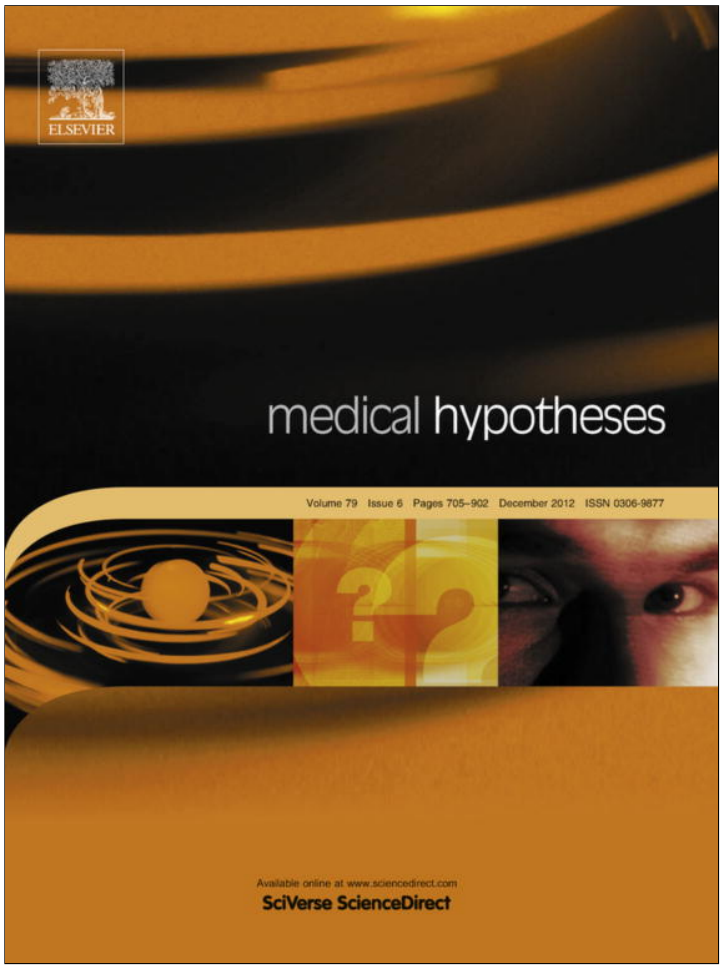

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Manipulation of the extrastriate frontal loop can resolve visual disability in blindsight patients

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ABSTRACT

Patients with blindsight are not consciously aware of visual stimuli in the affected field of vision but retain nonconscious perception. This disability can be resolved if nonconsciously perceived information can be brought to their conscious awareness. It can be accomplished by manipulating neural network of visual awareness. To understand this network, we studied the pattern of cortical activity elicited during processing of visual stimuli with or without conscious awareness. The analysis indicated that a re-entrant signaling loop between the area V3A (located in the extrastriate cortex) and the frontal cortex is critical for processing conscious awareness. The loop is activated by visual signals relayed in the primary visual cortex, which is damaged in blindsight patients. Because of the damage, V3A-frontal loop is not activated and the signals are not processed for conscious awareness. These patients however continue to receive visual signals through the lateral geniculate nucleus. Since these signals do not activate the V3A-frontal loop, the stimuli are not consciously perceived. If visual input from the lateral geniculate nucleus is appropriately manipulated and made to activate the V3A-frontal loop, blindsight patients can regain conscious vision.

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Under experimental conditions certain brain-damaged patients are able to accurately identify visual stimuli that they deny perceiving consciously [1]. This phenomenon of perception without awareness has been extensively studied on patients with lesions in the primary visual cortex (V1). These patients with 'blindsight', cannot see visual stimuli in the affected field of vision but when forced to make a choice, they show remarkable accuracy in describing location, color, stimulus orientation, target displacement and direction of motion of objects located in their 'blind' fields [2]. It suggests retention of nonconscious perception of visual stimuli.

Because of the retained nonconscious perception, the disability in these patients could be resolved if perceived stimuli are brought to conscious awareness by manipulating the neural network involved in conscious perception. We recently identified this network by analyzing the pattern of neural activation elicited during processing of visual stimuli with or without conscious awareness [3–11]. In a series of neuroimaging experiments we studied conscious and nonconscious retrieval of visual stimuli and found that the activity in the area V3A located in the extrastriate cortex, is significantly attenuated during nonconscious processing. This finding was replicated by other investigators and it is one of the most consistent changes observed in the brain activity during processing of nonconscious memory [12,13]. Interestingly, reduced activation in this area is observed also during conscious memory processing of visual [9,14] and auditory [6,8,15] stimuli. In this condition addition activation is found in the frontal and hippocampal areas. There is however a difference in the pattern of V3A attenuation observed during conscious and nonconscious processing. The activity is reduced for about 600 ms during processing of the conscious task but only for 200 ms (early attenuation) during nonconscious processing [8,16,17]. Further, the additional reduction of 400 ms (late attenuation between 200 and 600 ms) observed in the conscious condition temporally overlaps the increased activity in the frontal cortex observed during conscious processing. This finding is important because the frontal cortex is involved in the processing of conscious awareness [18,19].

Thus, in the conscious condition attenuation of the V3A activity is observed both in the early (in the first 200 ms) and late (between 200 and 600 ms) phases of the processing. Since the early attenuation is associated with nonconscious processing, finding of this attenuation in the conscious condition indicates that the stimuli are initially retrieved nonconsciously even in the conscious condition [9,14,16,20]. These stimuli are then 'held' for about 400 ms (during late attenuation). During this time period signals are relayed to the frontal cortex leading to the frontal activation and conscious awareness of stimuli. Further, the temporal overlap (between 200 and 600 ms) of the this activation with the late attenuation of the V3A suggests activation of a reverberating

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feedback circuit making a reentrant signaling loop between the V3A and frontal cortex – perhaps via intermediate inhibitory interneurons. This loop appears to be instrumental in bringing nonconscious information to conscious awareness. In this context the observation that activity in the loop is maintained for about 400 ms is important because experiments suggest that a signal cannot be consciously perceived unless it activates the cortex for about half a sec [21]. The V3A-frontal reentrant loop allows the signal to activate the cortex until it is consciously perceived. Additionally, many investigators believe that activation of a re-entrant signaling loop is essential for processing of multiple components of a metacognitive function such as conscious awareness [21,22].

The association of V3A-frontal loop with conscious awareness is consistent with Crick and Coch's meta-analysis of neurocognitive studies on awareness [18]. The analysis suggests that the neurons of only extrastriate and frontal areas possess necessary neuroanatomical and psychophysical properties to support conscious awareness. They argue that the awareness of visual information must involve connection between neurons of these areas. It is therefore not surprising that the frontal cortex is activated in blindsight patients [23] only when a visual stimulus is perceived consciously. It is not activated when the stimulus is perceived without awareness. Involvement of the V3A-frontal loop in conscious awareness is indicated also by lesion studies that have reported impaired awareness of visual stimuli when the loop is damaged. Thus, disruption of the ventral stream of visual projection, which connects the neurons of extrastriate cortex and frontal lobe, alters awareness of visual stimuli and leads to visual form agnosia. These agnostic patients cannot recognize geometric shapes but select slots of correct dimension and orientation when asked to match slots with wooden blocks of different shapes [24]. Further, lesions in the parietal cortex (which also disrupts the extrastriatal-frontal connectivity), makes the patients ignore visual stimuli in the affected filed. This condition is another form of perception without awareness [25].

The precise role of prefrontal cortex in processing of visual awareness however has been under intense debate. Even though the evidence suggests its involvement, cortical blindness following frontal lesions has not been frequently reported [26]. It led to the confusion concerning the role of frontal cortex. It however appears that the confusion is primarily due to the complexity of information processing in the frontal cortex. Since signals from the extrastriate cortex activate the frontal lobe of both hemispheres [23], unilateral frontal damage is not expected to affect visual awareness. Bilateral damage to specific frontal areas however should affect the awareness. While no study has reported complete blindness after bilateral lesion, a number of investigators have found impaired awareness of visual stimuli after the lesion. The impairments include higher temporal threshold for recognition of visual stimuli [27]. These patients become consciously aware of a visual stimulus when it is presented for a long duration. This finding is consistent with the observation of another experiment in which it was shown that the temporal threshold for perception reduces significantly after the frontal cortex is activated using transcranial magnetic stimulation (TMS) [28]. After the activation, essentially volunteers become consciously aware of otherwise subliminal stimuli. Expectedly, after suppression of the (dorsolateral) frontal activity by rTMS, volunteers find it difficult to consciously recognize changes in visual stimuli presented to them [29]. It also impairs metacognitive awareness of visual stimuli [30]. These findings suggest that the processing of visual awareness is impaired in patients with frontal lesions [31]. Thus, frontal lesions affect aspects of visual awareness but it does not completely abolishes it, possibly because aspects of visual awareness are processed in widely distributed areas within the frontal cortex. Therefore some aspect of the awareness remains intact even after extensive frontal damage.

It therefore appears that the V3A-frontal signaling loop activates several areas of the frontal cortex either directly or indirectly through relay neurons. Further, this loop is activated normally by visual signals that are relayed in the V1. These signals therefore are perceived consciously. If the V1 is damaged, the loop is not activated and signals are not consciously perceived. The damaged V1 however does not prevent visual stimuli to activate the brain via signals relayed in the lateral geniculate nucleus [32]. The studies suggest a direct neuronal connection between the lateral geniculate and the extrastriatal areas including the area V3. Significantly, a temporary lesion of the lateral geniculate nucleus abolishes behavioral response to visual stimuli in monkeys with damaged V1 [33]. It indicates that blindsight patients receive visual signals via the connection between the lateral geniculate nucleus and extrastriate cortex [34]. Signals arriving via this connection however, do not activate the V3A-frontal loop. Therefore, visual stimuli are not consciously perceived [2]. Visual signals arriving through this connection however, can possibly be manipulated to activate the V3A-frontal signaling loop. The manipulation could use neurochemical, neurosurgical, or cognitive techniques. These manipulations will enable blindsight patients to consciously perceive visual stimuli in their 'blind' fields and resolve visual symptoms. It is therefore important to explore the lateral geniculate-V3A connection and formulate a strategy to activate the V3A-frontal loop by the signals arriving via this connection.

Conflict of interest statement

None declared.

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