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Does vestibular stimulation activate thalamocortical mechanisms that reintegrate impaired cortical regions?

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Caloric stimulation induced a transient reversal of multimodal hemispatial cognitive deficits in an 81-year-old woman with an acute left cerebral hemisphere stroke. The patient had unawareness of her right hand (asomatognosia), right-sided visual unawareness (hemineglect), aphasia and right-sided weakness (hemiplegia) prior to the stimulation. Transient improvements in impaired sensory, motor, linguistic and cognitive function developed within 30 s following application of the caloric stimulus and onset of horizontal nystagmus. The effect persisted for 3 min and ceased completely after 5 min. While several recent reports have described the capacity of caloric stimulation to transiently improve or reverse a wide range of attentional, cognitive and motor impairments, most examples are in right-hemisphere-damaged patients with long-standing brain injury. Typically, patients have been tested several months or years after the onset of the deficit. A possible mechanism for the temporary reintegration of multiple cognitive functions in this patient is discussed.

Keywords: intralaminar thalamus; gating; cognition; awareness; hemi-neglect; attention

1. CASE

An 81-year-old, right-handed woman suffered an acute left hemispheric cerebral infarct following an elective repair of an aortic aneurysm. The patient had recovered well from the surgery and was scheduled for discharge to a rehabilitation facility. At 6 pm on post-operative day 23, she was found lying sideways on her bed unable to talk or move her right side. Vital signs were within the normal range with the exception of an elevated blood pressure of 175/90. On initial neurologic examination, she was awake and globally aphasic. Her eyes were fully deviated to the left at rest. This dense left lateral gaze preference could not be overcome by passive rotation of the head. The appearance of a loss of awareness of the right visual field (homonymous hemianopia) was noted as the patient did not blink to visual threat from the right side. Right-sided strength was markedly reduced (graded 1/5 in the upper extremity, 3/5 in the proximal lower extremity and 2/5 in the distal lower extremity). She withdrew from noxious stimuli bilaterally. Deep tendon reflexes were brisk and symmetrical. Right plantar response was extensor. The general medical exam was unremarkable. A CT scan of the head revealed no haemorrhage or early signs of a structural lesion. She was given aspirin and no further intervention. At 8 pm she was noted to be able to make gross movements of the right arm, lift the right leg and answer questions with brief one- or two-word answers.

At 10.30 pm she was awake, alert with a moderate expressive aphasia and a notable receptive aphasia. A dense right hemispatial neglect was noted. Eye deviation to the left was evident at rest and leftward eye movements were noted in response to auditory stimuli emanating from the right side. She was unable to visually track past the midline and demonstrated a loss of response to visual threat from the right, accompanied by unawareness of any right-sided stimuli when queried. Optokinetic nystagmus was elicited with bars moving to the left, but not to the right. An object-referenced visual extinction of one of two moving finger stimuli was noted within the left hemi-field depending on the head position of the examiner, i.e. leaning in from the right or left side of the bed. When testing the left visual field with outstretched hands each with a moving finger, the patient extinguished either the lower finger (examiner's head tilted 90° from the left side) or the upper finger (examiner's head tilted 90° from the right side). The patient's right hand and arm were tightly held against the side of her chest and exhibited no spontaneous movements. When this hand was moved with effort and brought into the left visual hemi-field the patient could not identify the hand as her own. Asked, 'Whose hand is this?', the patient tentatively replied, 'I don't know' and further denied the hand as her own when queried.

After otological examination revealed normal tympanic membranes and clear external auditory canals, the right external auditory canal was irrigated with 50 ml of ice water. Within 30 s she underwent notable functional improvement. She immediately orientated both head and eyes to right-sided auditory cues and held visual attention to the right hemi-space. Object-referenced neglect was no longer evident in the left hemi-space. Simultaneous with the change in her response to auditory and visual cues in right hemi-space, spontaneous 'exploratory' movements of the right arm and hand appeared. When the right arm was presented to the patient with the question 'Whose

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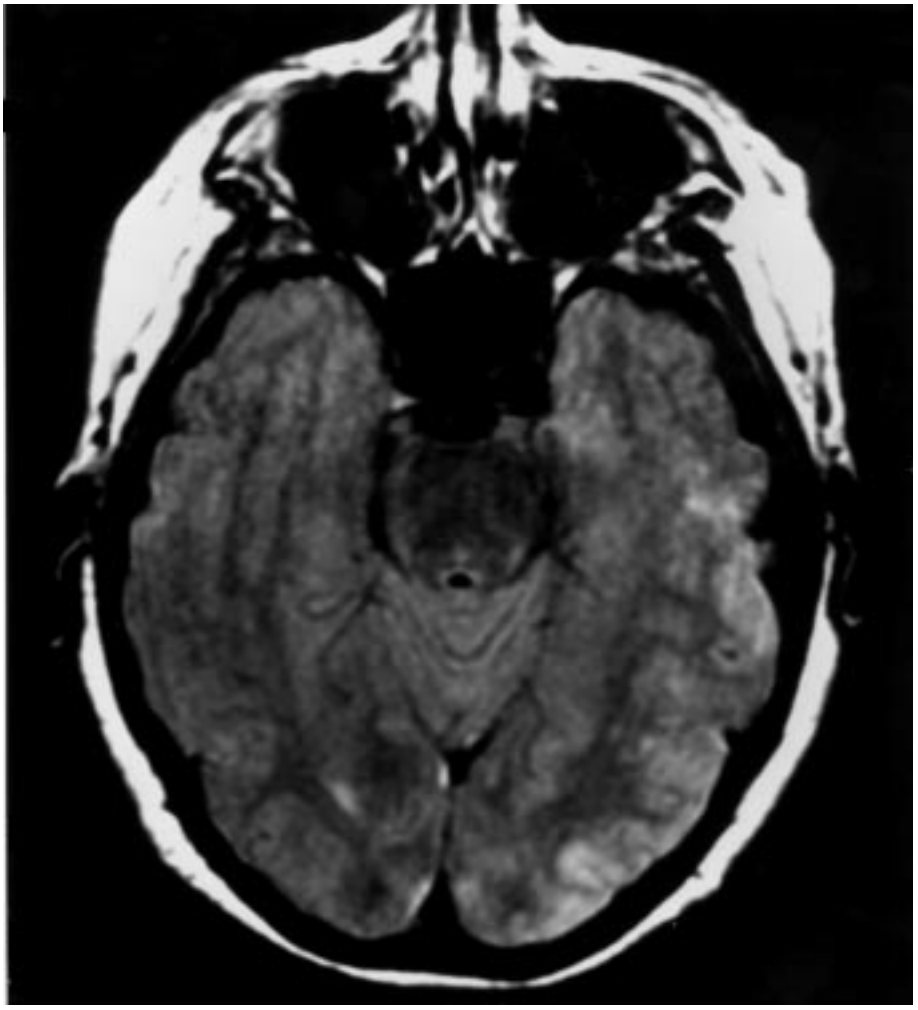

Figure 1. T2 weighted MRI axial images demonstrating hypodense lesions consistent with infarctions of the temporal lobe.

hand is this?', she now replied immediately and with emotional emphasis, 'That's my hand!' During the following 4 min, the patient slowly relapsed her resting body, head and eye positions back toward her post-stroke baseline.

A 1.5 Tesla MRI scan obtained 24 h after the stroke demonstrated multiple cortical infarcts with distribution of emboli from a proximal region of the middle cerebral artery. The left temporal lobe was most uniformly affected (figure 1) along with frontal, parietal and occipital ischaemic regions. A thallium SPECT examination showed normal regional cerebral perfusion to the left temporal-parietal occipital region and minimal reduction of blood flow in the contralateral cerebellum suggesting a mild reversed crossed cerebellar diaschisis phenomenon. Stroke evaluation was unremarkable, including a normal carotid Doppler exam and echocardiogram. A repeated attempt with caloric stimulation on post-operative day 30 elicited less recovery than the first stimulation. However, a similar pattern of improvement was evident with improved hemispatial localization of auditory and visual stimuli and movements of the right arm. At this point the patient did not consistently exhibit object-referenced neglect or asomatognosia at baseline. The patient remained with a dense right-sided neglect and mild right-sided weakness and was transferred to a nursing home on post-operative day 31. The reduced effect observed at this later examination likely reflects a further loss of cortical tissue due to the filling in of the penumbra of the stroke over the hours and few days following the initial examination. In addition, the inconsistent appearance of object-referenced neglect and asomatognosia at this stage of the patient's illness prevented an unequivocal evaluation of these aspects of cognitive function.

2. DISCUSSION

To our knowledge, this is the first report of cold caloric stimulation in the setting of an acute stroke inducing transient recovery of multiple cognitive impairments. Coslett and co-workers (1993) reported a single patient, JF, with multimodal hemispatial deficits following a left hemispheric stroke similar to those of our patient. Caloric testing, however, was not reported. The underlying mechanism for the observed recovery of function in our patient and others is unclear (Vallar *et al*. 1997). Bottini and colleagues (1994) used ^{15}O-PET to study one patient with recovery of mild somatosensory inattention following caloric stimulation. The improved sensory discrimination in this patient was interpreted in terms of

an increase past a threshold level of activation in multiple cortical areas. Another recent report (Nadeau *et al*. 1997) demonstrated a global hemispheric increase in blood flow in a patient with visual neglect who showed improvement with forced gaze deviation. The marked and widespread changes seen with this simple manoeuvre suggest that recovery of awareness may depend on specific, organized activations of distributed cortical and subcortical regions linked to eye movements. It is possible that a similar physiologic mechanism may underlie the transient recovery of our patient's deficits with caloric stimulation. It is important to note that, as in the above example, the recovery of deficits with caloric stimulation is also a selective phenomenon, not simply dependent on arousal. This is evident in the well-documented difference between contralesional ear canal stimulation, which may produce improved function and ipsilesional stimulation which results in no improvement or even worsening (Rubens 1985). Reintegration of function in our patient was not observed with ipsilesional ear canal irrigation.

Thus, the recovery of multiple cognitive capacities in our patient raises the question of whether a mechanism that influences the gating of long-range cortico-cortical processing may be engaged by caloric stimulation. This case raises these questions because of the simultaneous reintegration of multiple cortical functions observed following vestibular stimulation. The demonstration of this effect in the setting of an acute stroke eliminates the possibility that the response to vestibular stimulation is a result of later brain plasticity in the course of recovery. We tentatively suggest that the projections of the brainstem vestibular nuclei to the thalamic intralaminar nuclei (ILN) may mediate the observed reintegration of impaired cortical regions. Both clinical and experimental data provide evidence for similar multimodal neglect phenomena to arise with lesions of the ILN (Purpura & Schiff 1997; Steriade 1997). The vestibular nuclei directly project to the centromedian–parafascularis complex of the posterior intralaminar group, which has connections to the basal ganglia and distributed cortical regions including premotor and parietal cortex (Shiroyama *et al*. 1995). The caloric stimulation also activates ascending cerebellar outputs that project strongly to the central lateral nucleus of the anterior intralaminar group which projects to the frontal eye fields, prefrontal and visual association cortices (Steriade *et al*. 1997). A specific theory has been proposed for the role of these ILN connections in the integration of arousal inputs with attention, working memory and gaze control (Purpura & Schiff 1997). We hypothesize that caloric stimulation may generate a reallocation of these resources to the left hemisphere, via inputs to the intralaminar thalamus, that transiently results in global functional improvement. The brief duration of the recovery may specifically depend on the repetitive distribution of cortical activations based on an efference copy signal of eye movements generated in the ILN (Purpura & Schiff 1997). Cortical reintegration mediated by the ILN may be facilitated in this case by the nystagmus induced by vestibular stimulation.

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