby eliciting robust responses in lateral nucleus. Moreover, the independence of this specialized memory system from cortical pathways and resilience in terms of long-term retention have also been reported (thalamo-amygdala pathways⁷). For instance, Maren and Quirk² reported lateral amygdala-associated memory plasticity during auditory fear conditioning, even in the presence of large lesions in auditory cortex.⁴⁰ Nevertheless, despite extensive research confirming the unique ability of the “low road” pathway to govern motor action, perception and memory consolidation independent of cortical structures, its possible role in enhancing prognosis in cases of neocortical dysfunctions has never been discussed in the literature.

As mentioned earlier, neocortex, the outermost and latest evolutionary development of brain, accounts for ~76% of the brain volume.⁴¹ Any superficial damage to these structures in cases of trauma and cerebrovascular accidents might cause a wide array of cognitive^{42–44} and sensory–motor dysfunctions.⁴⁵ Such damages together inflict debilitating symptoms on both cognitive and motor domains, thereby adversely impacting the prognosis of such patients. For instance, damage to prefrontal cortex (dysexecutive syndrome⁴⁶) might considerably impair conscious perception;⁴⁷ self-control; task purportedly measuring fluency; concept formation; set shifting; inhibition; attention organization; abstract reasoning; novel problem-solving ability; stimuli inferencing decision-making

ability; ability to encode task relevant information in working memory;^{48,49} ability to select, monitor, manipulate and access current task information⁴⁴ and others.⁵⁰ Shumway-Cook and Woollacott⁵¹ suggested that such deficits in attention, working memory allocation and short-term memory might considerably prolong the prognosis in a rehabilitation protocol, where explicit instructions are mainly emphasized.^{52,53} In this study, we attempt to explain how the specialized abilities of these “low road” pathways could be exploited to enhance motor relearning for aiding in rehabilitation independent of such higher cortical functioning.

Accessing the “low” roads: the novel strategy

In this article, we attempt to suggest possible strategies that could be used to access the subcortical “low road” routes of the brain to facilitate or stimulate the damaged or dormant structures of the brain and aid in rehabilitation. We suggest utilizing task-specific multimodal neuroprosthetics to deliver aversive sensory stimuli subliminally to enhance motor perception and facilitate the process of motor relearning.⁵⁴ Real-time kinematic auditory feedback (sonification) and kinematic visual feedback generated in some of the widely researched rehabilitation approaches which allow comprehensive and efficient multisensory integration.^{55,56} Kinematic auditory feedback is a relatively new interdisciplinary approach which has been utilized and demonstrated to enhance motor perception, motor control and learning in rehabilitation.^{57,58} This methodology takes advantage of the strong relationship between auditory perception and motor control,^{59–62} and has been reported to trigger neural centers associated with biological motion perception.^{63,64} Also, sonification might provide valuable assistance toward enhancing movement perception of motor patterns associated with/without expertise, further aiding in enhancing representation and internal simulation of a motor task in the action observation system.^{65,66}

Likewise, virtual reality is effective in rehabilitation.⁶⁷ The environment designed in virtual reality can be customized very similar to real-life settings⁶⁸ and can possess benefits in terms of transmitting kinematic visual stimuli for augmenting the brain functions by enhancing motor perception,⁶⁹ especially related to biological motion perception.⁷⁰ Moreover, the sensorimotor lability of both kinematic auditory and visual stimuli can be used to induce a compelling sense of immersion even when sensory inputs are incongruent and below the conscious threshold.⁶⁹ Therefore, coupling the use of methodologies can possibly provide opportunities to deliver multimodal multisensory information in terms of kinematic

auditory and visual information concomitantly.^{58,64,65,71} These methodologies have demonstrated to enhance perception,⁶⁴ efficient human behavior,^{68,72} motor learning,⁶⁴ relearning⁶⁴ and performance,⁷³ thereby allowing benefits in the due course of rehabilitation. Radiological evidence by Schmitz et al⁶⁴ demonstrated robust activation of a specialized mirror–neuron system and human action observation system, precisely the activation of cortical: superior temporal sulcus, Brodmann’s area 45, 6, and subcortical areas comprising striato-thalamo-frontal motor loop, ie, caudate nucleus, putamen and thalamus. The authors further speculated that such an activation of the action observation system while listening to motor activities might lead to an internal stimulation of perceived movement. Therefore, suggesting an association for increase in mental, auditory imagery.⁵⁵

Utilizing such multisensory modalities for transmitting aversive subliminal stimuli might allow multifaceted benefits in perceptual domain, for instance, providing kinematic stimuli associated with fearful postures. Supposedly, a wild environment could be generated where a distant predator or imminent danger leads the person to choose a flight response and run away from the situation. Here, the patient could either be subjected to a first person or a third person view i.e., patient perceiving the threat on themselves or on a virtual avatar, respectively. This difference could be selected based on the level of cognitive and meta-cognitive dysfunctions. Further, coupling the audiovisual kinematic information for fearful postures and locomotion might instigate similar changes in the patient’s action observation system and enhance internal simulation associated with locomotion for a “flight” response. For instance, Johansson⁷⁴ suggested that higher cortical centers are not the main components for perceiving basal biological motion, and therefore, this approach might be efficient in the condition of no-cortical dysfunction. Moreover, the stimuli might also be used to instigate reflexive behavior. For instance, Tamietto and De Gelder⁷⁵ suggested a strong relationship between the motor domain and amygdala while processing fearful stimuli to elicit reflexive behavior. In this study, we again suggest to possibly exploit this strong network and utilize multisensory integration modalities to address the deficits in motor execution. For instance, virtual reality can be used to generate a specific environment where a predator, such as a snake, tries to attack an extremity, eliciting a reflexive withdrawal reflex. Sonification in such a strategy can be used to superimpose on the executed reflexive action, for instance, aversive auditory feedback can be superimposed on the elbow imitating a flexor withdrawal reflex. Although due to motor restrictions these movements might not be physically executable, simulating

these motor movements might allow preemptive facilitation (feed-forward manner) essential for execution.⁷⁶

Such internal representations should elicit internal representations of motor tasks and thereafter aid in kinesthetic motor imagery for the perceived movement pattern. Moreover, facilitation of neural pathways might also be elicited as a rehabilitation perspective neural pathway for motor execution and imagery, and actively executed motions share a similar neural circuitry.⁷⁷ Ietswaart et al⁷⁸ suggested that enhanced brain plasticity because of mental practice can play a very important role in recovery following brain damage. Precisely, imagining or practicing movements could stimulate restitution and redistribution of brain activity, which can enhance the recovery of motor functions (refer “Hebbian theory”⁷⁹). This when superimposed with conventional passive and active movements by a physiotherapist might provide additional benefits for relearning and performance.^{80–82} Although highly speculative the fearful stimuli provided with biological motion might also instigate memory consolidation of movement patterns in a habitual manner, which in rehabilitation and performance settings have been demonstrated to be extremely beneficial.^{83–87}

Moreover, to avoid the detrimental perceptual repercussions in behavior, the stimuli can be delivered subliminally. Perception of fear stimuli has been reportedly maintained even when a stimulus is masked,⁸⁸ with dichoptic stimulation,⁸⁹ when stimulus is presented at thresholds⁹⁰ and in the peripheral vision.^{91,92} Additionally, visual activation of invisible stimuli can also be strong, when the invisibility is induced by neglect⁹³ or inattention.⁹⁴ Dehaene et al⁹⁵ suggested a state of contrast between subliminal and preconscious processing, which possibly could be an appropriate tool or the application of audiovisual stimuli, ie, masking of stimuli combined with inattentiveness. The author implied that within the conscious perception, a subject would be able to recognize and identify the presented stimuli.⁸ On the contrary, the preconscious state of perception implies that the subject has a relatively strong neural response to the presentation, but either is not yet consciously aware or will miss it due to the absence of attention.⁹⁵ Finally, we hypothesize this methodological approach to attain perceptual and learning benefits by two mechanisms: first, by eliciting reflexive mechanisms in patients and activating dormant or damaged cortical pathways. Furthermore, this approach can be allocated with activities of daily living, where certain activities can be coupled with aversive sensory inputs. Together they are hypothesized to enhance biological motion perception, higher neural center activation, mental practice, cortical restructuring and regeneration and when coupled with physical therapy, they can lead to additional

motor activity in terms of rehabilitative benefits. This perspective for the first time proposes the utilization of “low” road pathways for facilitating higher neocortical structures in case of damage. This approach could also have applications for patients in minimal conscious states where prognosis is exceptionally poor.⁹⁶ These patients exhibit characteristics similar to higher order cortical dysfunctions.^{97,98} Additionally, the patients under minimal conscious states as per the categorization by Giacino et al⁹⁹ and Vincent⁹⁸ exhibit reproducible visual fixation, emotional and motor behavior. Producing reflexive motor actions via multisensory integration of aversive stimuli can allow the development of increased awareness and elicit neural reorganization. Finally, the main aim of this perspective is to elicit a scientific discussion on the topic, and we strongly urge future studies to analyze this gap in the literature.

As a future prospect, we would like to propose utilization of aversive olfactory stimuli as a possible medium in multisensory integration for enhancing fear perception. Studies have reported the effects olfactory stimuli possess on motor control of human body.^{100–102} Sakamoto et al¹⁰² speculated that olfaction possibly could have enhanced stability and motor performance by activating the insular cortex. Similarly, a multisensory integration pattern has been demonstrated in studies evaluating audio-olfactory domain¹⁰³ and visuo-auditory domain.¹⁰⁴ Nonetheless, the most important aspect why we are interested in incorporating olfaction in multisensory integration is its association with the limbic system. Baars and Gage¹ suggested that the afferent signals to amygdala arrive via four main pathways. However, the information drawn from olfactory stimuli is perpetuated directly at amygdala from the olfactory cortex without preprocessing at the thalamus, thereby suggesting a profound ability of odor as compared to other sensory stimuli on emotional consolidation of memories. Likewise, the findings of De Groot et al¹⁰⁵ are also important where olfactory fear stimuli were described to be as potent as audiovisual fear signals in inducing fear. This could considerably add toward the development of a comprehensive environment to elicit a fear response. Not only this but recent research by Jacobs et al¹⁰⁶ have also confirmed the presence of spatial coding information with high precision with olfaction in humans. These findings considerably add toward the prospective use of olfaction with movement perception and virtual reality where the spatial information about the motor movements derived from sensory inputs is a key component.¹⁰⁷ Nonetheless, the concept of utilization of olfaction as a possible medium of multisensory integration in movement perception is rather new and has been never discussed in

published literature earlier. Recent advancements in virtual reality domain by coupling olfactory inputs by Ubisoft can possibly ascertain future application. Gaming modalities such as Nosulus rift can precisely incorporate aversive scents and couple them in a simulated environment providing enhanced perception benefits. This has been previously described by Richard et al.¹⁰⁸ Additionally, we would also suggest utilization of modern neuroprosthetics such as smart skins to enhance afferent inputs from skin receptors to aid in multi-sensory integration, and relearning.¹⁰⁹

Summary

In this article, we propose a possible methodological approach which utilizes the “low” road fear pathways in rehabilitation of neurological disorders characterized by cortical damage primarily leading to executive dysfunctions. Based on the previous findings, this article bridges the published empirical findings and suggests that perception of fear can occur without consciousness. The article also proposes a methodological approach by using multisensory integration modalities, such as real-time kinematic auditory feedback, virtual reality to transfer aversive stimuli via audiovisual input, without conscious awareness to enhance biological motion perception, associated with activities of daily living to enhance mental imagery, practice, preparedness and possibly neural regeneration. Moreover, we also discuss possibly eliciting reflexive motor actions incurred by an aversive stimulus to enhance motor relearning. This coupled with physical rehabilitation can allow more benefits in terms of prognosis. This methodological perspective is aimed to address the poor prognosis faced by patients suffering from neocortical dysfunctions.

Acknowledgments

This article was funded by the open access funds of Leibniz University Hannover. The authors thank Prof Robert Isler and Prof Thomas Münte for their constructive comments and guidance.

Author contributions

Shashank Ghai conceptualized the perspective and wrote the article. Ishan Ghai and Alfred O Effenberg provided useful discussions and reviewed the paper. All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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