Acta Neuropsychiatrica 2007: 19: 183–203

DOI: 10.1111/j.1601-5215.2007.00208.x

ACTA NEUROPSYCHIATRICA

Studies of caloric vestibular stimulation: implications for the cognitive neurosciences, the clinical neurosciences and neurophilosophy

Steven M. Miller[1,2,3], Trung T. Ngo[1,2]

[1]Caulfield Pain Management and Research Centre, Caulfield General Medical Centre, Melbourne, Victoria, Australia; [2]Brain Stimulation Laboratory, Alfred Psychiatry Research Centre, The Alfred Hospital, Melbourne, Victoria, Australia; and [3]Department of Psychological Medicine, Monash University, Melbourne, Victoria, Australia

Miller SM, Ngo TT. Studies of caloric vestibular stimulation: implications for the cognitive neurosciences, the clinical neurosciences and neurophilosophy.

Objective: Caloric vestibular stimulation (CVS) has traditionally been used as a tool for neurological diagnosis. More recently, however, it has been applied to a range of phenomena within the cognitive neurosciences. Here, we provide an overview of such studies and review our work using CVS to investigate the neural mechanisms of a visual phenomenon – binocular rivalry. We outline the interhemispheric switch model of rivalry supported by this work and its extension to a metarivalry model of interocular-grouping phenomena. In addition, studies showing a slow rate of binocular rivalry in bipolar disorder are discussed, and the relationship between this finding and the interhemispheric switch model is described. We also review the effects of CVS in various clinical contexts, explain how the technique is performed and discuss methodological issues in its application.
Methods: A review of CVS and related literature was conducted.
Results: Despite CVS being employed with surprising effect in a wide variety of cognitive and clinical contexts, it has been a largely underutilized brain stimulation method for both exploratory and therapeutic purposes. This is particularly so given that it is well tolerated, safe, inexpensive and easy to administer.
Conclusion: CVS can be used to investigate various cognitive phenomena including perceptual rivalry, attention and mood, as well as somatosensory representation, belief, hemispheric laterality and pain. The technique can also be used to investigate clinical conditions related to these phenomena and may indeed have therapeutic utility, especially with respect to postlesional disorders, mania, depression and chronic pain states. Furthermore, we propose that based on existing reports of the phenomenological effects of CVS and the brain regions it is known to activate, the technique could be used to investigate and potentially treat a range of other clinical disorders. Finally, the effects of CVS (and its potential effects) on several phenomena of interest to philosophy suggest that it is also likely to become a useful tool in experimental neurophilosophy.

Keywords: anterior cingulate cortex; attentional neglect; binocular rivalry; caloric vestibular stimulation; chronic pain; neurophilosophy; phantom limb

Dr Steven M. Miller, Caulfield Pain Management and Research Centre, Caulfield General Medical Centre, 260 Kooyong Rd, Caulfield, Melbourne, VIC 3162, Australia.
Tel: +61 3 9076 6834;
Fax: +61 3 9076 6675;
E-mail: steven.miller@med.monash.edu.au

Introduction

Caloric vestibular stimulation (CVS) is a routine diagnostic technique in the neurological assessment of vestibular function and brain death (1,2). Irrigating the external ear canal with water was reportedly used in the first century A.D. to purge foreign material (3); however, it was not until two millennia later that Bárány developed caloric stimulation as a vestibular diagnostic test (4–6). The caloric test requires the instillation of cold or warm water into the external ear canal ('CVS' hereafter refers to cold-water irrigation, unless

otherwise indicated). CVS elicits semicircular canal fluid movement, afferent vestibular nerve signals to vestibular nuclei and activation of *contralateral* cortical and subcortical structures. After 10–20 s of irrigation, the subject shows nystagmic eye movements (through the vestibulo-ocular reflex) and experiences vertigo.

In recent years, CVS has been applied beyond the neurodiagnostic realm in a wide range of contexts with often striking effects. These effects provide insights into the neurobiology of the phenomena in question because the brain regions activated by CVS have been well documented. As with many phenomena targeted by brain-imaging studies, the CVS imaging studies are complex however consistent findings of contralateral hemispheric activation have been shown. These activated regions include anterior cingulate cortex (ACC), temporoparietal cortex and insular cortex [detailed below (7–15)]. Such regions have been linked by brain-imaging, lesion and other studies to the various phenomena affected by CVS. Because these areas are also functionally linked to cognitive and clinical contexts in which CVS has not yet been applied, there is fertile ground for future experimental work using the technique.

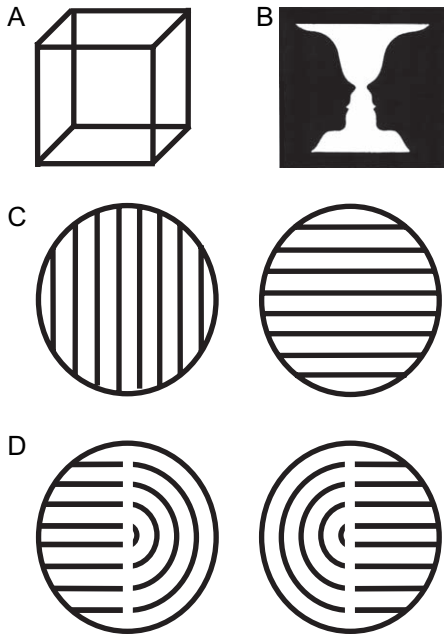

Fig. 1. Types of perceptual rivalry. (A) The Necker cube induces perceptual reversals of depth perspective. (B) Rubin's vase-faces illusion induces perceptual reversals between figure and ground. (C) Conventional BR stimuli induce alternating perception of each image. Try this for yourself by free fusing or using a piece of cardboard to separate each eye's presented image. (D) Díaz-Caneja BR stimuli induce alternations between four percepts: two that reflect each eye's presented image (half-field percepts) and two that are perceptually regrouped into coherent images (coherent percepts).

In what follows, we aim to show that CVS is a largely underutilized exploratory tool in the cognitive and clinical neurosciences. This is illustrated by outlining the success of applying CVS in novel contexts across several domains. We then argue that the technique may serve not only as a useful exploratory tool but also as a potential clinical therapeutic intervention for conditions that are (i) known to be affected by CVS and (ii) known to involve brain regions activated by CVS. These conditions span psychiatry, neurology, neuropsychiatry, rehabilitation medicine and pain medicine. Having discussed the utility of CVS as an exploratory tool and potential clinical intervention, we conclude by arguing with reference to such discussion that CVS is also a valuable tool for empirical studies in neurophilosophy.

CVS during binocular rivalry

We applied CVS to the investigation of neural mechanisms of binocular rivalry (BR). BR is a well-studied visual phenomenon in which the presentation of conflicting images, one to each eye, induces an alternating perception of each image, every few seconds. While one image is perceived, the rival image is suppressed from visual consciousness and this to-and-fro alternation continues for as long as the conflicting stimuli remain presented to the eyes. The perceptions during BR are similar to the alternations that occur with the well-known Necker cube, a perspective-reversing ambiguous figure (Fig. 1A) and with Rubin's vase-faces illusion, a figure-ground ambiguous figure (Fig. 1B; see also Fig. 1C to experience BR directly, either by free fusing or using a piece of cardboard to limit presentation of one image to one eye and the other image to the other eye). The neural mechanisms of BR have been the subject of intense controversy for over a hundred years (16). Around the time of our initial experiments (the mid-late 1990s), a shift was occurring in understanding the level at which rivalry is resolved in the brain. The psychophysical evidence by the late 1980s had been weighted in favor of an eye-rivalry model, which held that the perceptual alternations arose as a result of reciprocal inhibition between low-level monocular neurons (17).

In the following decade, however, direct single-unit recordings in alert macaque monkeys reporting their perceptions during BR cast doubt on this monocular channel model [reviewed in Logothetis (18); see also Miller (19), this issue]. Accompanied

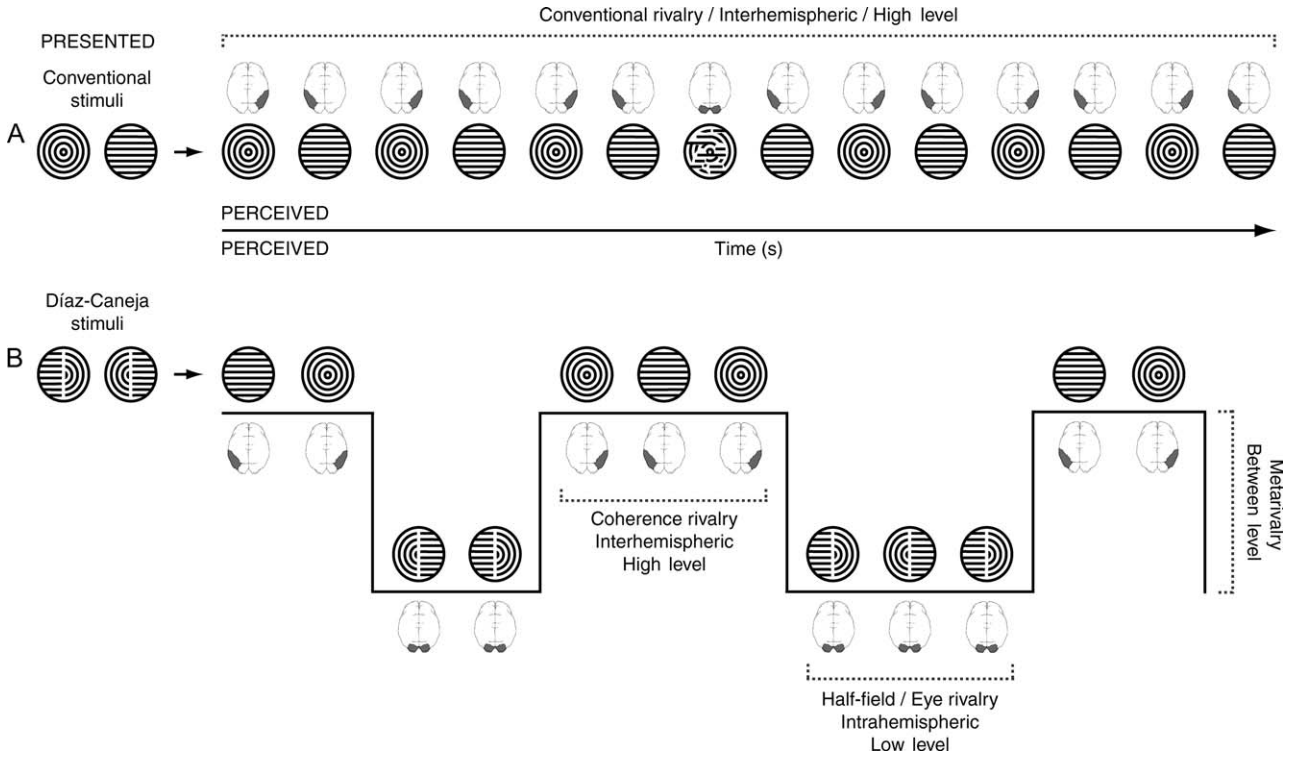

Fig. 2. Models and levels of rivalry with conventional stimuli and DC stimuli. (A) Our previous CVS experiments with conventional stimuli showed that *inter*hemispheric switching at a high level of visual processing mediates this type of rivalry (35). (B) In our most recent experiments (21), the finding that CVS significantly changed predominance of coherent percepts during viewing of DC stimuli showed that high-level interhemispheric switching also mediates coherence rivalry. However, half-field rivalry predominance with the same stimuli was not significantly affected by CVS, suggesting that the rivaling half-field percepts are mediated by *intra*hemispheric mechanisms at a low level of visual processing (eye rivalry). These findings therefore showed discrete neural mechanisms for coherence rivalry and eye rivalry. In addition, we proposed that these discrete high- and low-level rivalries themselves rival for visual consciousness (metarivalry). Figure and caption adapted from Ngo et al. (21).

by psychophysical studies [e.g. Logothetis et al. (20)], the emerging data supported instead a high-level BR mechanism. Subsequent brain-imaging studies provided conflicting data, with evidence in favor of both low- and high-level interpretations [discussed in Ngo et al. (21)]. These late-20th-century opposing low- vs. high-level views on BR mechanisms reflected similar theoretical positions in early BR research. Thus, Hering argued for a bottom-up explanation while Helmholtz, James and Sherrington argued in favor of attentional top-down interpretations.

Despite the evidence that emerged in the past decade supporting high-level mechanisms of BR, there were few high-level mechanistic models of the phenomenon in the literature. More recently, an amalgam view has been proposed by Blake and Logothetis (22) in which BR is considered to occur through a series of both high- and low-level processes, and this is probably the consensus view today. However, a novel high-level mechanistic model of perceptual rivalry had been proposed earlier (by author S. M. M. and Jack Pettigrew) — the interhemispheric switch (IHS) hypothesis — and it was this model we assessed with CVS. The IHS model suggested that during BR and rivalry with ambiguous figures such as the Necker cube, one hemisphere selects one image/perspective, while the opposite hemisphere selects the rival image/perspective, and the perceptual alternations are mediated by a process of alternating hemispheric activation (i.e. interhemispheric switching; Fig. 2A).

Several factors contributed to the generation of the IHS model and these have been detailed elsewhere (21). The model was consistent with evidence for alternating hemispheric activation in humans (23) and non-human species (24,25) on the one hand, and on the other, the conjunction of (i) attentional interpretations of rivalry (see above), (ii) evidence for independent hemispheric attentional processing in humans [e.g. Luck et al. (26)] and (iii) evidence that a single cerebral hemisphere can sustain coherent visual perception (27). CVS was used to assess the IHS model according to the following rationale. The technique has shown effects on attentional function, inducing temporary

amelioration (10–15 min) of attentional neglect following unilateral brain lesions (28,29). Conversely, attentional neglect is known to potentially follow lesions to any of the above-mentioned regions that are activated by CVS (30–32; particularly on the right side: 33,34). Given the effect of CVS on mechanisms of attention and the fact that such effects are exerted through *unilateral* hemispheric activation, it was reasoned that CVS applied during BR should shift the relative time spent perceiving one or the other image (predominance), if indeed BR is mediated by an IHS process.

Prior to the proposal of the IHS model of BR, there would be no expectation that CVS should affect what is perceived during rivalry because all models of the phenomenon had taken for granted that, at any one time, what happened in one hemisphere during rivalry was no different to what happened in the other hemisphere. On such views, specifically activating one hemisphere should not therefore perturb the rivalry process. However, Miller et al. (35) showed in a series of BR experiments using horizontal and vertical gratings, orthogonal oblique gratings and the Necker cube that perceptual predominance during rivalry is indeed significantly affected by CVS. In all three experiments, only left hemisphere activation (induced by right ear CVS) significantly affected rivalry predominance, with stimulation of the opposite hemisphere having no significant effect. This asymmetry was interpreted with respect to known hemispheric asymmetries of BR transitions (36) and of spatial representation (34,37).

The finding that CVS-induced unilateral (left) hemisphere activation reliably affected rivalry predominance supported both the IHS model and the early (involuntary) attention-based BR theories (37). An interpretation of the CVS effect based on residual horizontal nystagmic eye movements was excluded given the similar results found for BR with horizontal/vertical gratings and for BR with orthogonal oblique gratings (35). These CVS findings were also subjected to further assessment by applying a single pulse of transcranial magnetic stimulation (TMS) to the left temporoparietal region during BR. This induced phase-specific perceptual disruption effects (35) that also could not be explained by standard BR models but were exactly predicted by the IHS model.

Ngo et al. (21) recently proposed additional novel interpretations of BR based on experiments with CVS during viewing of Díaz-Caneja (DC) stimuli (38). These stimuli induce rivalry with four resulting percepts (Fig. 2B; experience this using the stimuli in Fig. 1D): two of these percepts mirror the images presented to the eyes (referred to as half-field images) and the other two involve the reconstruction of aspects of each eye's presented image into global coherent percepts. Ngo et al. (39) had earlier shown that during rivalry with DC stimuli, coherent percepts are visible for around half the viewing time while half-field, nongrouped percepts account for the remaining half.

The phenomenon of interocular grouping during rivalry [eg, Kovács et al. (40); earlier reviewed in Papathomas et al. (41)] in itself suggests that rivalry involves higher order top-down influences (35); however, Ngo et al. (21) directly assessed whether predominance of both the grouped and nongrouped percepts would be affected by CVS. They found that in fact only the predominance of coherent percepts was susceptible to influence by CVS, while the predominance of half-field percepts was unaffected by the intervention. The findings showed that coherence rivalry and half-field rivalry are mediated by discrete neural mechanisms.

In addition, Ngo et al. (21) suggested that these discrete neural mechanisms included interhemispheric rivalry at a high level (accounting for the grouped percepts, affected by CVS) and *intra*hemispheric rivalry at a low level (accounting for the nongrouped percepts, unaffected by CVS). The fact that both sets of percepts themselves compete for visual consciousness in a given viewing period further suggested that these high- and low-level processes engage in a third type of rivalry – a between-level competitive process (Fig. 2B). Thus, a 'metarivalry' model was proposed to account for perception during viewing of rivalry stimuli that induce interocular grouping. While the neural mechanisms of BR remain to be conclusively determined, our data show that application of the CVS technique in novel contexts (such as visual processing) can have surprising and challenging results. As explained in the next section, the implications of our CVS and BR experiments are not limited to visual neuroscience.

A novel pathophysiological model of bipolar disorder

Pettigrew and Miller (42) presented a novel pathophysiological model of bipolar disorder that was based on three factors: (i) they had discovered that the rate of BR was slower in subjects with bipolar disorder than in controls, (ii) they had conceived of a novel neurophysiological mechanism of BR (the IHS model) and (iii) they merged these two facts with a wide variety of evidence for hemispheric asymmetries of mood and mood disorders. The result was a pathophysiological model (the 'sticky switch' model) that viewed mania as the

endpoint of unopposed (relative) left hemispheric activation and depression as the endpoint of unopposed (relative) right hemispheric activation.

The issue of lateralization in the neurobiology of mood and its disorder is contentious and is not reviewed in detail here. Suffice to say that the mood-related hemispheric asymmetries that influenced Pettigrew and Miller's proposal (42) included evidence from studies of brain imaging [e.g. Bench et al. (43), Martinot et al. (44), Migliorelli et al. (45)], electroencephalography [e.g. Henriques & Davidson (46)], lesion patients (47), hemisphere inactivation (48,49) and TMS (50,51). In the current literature, there exists evidence in favor and evidence against the notion of mood lateralization (52,53). While some studies fail to find mood-related hemispheric asymmetries, there are relatively few reports of mood lateralization in the opposite direction to that entailed in the sticky switch model.

The development of Pettigrew and Miller's model (42) was also influenced by results from a CVS study by Ramachandran [(54); see also Cappa et al. (55)] who reported that following a right hemisphere lesion, anosognosia [denial of disease, e.g. denial of hemiplegia; Bisiach et al. (56), McGlynn & Schacter (57), Jehkonen et al. (58)] can, like unilateral neglect, be temporarily ameliorated by left ear CVS. This led Ramachandran (54) to propose that each cerebral hemisphere has a unique cognitive style – the left goal oriented and tending to deny discrepancies (resulting in anosognosia when a right hemisphere lesion leaves the left unopposed), while the right hemisphere, in contrast, identifies and focuses on discrepancies (the 'devil's advocate'). These complementary cognitive styles and their lateralization are broadly consistent with similar proposals for neural mechanisms of 'affective style' [approach/withdrawal theory: Davidson (59); valence theory: Silberman & Weingartner (60); reviewed in Demaree et al. (61)].

Furthermore, neuropsychiatric corollaries of such cognitive styles (taking them to their extremes) suggest that not just postlesional anosognosia could result from pathological hemispheric activation asymmetries but also postlesional mania and depression [consistent with the literature (62–71)]. As proposed by Pettigrew and Miller (42), these corollaries could also be extended to the general psychiatric setting (i.e. mania and depression in the absence of brain lesions). Indeed, prior to the proposal of their model, evidence already existed for the left lateralization of mania and the right lateralization of depression (as per the studies cited above); however, such evidence had not been synthesized into a coherent mechanistic model of bipolar disorder that accounted for the *alternation* between these hemispheric activation asymmetries.

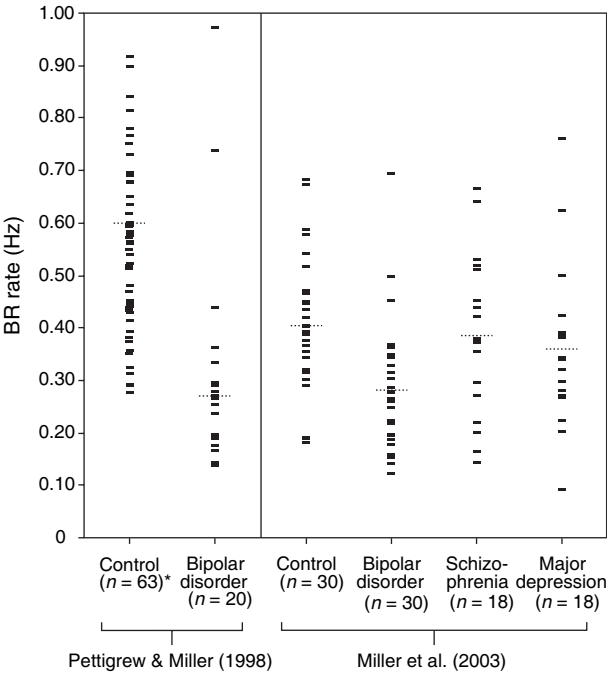

Fig. 3. Rates of BR in normal subjects, bipolar disorder, schizophrenia and major depression [adapted from Miller et al. (72)]. See main text for an explanation of the stimuli used in the two studies. Slow BR rate in bipolar disorder was considered to be a trait- rather than a state-dependent finding, also unaffected by medication, but further research is required to verify these contentions. The central tendency for each subject group is indicated by the dotted lines in the respective studies [medians in Pettigrew & Miller (42); means in Miller et al. (72)]. *Four control outliers are not shown: 1.11, 1.11, 1.19 and 1.48 Hz (42).

In proposing this synthesis, Pettigrew and Miller's model (42) was most fundamentally driven by a serendipitous discovery during their CVS experiments with BR. They found that the rate of BR was slower in a subject with bipolar disorder than in subjects without the disorder. They subsequently assessed 20 out-patient bipolar subjects and 63 control subjects and found the two groups to be significantly different in their BR rates (Fig. 3). That study (42) involved the use of high-strength rivalry stimuli consisting of drifting horizontal and vertical gratings of a high spatial frequency. A later study (72) used stationary gratings with a lower spatial frequency to induce BR, in a different group of 30 in-patients and out-patients with bipolar disorder and in 30 control subjects, and showed the same finding (Fig. 3). The separation between the bipolar and control groups, however, was less with these lower strength stimuli. This latter study also assessed rates of BR in a small group of subjects with schizophrenia ($n = 18$)

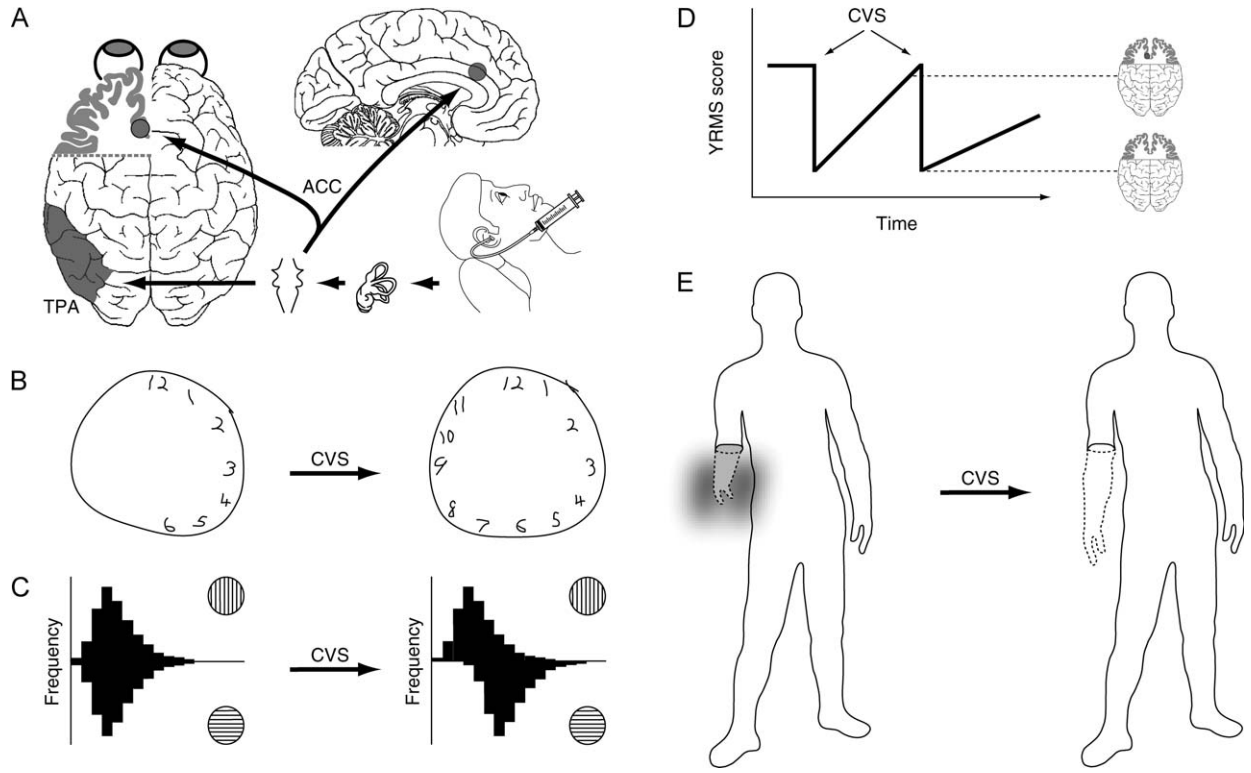

Fig. 4. The CVS procedure and some of its demonstrated effects. (A) Right ear CVS with cold-water activates, through the semicircular canals and vestibular nuclei, brain regions in the contralateral hemisphere such as the ACC and temporoparietal areas (TPA; activation of other areas such as insular cortex and the putamen in the basal ganglia are not indicated). (B) One pencil-and-paper test used to detect (left) unilateral neglect involves the patient being instructed to draw a complete symmetrical clock face. Patients with the disorder fill in numbers on the right side only (as depicted, despite having drawn a whole circle) or may include more digits on the right than the left side. Following CVS of the left ear (ie, activation of the lesioned right hemisphere), subjects' left-sided attentional neglect is temporarily ameliorated for 10–15 min (28,29) as represented by the subsequent drawing of a complete clock face. (C) The schematic BR interval duration frequency histograms represent the time an observer perceives one image (eg, vertical lines) relative to the other (eg, horizontal lines) within a given viewing period. Before CVS, the vertical and horizontal gratings are perceptually dominant for a roughly similar duration. Following CVS, predominance of horizontal image perception increases, reflected in the higher frequency of longer horizontal interval durations [see Miller et al. (35)]. (D) According to Pettigrew and Miller's (42) pathophysiological model of bipolar disorder, left ear CVS (right hemisphere activation) restores toward normal the disordered left-over-right hemispheric activation asymmetry associated with mania (75). This specific prediction was assessed and verified in a case study by Dodson [(76); see main text]. The graph represents the effects of CVS on the patient's YMRS score. (E) In patients experiencing phantom limb following amputation, CVS has been reported to restore abnormal phantoms (eg, telescoped phantoms, as depicted in left figure) to normal phantoms, and painful phantoms to nonpainful phantoms (141).

and unipolar depression ($n = 18$) and found that alternation rate in these groups was not significantly different from that in controls. These findings were consistent with early-20th-century reports of slow ambiguous figure rivalry in bipolar disorder but not in schizophrenia [(73,74); including Necker cube rivalry].

A number of conceptual steps are taken by Pettigrew and Miller (42) in linking slow BR rate in bipolar disorder to the IHS model and the phenomenology of the disorder. The key elements are the following: temporoparietal IHSs mediating BR (of the order of seconds) are genetically coupled to more anterior (prefrontal) IHSs mediating alternations of cognitive style and mood (of the order of minutes). This coupling implies that in bipolar disorder, slowed temporoparietal IHSs are associated with slowed anterior IHSs. Slower switches are biophysically more easily held in one or the other position (i.e. are considered 'stickier' than faster switches); thus, once 'stuck' in the left or right position (perhaps following environmental triggers with top-down modulation of the subcortical switch), the resulting hemispheric activation asymmetry in turn results in extremes of that hemisphere's cognitive style and thus the phenomenology of mania and depression, respectively (of the order of days to weeks).

Furthermore, a clearly stated prediction of the sticky switch model was the potential hemisphere-specific therapeutic utility of CVS in mania and depression. Thus, it was predicted that left ear

CVS, through its activation of the right hemisphere, would restore toward normal the hemispheric imbalance in mania [left over right; eg, Blumberg et al. (75)] and thus reduce manic signs and symptoms. Conversely, CVS of the right ear was predicted to reduce the signs and symptoms of depression. The prediction of a left ear CVS effect on the signs and symptoms of mania has since been assessed, albeit in a single case study, and the results were impressive.

Dodson (76), based on Pettigrew and Miller's (42) proposal (Dodson, personal communication), reported the effects of left ear CVS in an acutely manic female patient with a long history of bipolar disorder. Her elevated mood had heightened gradually over several weeks and her manic episodes had previously been responsive to electroconvulsive therapy (ECT). Following admission, both an increase in dosage of atypical antipsychotics and multiple ECT treatments were ineffective and the patient became intolerant of pharmacotherapy. However, in a therapeutic trial, left ear CVS reduced her Young Mania Rating Scale (YMRS) score almost immediately from 32 to 10, with a lowering of mood and return of appropriate behaviour. The patient, who had previously lacked insight into her elevated mood and inappropriate behaviour, regained insight following CVS and felt embarrassed by her pre-CVS behaviour [in a manner that invites comparison between mania and anosognosia; see also Benke et al. (77), Liebson (78), Migliorelli et al. (79)]. The CVS effect wore off after approximately 24 h but repeated administration 72 h later, again caused a reduction in YMRS score that appeared to be longer lasting.

Clearly, a single case study is not proof of Pettigrew and Miller's model (42), but it is a striking finding and again shows the surprising potential of CVS in novel contexts (summarized in Fig. 4). Replication of such effects in a larger sample of subjects with mania, and demonstration of the corresponding prediction for depression, would be sound evidence in favor of their model. In one recent study, CVS was indeed performed in subjects with depression but only eye movement patterns were studied, without concurrent assessment of mood change (80). Nevertheless, the investigators reported that depression was associated with bilateral reduced vestibular nuclei function, with the right side more affected than the left [a finding consistent with the above asymmetry discussion, given neuroanatomical evidence for crossed vestibular projections; Shiroyama et al. (81), Barmack (82); see also Halmagyi et al. (83)]. The authors further drew on known connections between vestibular nuclei, suprachiasmatic nuclei (circadian) and raphe nuclei (serotonergic), in linking their results to the phenomenology of depression. While this study did not assess Pettigrew and Miller's (42) CVS prediction for depression, it is nevertheless relevant given the finding of a left–right subcortical asymmetry in this disorder and because the suprachiasmatic nucleus has been shown to exhibit antiphase (left–right) alternations (84). The notion of subcortical bistable (antiphase) oscillators was an important component of Pettigrew and Miller's model [with the genetic anomaly in bipolar disorder postulated to be a reduction in cationic channels that control oscillator switch rate; Pettigrew & Miller (42); see also Pettigrew (85)].

Effects of CVS in other clinical conditions

Further studies of CVS in mania and depression would not only potentially support Pettigrew and Miller's (42) model of bipolar disorder but would also address the intriguing possibility that the technique may be of clinical therapeutic benefit. Furthermore, potential clinical utility may not be limited to mood disorders, as illustrated by the following overview of CVS effects in several other clinical disorders. First though, we discuss CVS neurophysiology in more detail, describe more fully the functions performed by some of the structures activated by CVS and compare CVS (and related techniques) with other novel brain stimulation modalities.

As briefly mentioned earlier, CVS induces activation of a number of contralateral cortical structures. Some of these, including posterior insular and retroinsular cortex, temporoparietal junction, somatosensory area SII, inferior parietal lobule, parietal operculum and superior temporal gyrus, have been considered as representing the human homologue of monkey parietoinsular vestibular cortex (8,9,86–90). In monkeys, this core region forms part of a polymodal system that is responsive to vestibular, visual, somatosensory and optokinetic stimuli (82,91). Brain-imaging studies have shown a functional–anatomical correspondence of this system in humans (92), with some overlap in the cortical areas activated by CVS, galvanic vestibular stimulation (GVS), neck muscle vibration (NMV; through proprioceptors), optokinetic stimulation (OKS) and visually induced apparent self-motion (9,88,92–102). CVS and GVS have also been found to induce bilateral deactivation of primary visual cortex, extrastriate areas (fusiform gyri, middle temporal gyri), and

superior and middle frontal gyri (9,15,93,103). Clinically, it has been shown that (like CVS) NMV, OKS and GVS also have ameliorating effects on postlesional attentional neglect (104–112).

Along with the above activations, CVS has been shown to activate contralateral ACC and the putamen in the basal ganglia [(7–9,15); such activations have been reported less consistently following OKS and GVS, and not at all following NMV: (9,93–99,113–115); see also Bottini et al. (7–9) and Wenzel et al. (15) regarding thalamic activation following CVS]. Located medially, the ACC is considered, based on earlier functional–anatomical evidence, to comprise a rostral–ventral affective division and a dorsal cognitive division (116). The rostral–ventral component has connections to areas such as the orbitofrontal cortex, anterior insula, temporal pole, amygdala and medial dorsal nucleus of the thalamus and contributes mainly to the processing of motivational and affective content. Regions with connections to the dorsal component include premotor and supplementary motor areas, posterior insula, parietal cortex, dorsolateral prefrontal cortex, medial dorsal nucleus of the thalamus and putamen (117–119). This dorsal subdivision of the ACC participates mainly in sensory-related attentional processing, conflict monitoring, error recognition, reward-related responses and motor execution [eg, Weissman et al. (120), Yücel et al. (121), Holroyd et al. (122), Williams et al. (123)]. Recent brain-imaging evidence and reviews also support a third caudal subdivision involved in motor control (124–127) and a key role of the ACC in the functional neuroanatomy of mania and depression (75,128–130).

Novel brain stimulation treatment modalities were recently reviewed by Malhi and Sachdev (131) and include TMS (131,132), deep-brain stimulation [DBS (134–136)] and vagus nerve stimulation [VNS (137,138)]. All of these techniques have reported effects in psychiatric disorders (131) and CVS could also be tentatively added to this list (76). TMS and DBS involve condition-specific targeted application, though with spreading effects. CVS, on the other hand, activates largely the same network each time it is applied (see methodology box). CVS, each time it is applied, activates a polymodal 'endogenous' network of interrelated structures that mediate a wide range of sensory and higher order functions (see below). DBS and VNS are invasive, while CVS and TMS are not. Although TMS is noninvasive, CVS is far easier to administer, with the desired activation easily verified by observed nystagmus and subject reports of vertigo. CVS is also inexpensive and well tolerated (with mild cold-related discomfort to contend with, and the main side-effects being infrequent mild headache and nausea, rarely with vomiting). Given its mild nature, CVS is also a notably less severe (potential) treatment modality than ECT in the psychiatric setting.

Above we have suggested that the effect of CVS in mania (and depression, if the corresponding prediction is confirmed) warrants further investigation regarding whether the technique is able to induce *sustained* therapeutic effects. In support of this notion, NMV has recently been shown to have long-lasting restorative effects in postlesional neglect. This sustained rehabilitation benefit involved at least 2 months of significantly improved measures of attentional function and activities of daily living. That is, NMV plus standard attentional retraining measures produced better attentional outcomes than standard measures alone. This beneficial effect followed a stimulation protocol consisting of daily NMV (5 days/week), repeated for 3 weeks (143). More recently, it was also shown that repeated NMV *alone* can induce sustained rehabilitation benefit (144). Longer term benefits imply that the technique induces neuroplastic changes in at least some of the sites it activates [see Michel (145), Kerkhoff & Rossetti (146)]. It remains to be seen whether such neuroplastic effects also occur following repeated CVS (Dodson's case study is promising but involved too short a follow-up period). Clearly, further work on the potential clinical utility of CVS and related techniques in the context of neglect rehabilitation (147) and mood disorders is required.

Furthermore, neglect [including attentional, intentional and representational neglect (148–150)] is not the only postlesional disorder temporarily ameliorated by CVS. Other such conditions include hemianesthesia (151,152), anosognosia [as discussed above (54,55,153)], somatoparaphrenias [such as bizarre beliefs that one's hemiplegic limb belongs to someone else (154,155)] and motor neglect (153). In all these conditions, the potential therapeutic effects of repeated CVS (and related techniques) could be assessed. Another clinical arena that holds intriguing potential for the application of CVS, with respect to investigating mechanisms and therapeutic utility, is chronic pain. TMS has been investigated in the treatment of chronic pain with as yet disappointing results [(156,157); though see Pleger et al. (158)], while DBS appears to be more effective [(134,159); though with far greater invasiveness and expense]. There is preliminary evidence that VNS may also have an effect on pain conditions (160–162) though pain side-effects may be associated with this

technique [e.g. Privitera et al. (163), Rush et al. (164), Shih et al. (165)]. In relation to CVS, its reported temporary effects in the context of chronic pain are just as striking as its above-mentioned postlesional and antimanic effects.

André et al. (141) administered CVS to amputees and reported that 10 of 10 subjects with phantom limb pain had their pain significantly ameliorated, albeit temporarily, following the intervention. In other subjects, deformed phantom limbs were felt as normal phantoms following CVS. The authors concluded that CVS reconstructs the global body schema, restoring normal somatosensory representation. They did not, however, mention potential pain management implications perhaps because the work by Schindler et al. (143) showing sustained therapeutic benefit of NMV (in attentional neglect) was not yet known. In addition, Le Chapelain et al. (166) reported that of four subjects with pain following spinal cord injury, two considered that CVS greatly relieved their pain. In yet other chronic pain contexts, there is recent preliminary case study evidence for the alleviation of pain following CVS in thalamic pain syndrome [notably with relief obtained for at least several weeks duration (167)] and in complex regional pain syndrome [CRPS (168)]. The latter finding is of particular interest given that a motor neglect component has been considered to be associated with CRPS (169,170) and that CVS is known to temporarily ameliorate postlesional motor neglect (153). Pain in CRPS has also been recently found to be alleviated (for up to a week) with yet another technique, prism adaptation (171), which also ameliorates postlesional neglect [for up to 5 weeks: (172); reviewed in Luauté et al. (173), Redding & Wallace (174)].

The mechanism underlying CVS-induced pain reduction in phantom limb pain, spinal cord injury pain and other chronic pain conditions is likely to involve the ACC given its key role in encoding the motivational and affective content of pain states [e.g. Rainville et al. (175)]. Compared to experimentally induced pain in healthy individuals, it has been generally found that in chronic pain states, activity in prefrontal cortical areas is enhanced while activity in a network of structures including the thalamus, somatosensory areas SI and SII, insular cortex, and ACC is diminished (176). In contrast, in healthy individuals, the ACC has been linked both directly and indirectly to the cortical representation of pain. Consistent with its two main functional–anatomical subdivisions, stimulation that induces pain has been found to activate the rostral affective ACC (177,178), while sensory processing of the same stimulation and pain-related motor responses are associated with activity in the dorsal cognitive division (177,179).

Implicating ACC in the mechanism by which CVS reduces pain also stems from reports that surgical removal of the ACC (or disruption of the cingulum bundle) has been used successfully in cases of severe intractable chronic pain states (180–192). Not surprisingly in the current context, such surgical procedures have also been shown to affect intractable psychiatric illness [including mood disorders and obsessive-compulsive disorder (193–197)]. Right ACC activation presumably also mediates the mania-diminishing effect of left ear CVS because asymmetric activation of left ACC has been observed in the acute manic state (75). Regions such as ACC that are known to be involved in depression and pain conditions (see above) may also hold clues to the comorbidity commonly observed in such disorders (198–200). It will also therefore be worthwhile to assess the therapeutic effects of CVS in comorbid chronic pain and depression.

In none of the studies of CVS effects in chronic pain conditions has the stimulation been administered repeatedly to assess for sustained pain reduction. Controlled trials of CVS as a stand-alone or adjunctive intervention in the management of chronic pain conditions are thus required. This is particularly so given the debilitating nature of these conditions (201,202), the often poor efficacy of current interventions [and limited evidence for them (203,204)] as well as the invasiveness and expense of current interventions. Furthermore, given the reported pain-alleviating effects of CVS across a variety of pain states, the technique's utility may also extend to other debilitating and often refractory conditions such as (i) failed back surgery syndrome [(205); see Rasche et al. (206) regarding ACC activation in this condition and the effects on ACC following spinal cord stimulation] and (ii) postlesional pain, that is, postlesional pain more generally than just thalamic pain syndrome (167), given reports of lesion (207) and brain-imaging (208) evidence associating postlesional pain with another CVS-activated brain region – insular cortex [see also Brooks & Tracey (209)].

In summary, we suggest that investigations of potential therapeutic utility of CVS (and related techniques) in a range of postlesional conditions, in psychiatric and neuropsychiatric mania and depression, and in several chronic pain conditions is warranted based on existing evidence of CVS effects as detailed above. The assessment of CVS-induced clinical effects compared with other novel

brain stimulation methods such as TMS, DBS, VNS and with established treatments such as ECT and pharmacotherapy will also be of great interest given relative factors such as technical requirements, tolerability, side-effects, invasiveness and costs. Indeed, assessment of potential CVS effects in patients for whom highly invasive procedures such as DBS (or spinal neuromodulation techniques) are being considered would seem most urgent. Any findings of positive short-term temporary effects in such patients should then be followed by repeated-stimulation protocols to assess for sustained effects (to thus avoid invasive surgery). Finally, of all the novel brain stimulation methods currently being researched, CVS is the most relevant for application in developing countries. Here treatment options may not exist at all; yet, a syringe and iced water would be readily accessible.

Further clinical contexts for CVS application

There are a range of other clinical phenomena to which CVS could be applied for exploratory neurobiological and clinical purposes. Postulating (and assessing) such novel contexts can be driven by the known functional and dysfunctional roles of brain regions activated by CVS. Thus, for example, cognitive functions and clinical disorders involving the ACC are potential novel targets of CVS studies. Here autism illustrates the point. Considered to involve disordered ACC function (210–214), this pervasive disorder is extremely difficult to treat, entails possible links to vestibular dysfunction [(215,216); cf. Goldberg et al. (217)] and has reported beneficial effects following visuospatial intervention [prism lenses (218)]. Furthermore, autism clearly involves disordered approach/withdrawal behaviour. Similarly, obsessive-compulsive disorder has been considered to involve disordered ACC function (195,197,219–221) and the phenomenology and behaviour in this disorder, in particular with respect to error detection/conflict monitoring, approach/withdrawal functions and cognitive style [e.g. López-Ibor & López-Ibor (222)], suggest its assessment with CVS may be especially illuminating.

A functional role of the ACC has also been shown in motivation (223,224) and decision-making (123,225–227) and it is not surprising, therefore, that impaired motivation and decision-making (197,228–230) are also associated with disorders of the ACC. Excessive motivation [and impaired decision-making; e.g. Minassian et al. (231)] are classical features of the acute manic state [with implications of a left hyperactive ACC (75)]. Diminished motivation and apathy are classical of depression with studies confirming a role of the ACC in depression [though with less evidence for functional ACC lateralization; see above and Mayberg et al. (232)]. The ACC, the nucleus accumbens, the ventral pallidum and the medial dorsal nucleus of the thalamus are thought to constitute a cortico-striatal-pallidal-thalamic circuit that mediates motivation (233,234). Damage to this circuit can result in disorders of diminished motivation (specifically in the absence of depression), as reviewed by Marin and Wilkosz (233).

Disorders of diminished motivation include akinetic mutism (absence of spontaneous behaviour and speech but with spared visual tracking), abulia (a disorder of 'will' – a less severe form of akinetic mutism involving poor initiative, poverty of and slowed behaviour and speech, and decreased emotional responses) and apathy (generalized diminished motivation in otherwise normal individuals). Akinetic mutism can follow bilateral or unilateral ACC lesions, with recovery from the latter usually being better (235,236). One patient who had a left frontal lobe infarction that included the ACC, remarked (following recovery) that her muteness had been characterized by a loss of will to talk with medical staff, having 'nothing to say', that her mind was 'empty', nothing 'mattered' and that she still felt relatively unconcerned after being discharged (237). It is also noteworthy that other investigators have interpreted reports of nonaphasic mutism (including akinetic mutism) following left-sided lesions and nonaphasic hyperlalia following right-sided lesions in the context of the sticky switch model of bipolar disorder (238). CVS would certainly be worth performing in patients with disorders of diminished motivation given a lack of alternative treatment options and the possibility that ACC activation following CVS may assist in restoring motivational functioning toward normal, much like CVS restores toward normal, somatosensory representation in phantom limb, attentional function in neglect, and mood and behaviour in mania. Positive short-term effects in patients with disorders of diminished motivation would then necessitate further study of repeated stimulations to assess for sustained therapeutic effects.

The motor component of disorders of diminished motivation, most extreme in akinetic mutism, can be linked to the motor functions of the ACC (described above) and the output of the motivation-related cortico-striatal-pallidal-thalamic circuit to motor cortex, basal ganglia and the reticulospinal tract (233). Recall that CVS induces basal ganglia

activation (putamen) along with ACC activation, raising the issue of potential CVS effects on not just the disorders already discussed (including disorders of diminished motivation) but also on movement disorders more generally. One such example is the group of dystonias, thought to be primarily basal ganglia disorders (239,240), that interestingly are comorbid with CRPS (241,242), treatable with DBS (243,244) and shown in case studies (of cervical dystonia) to be ameliorated with GVS (245), acoustic vestibular stimulation (245) and NMV [(246,247); see also Münchau & Bronstein (248), Bove et al. (249,250)].

Furthermore, catatonia is thought to be primarily a motor disorder (251) that occurs in association with depression, mania and schizophrenia (along with metabolic disorders, neurological disorders and drug-induced/toxic states). It involves a range of symptoms and signs including mutism, stupor, posturing, automatic obedience, mannerisms and a variety of abnormal movement patterns and behaviours. Catatonia has also been proposed to involve right orbitofrontal cortex hypoactivation that leads to ACC and basal ganglia activity changes (252). Consideration should therefore be given to CVS as a potential intervention for catatonia (notwithstanding difficult issues of consent). This suggestion is also of relevance for the present discussion given recent interest in links between catatonia and autism [e.g. Dhossche et al. (253)].

Thus, we propose, admittedly in a speculative manner, that CVS (and related techniques) could be applied to clinical contexts in which the underlying neurobiology (and phenomenology) is suggestive of potential modulation. This includes clinical conditions such as autism, obsessive-compulsive disorder, disorders of diminished motivation, dystonia and catatonia. There are many issues associated with our suggestion that CVS be considered as an intervention in such conditions, and indeed in the conditions discussed earlier including attentional neglect, mood disorders and chronic pain states (see methodology box). We certainly do not expect, nor wish to propose, that CVS is likely to be a brain stimulation panacea. On the contrary, we wish to emphasize that there currently exist no clinical trials showing therapeutic efficacy of CVS. However, there do exist studies reporting dramatic modulation by CVS (reversing neglect, mania and several chronic pain states), along with evidence for sustained benefit (neuroplastic effects) using a closely related technique (NMV). Such evidence, together with the fact that most of the conditions we have listed can be refractory to current treatments or are often treated only with invasive and expensive interventions (or not treated at all in developing countries) suggests that our proposal for widespread assessment of CVS in clinical contexts is not unwarranted.

CVS studies and neurophilosophy

In addition to potential clinical utility as discussed above, reported CVS effects on vision, attention, anosognosia, somatoparaphrenias, mood, somatosensory representation and pain suggest that the neural mechanisms of these phenomena are amenable to investigation with this novel brain stimulation technique. Cognitive neuroscience studies involving phenomena such as decision-making and motivation in normal subjects can also be performed using CVS. Moreover, laterality research has generally not taken advantage of CVS as a means to selectively activate one or the other cerebral hemisphere [Bächtold et al. (254) being a notable exception]. As should by now be clear, the type and range of phenomena modulated by CVS also suggests that the technique has potentially important implications for experimental neurophilosophy.

Broadly defined, neurophilosophy [a term introduced by Churchland (255)] entails two approaches – empirical neuroscience studies of cognitive (mental) phenomena of specific interest to philosophy, on the one hand, and philosophic analyses of the phenomena and their study in the context of neuroscientific advances, on the other. In the remaining discussion, we consider the first of these approaches, in particular with respect to existing and future studies of CVS. We do not propose specific neurophilosophic hypotheses or experiments. Rather, we wish to point out that CVS, given its effects on many phenomena of interest to philosophy (often experimentally elusive phenomena), and given its safe, inexpensive and non-invasive nature, ought to be an extremely useful tool for doing neurophilosophy.

In the case of CVS studies of BR, the neurophilosophic target of interest is consciousness, specifically visual consciousness. The broad implications of BR research for the scientific study of consciousness are addressed in detail elsewhere [Miller (19), this issue; an example of the second type of neurophilosophic approach; see also Miller (37)], and specific issues raised by the IHS model are also discussed in that paper [see Footnote 8 in Miller (19)]. Another target for neurophilosophy that can be addressed using CVS is belief. Recall that CVS induces short-term reversals of lesion-related anosognosia (denial of disease). Thus, the patient prior to CVS is unaware of their paralysis

or, even if made 'aware' of the deficit, believes there is no reason to be concerned by it. Following CVS, the patient is temporarily able to acknowledge their hemiparesis and further that their paralysis is indeed cause for concern. Belief is a prominent issue in the philosophy of mind and is an elusive phenomenon to study empirically, certainly with respect to directly modulating it by brain stimulation. Thus, CVS investigations of mechanisms of belief, its dysfunction and repair, are a potentially fruitful empirical approach for neurophilosophy.

Progressing from a cognitive neuroscience study of anosognosia (e.g. assessing brain-imaging activations associated with pre-CVS anosognosia and post-CVS return of insight) to a more specifically neurophilosophic study of belief is best served by the development of particular neurophilosophic questions. Thus, the types of questions asked by a neurophilosophic study ought to be different to those asked by standard cognitive neuroscience studies. Distinctive neurophilosophic questions on belief, for example, should emerge from problems in philosophy posed by notions and theories of belief. Not all such problems will require empirical investigation (many rather, being problems of logic) but some will indeed be amenable to direct empirical enquiry. A simple brain stimulation technique that has demonstrable effects on an individual's beliefs must therefore be regarded as a useful neurophilosophic tool, notwithstanding interpretation issues associated with brain stimulation methods [see Miller (19), this issue] and inference from pathological to normal mechanisms.

To avoid being limited to pathology-based neurophilosophic experiments, CVS could also be applied in normal subjects, ideally assessing neurophilosophic phenomena with known laterality components, or assessing neurophilosophic phenomena *for* laterality components. Thus, we wonder whether subtle belief-based experiments [e.g. Bechara et al. (256)] in normal subjects may detect CVS-induced modulation of cognitive style. In this regard, it is noteworthy that hemisphere-specific CVS modulations of lateralized verbal and spatial performance measures in normal subjects have been reported (254). In addition, it has been recently shown in healthy volunteers that TMS-induced disruption of right but not left dorsolateral prefrontal cortex led to significantly greater risk taking in a gambling (decision-making) task (257).

Returning to the pathological domain, bizarre distortions of belief such as those seen in postlesional somatoparaphrenia ('My paralyzed arm and leg are not *mine* doctor, they are *yours* aren't they?' or 'Oh, that arm and leg were put there by the cleaner last night!') also suggest further CVS investigations, in this case entailing beliefs about self and other. Similarly, autism, as many investigators have considered (258–260), entails notions of self and other (theory of mind). Thus, beneficial CVS effects showed in these conditions would also be of neurophilosophic interest. In addition, it is particularly worth noting that recent brain stimulation experiments have directly implicated the temporoparietal junction as a key region in the polymodal processing of embodiment or localization of self. TMS of this cortical area in the right hemisphere in healthy volunteers was found to disrupt processing of mental imagery changes of body position and visual perspective (261). In keeping with this finding, it has also been shown in healthy subjects that CVS-induced activation of the left hemisphere impaired performance on a task that engaged high-resolution mental imagery (262).

Furthermore, it was recently found that the discharge of a seizure focus (in an epilepsy patient), which partially overlapped with the temporoparietal junction, caused an 'out-of-body' experience (disembodiment). Conversely, when the patient engaged in voluntary, imaginal own-body movements (which also occurred spontaneously during her out-of-body experiences), activation was observed in the temporoparietal junction (261). Remarkably in a separate study on the same patient, electrical stimulation of this region was found to reliably induce the illusory perception of a person shadowing the patient's bodily movements (263). It has also recently been argued that GVS could be used to investigate the neural mechanisms of self-processing and embodiment in neurologically intact subjects [see Lenggenhager et al. (264)]. In relation to CVS, consistent activation of the temporoparietal junction shown in brain-imaging studies (see above), along with its effects on restoring somatosensory representation in phantom limb, suggests that this technique is also likely to be useful in neurophilosophic studies of self and embodiment.

Still other potential neurophilosophic applications of CVS can be considered, including, for example, CVS studies of psychosis (in addition to manic psychosis). Thus, given the linking of anosognosia to the lack of insight commonly seen in schizophrenia (265–267), CVS studies in this condition may prove of interest with respect to understanding belief and insight, and their distortion and loss respectively (perhaps also with therapeutic potential). Similarly, the experience of pain is well-trodden territory within the philosophic and neurophilosophic literature and its

alleviation by CVS may shed light on the experience of pain and attitudes toward pain [see Price et al. (268)]. Furthermore, the neurophilosophic relevance of CVS investigations of phenomena such as mania, depression, disorders of diminished motivation, movement disorders and decision-making may have relevance to neurophilosophic targets as elusive as volition and free will [see eg, Tibbetts (269), Burns & Bechara (270), Gomes (271), Tancredi (272)].

Finally, rather than suggest that CVS will be of important utility in doing experimental neurophilosophy, it could be argued that, on the contrary, the wide range of conditions and phenomena the technique modulates actually diminishes its exploratory utility. Thus, it could be asked how the effects of CVS on one neurophilosophic phenomenon can be distinguished from its effects on another? One solution to this quandary is to combine CVS with other more focal brain stimulation methods or with imaging or electrophysiology protocols, to attempt to tease apart distinct functional–anatomical contributions to the various phenomena. Another is to argue that the reality for cognitive neuroscience is quite the converse and that functional–anatomical overlap for distinct phenomena, far from hindering progress, in fact illuminates understanding at the systems level. While it is not yet clear just how far CVS will reach into the neurophilosophical domain, the existing reports of its effects on visual consciousness, attention, mood, pain, somatosensory representation, phantom sensations and belief make its reach already impressive.

Conclusions

We have provided an overview of the effects of CVS in a wide range of contexts in the cognitive and clinical neurosciences. The application of the technique in the visual neuroscience arena in assessing novel models of BR was detailed, as was the link between BR, CVS and bipolar disorder. It was further argued that the reported effects of CVS, and its capacity to activate structures such as temporoparietal cortex, insular cortex and especially ACC, makes its future application in the cognitive and clinical neurosciences (including studies of potential therapeutic utility) an exciting prospect. This is particularly so given its safe, inexpensive and noninvasive nature as well as its ease of administration. We have also suggested that CVS represents a unique experimental method for neurophilosophic studies, through its dramatic modulation of phenomena of great interest to philosophy and by virtue of its activation of brain structures implicated in such phenomena. A century ago, Bárány (4) proposed the use of CVS as a neurological diagnostic test. One hundred years later, the potential of CVS as an exploratory and clinical tool appears to only now be dawning on the neurosciences.

Acknowledgements

We thank Anthony Hannan and an anonymous reviewer for helpful comments on an earlier draft of the manuscript. We also thank all participants of the conference workshop and its organizers.

***CVS administration*:** In our use of the CVS technique, subjects are screened by a medical practitioner to determine suitability for participation. Exclusion criteria we have used (which will obviously vary depending on the study, in particular the clinical group under investigation) include (i) a diagnosis or family history of an axis I psychiatric disorder; (ii) epilepsy or any brain disorder such as a brain injury, tumor or other significant neurological disease; (iii) significant cardiac or respiratory disease; (iv) ear disease such as a perforated ear drum or otitis media/externa; (v) vestibular disease or significant motion sickness and (vi) pregnancy. Written informed consent is obtained. Subjects are otoscopically examined by the medical practitioner for any signs of significant ear disease. The subject lies on a couch maintaining a vertical midsagittal plane, with head orientation kept at 30° from the horizontal plane. Iced water is irrigated into the external auditory canal using a 50-ml plastic syringe with a short piece of soft silastic tubing attached (the silastic tubing is readily available from intravenous cannulas, with the needle end removed). The end of the tubing is positioned near but not touching the tympanic membrane. Irrigation continues until there are demonstrable signs of nystagmus and reports of vertigo. The refluent water is collected in a kidney dish placed on the subject's shoulder. In the authors' experience of administering CVS to several hundred subjects, only three subjects requested that CVS be ceased (as a result of cold-related discomfort). Many find the experience of vertigo interesting. A mild headache may follow CVS (easily relieved with simple analgesics), as may mild nausea. Rarely vomiting may occur (in only two of our test subjects out of several hundred). Sham stimulation can be administered by irrigating the ear canal with water at body temperature (which does not induce vestibular stimulation); however, the lack of vertigo may suggest to the subject that actual stimulation has not occurred.

***Methodological and application issues*:** In planning a CVS study, particularly in relation to clinical conditions, several issues need to be considered. Informed consent is one such issue, especially in relation to conditions in which this may be compromised. Also, which technique is most appropriate? Thus, for example, CVS might be best applied to mania and autism compared with NMV because the latter requires active participation from the subject (in determining the subjective midline for purposes of placement of the vibrator tip). Of course, subjects with mania or autism may not tolerate cold-water irrigation (though we note that CVS was well tolerated by Dodson's case study subject). In such cases, OKS may be considered though the wearing of a virtual reality headset to induce this or sitting within a rotating striped drum may also not be tolerated. Perhaps all of the related techniques could be available to the clinician and patient, thus enabling a second option if the first is not tolerated. It is not clear, however, whether all the related techniques would work with equal efficacy. In particular, NMV has not been reported to induce ACC activation and such a factor may be relevant in the choice of technique depending on the neurobiology of the clinical condition under investigation. Also, patient selection will be important. Thus, for example, if autism is being studied, it will practically be preferable to begin investigations with higher functioning subjects (noting, however, that such subjects may be more *or* less likely than lower functioning subjects, to benefit from CVS).

It should also be noted that whether CVS produces contralateral neural activation or disruption/inhibition is not in itself clear from the brain-imaging studies; however, activation would appear most likely when considering the CVS literature as a whole (i.e. in relation to modulation of lateralized phenomena, CVS-induced activation rather than inhibition, is far more consistent). Furthermore, it could be argued that the effects of CVS are the result of general arousal or a 'shock to the system' from the cold-water irrigation. However, this explanation is refuted by exact opposite effects on attentional neglect when cold water is administered contralesionally (restoration) and ipsilesionally [worsening (139,140)] and, moreover, by the finding of no effect on neglect when cold water is irrigated in both ears simultaneously (140). Indeed, the issue of left ear vs. right ear stimulation needs to be considered carefully in planning CVS studies. The selection may be obvious from the underlying neurobiology of the disorder being investigated (e.g. left ear for mania treatment, right ear for depression treatment); however, for many of the disorders we have listed, it is not clear which ear/hemisphere should be stimulated. This will be especially so for disorders without a known laterality component but even the presence of laterality factors may not always be instructive. Thus, one might expect the contralaterality of phantom limb perception to suggest ipsilateral ear irrigation (i.e. CVS of the ear ipsilateral to the phantom). However, the reports of pain alleviation and phantom limb normalization suggest that irrigation of either ear can be effective [though with less data available for contralesional ear CVS (141)]. It may therefore be prudent in repeated-stimulation studies to irrigate the ear (hemisphere) which holds the least likelihood of worsening comorbid depression should this exist in the case of chronic pain states, for example. Thus, as a general rule, unless laterality considerations suggest otherwise, it is probably best for studies of repeated CVS to start with irrigation of the right ear (thus avoiding the theoretical risk of depression as a side-effect). Indeed for CVS studies of mood disorders, the possibility of rebound mania or depression needs to be taken into account and monitored during follow-up periods. Any such side-effects, along with other adverse events in repeated-CVS studies, should be reported in the literature in the manner that occurs currently for other novel brain stimulation techniques.

Other unanswered questions with respect to CVS include (i) whether water at 30°C would induce stimulation as clinically effective as iced water; (ii) whether warm water will induce stimulation as effective as cold water [warm water induces ipsilateral rather than contralateral hemispheric activation and so would be administered to the ear opposite to that used with cold water; see Dieterich et al. (142)]; (iii) how often the stimulation is required to be repeated and whether different repeated-stimulation protocols will induce substantially different clinical efficacy; (iv) whether a 3-week repeated-stimulation protocol as used with NMV (143), for example, would need to be repeated some months/years later (as occurs with ketamine infusions or radiofrequency denervation for some chronic pain states, for example); (v) whether the duration of CVS administration affects efficacy (i.e. what the effect would be of continuing irrigation for several minutes beyond the onset of nystagmus and vertigo, rather than ceasing irrigation at this point); (vi) whether combined cold-water CVS in one ear and warm-water CVS in the other will produce stronger effects than either alone; (vii) when in the course of a disorder the clinical efficacy of CVS would be most potent; (viii) when following the CVS protocol is the optimal time to collect outcome data; (ix) whether short-term (temporary) modulations will always be an indicator of likely therapeutic benefit (i.e. whether a condition may nevertheless improve following repeated CVS, despite there having been no observable, temporary phenomenological or behavioural improvements following a single CVS session); (x) whether CVS and related techniques are best administered alone or as adjunctive therapies and (xi) the effect of handedness with respect to laterality and CVS efficacy [see Bense et al. (10), Dieterich et al. (142)]. Many more questions no doubt remain to be raised and answered.

References

1. Fife TD, Tusa RJ, Furman JM et al. Assessment: vestibular testing techniques in adults and children. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2000;**55**:1431–1441.
2. The Quality Standards Subcommittee Of The American Academy Of Neurology. Practice parameters for determining brain death in adults (Summary Statement). Neurology 1995;**45**:1012–1014.
3. Feldmann H. Die zweitausendjährige Geschichte der Ohrenspritze und ihre Verflechtung mit dem Klistier. Bilder aus der Geschichte der Hals-Nasen-Ohren-Heilkunde, dargestellt an Instrumenten aus der Sammlung im Deutschen Medizinhistorischen Museum in Ingolstadt. Laryngo-Rhino-Otol 1999;**78**:462–467.
4. Bárány R. Untersuchungen über den vom Vestibularapparat des Ohres reflektorisch ausgelösten rhythmischen Nystagmus und seine Begleiterscheinungen. Monatsschr Ohrenheilkd 1906;**40**:193–297.
5. Bárány R. Some new methods for functional testing of the vestibular apparatus and the cerebellum. Nobel Lecture, September 11, 1916. In: Nobel lectures including presentation of speeches and laureates' biographies, physiology or medicine 1901–1921. Amsterdam: Elsevier Publishing Company, **1967**: 500–511.
6. Baloh RW. Charles Skinner Hallpike and the beginnings of neurotology. Neurology 2000;**54**:2138–2146.
7. Bottini G, Sterzi R, Paulesu E et al. Identification of the central vestibular projections in man: a positron emission tomography activation study. Exp Brain Res 1994;**99**:164–169.
8. Bottini G, Paulesu E, Sterzi R et al. Modulation of conscious experience by peripheral sensory stimuli. Nature 1995;**376**:778–781.
9. Bottini G, Karnath H-O, Vallar G et al. Cerebral representations for egocentric space. Functional-anatomical evidence from caloric vestibular stimulation and neck vibration. Brain 2001;**124**:1182–1196.
10. Bense S, Bartenstein P, Lutz S et al. Three determinants of vestibular hemispheric dominance during caloric stimulation. A positron emission tomography study. Ann N Y Acad Sci 2003;**1004**:440–445.
11. Emri M, Kisely M, Lengyel Z et al. Cortical projection of peripheral vestibular signaling. J Neurophysiol 2003;**89**:2639–2646.
12. Kisely M, Emri M, Lengyel Z et al. Changes in brain activation caused by caloric stimulation in the case of cochleovestibular denervation – PET study. Nucl Med Commun 2002;**23**:967–973.
13. Indovina I, Maffei V, Bosco G, Zago M, Macaluso E, Lacquaniti F. Representation of visual gravitational motion in the human vestibular cortex. Science 2005; **308**:416–419.
14. Vitte E, Derosier C, Caritu Y, Berthoz A, Hasboun D, Soulié S. Activation of the hippocampal formation by vestibular stimulation: a functional magnetic resonance imaging study. Exp Brain Res 1996;**112**:523–526.
15. Wenzel R, Bartenstein P, Dieterich M et al. Deactivation of human visual cortex during involuntary ocular oscillations. A PET activation study. Brain 1996;**119**: 101–110.
16. Blake R. A primer on binocular rivalry, including current controversies. Brain Mind 2001;**2**:5–38.
17. Blake R. A neural theory of binocular rivalry. Psychol Rev 1989;**96**:145–167.
18. Logothetis NK. Single units and conscious vision. Philos Trans R Soc Lond B Biol Sci 1998;**353**:1801–1818.
19. Miller SM. On the correlation/constitution distinction problem (and other hard problems) in the scientific study of consciousness. Acta Neuropsychiatr 2007;**19**: 159–176.
20. Logothetis NK, Leopold DA, Sheinberg DL. What is rivalling during binocular rivalry? Nature 1996;**380**: 621–624.
21. Ngo TT, Liu GB, Tilley AJ, Pettigrew JD, Miller SM. Caloric vestibular stimulation reveals discrete neural mechanisms for coherence rivalry and eye rivalry: a meta-rivalry model. Vision Res 2007 (in press).
22. Blake R, Logothetis NK. Visual competition. Nat Rev Neurosci 2002;**3**:13–21.
23. Shannahoff-Khalsa D. The ultradian rhythm of alternating cerebral hemispheric activity. Int J Neurosci 1993; **70**:285–298.
24. Pettigrew JD, Collin SP, Ott M. Convergence of highly-specialised behaviour, eye movements and visual optics in the sandlance (Teleostei) and the chameleon (Reptilia). Curr Biol 1999;**9**:421–424.
25. Rattenborg NC, Amlaner CJ, Lima SL. Behavioral, neurophysiological and evolutionary perspectives on unihemispheric sleep. Neurosci Biobehav Rev 2000; **24**:817–842.
26. Luck SJ, Hillyard SA, Mangun GR, Gazzaniga MS. Independent hemispheric attentional systems mediate visual search in split-brain patients. Nature 1989; **342**:543–545.
27. Bogen J, Berker E, Van Lancker D et al. Left hemicerebrectomy: vision, olfaction and mentation 45 years later. Soc Neurosci Abs 1998;**24**:173.
28. Vallar G, Guariglia C, Rusconi ML. Modulation of the neglect syndrome by sensory stimulation. In: Their P, Karnath H-O, eds. Parietal lobe contributions to orientation in 3D space. Berlin: Springer-Verlag, 1997: 555–578.
29. Rossetti Y, Rode G. Reducing spatial neglect by visual and other sensory manipulations: noncognitive (physiological) routes to the rehabilitation of a cognitive disorder. In: Karnath H-O, Milner D, Vallar G, eds. The cognitive and neural bases of spatial neglect. Oxford: Oxford University Press, 2002: 375–396.
30. Karnath H-O, Berger MF, Küker W, Rorden C. The anatomy of spatial neglect based on voxelwise statistical analysis: a study of 140 patients. Cereb Cortex 2004; **14**:1164–1172.
31. Leibovitch FS, Black SE, Caldwell CB, Ebert PL, Ehrlich LE, Szalai JP. Brain-behavior correlations in hemispatial neglect using CT and SPECT: The Sunnybrook Stroke Study. Neurology 1998;**50**:901–908.
32. Leibovitch FS, Black SE, Caldwell CB, Mcintosh AR, Ehrlich LE, Szalai JP. Brain SPECT imaging and left hemispatial neglect covaried using partial least squares: The Sunnybrook Stroke Study. Hum Brain Mapp 1999;**7**:244–253.
33. Bowen A, Mckenna K, Tallis RC. Reasons for variability in the reported rate of occurrence of unilateral spatial neglect after stroke. Stroke 1999;**30**:1196–1202.
34. Heilman KM, Van Den Abell T. Right hemisphere dominance for attention: the mechanism underlying hemispheric asymmetries of inattention (neglect). Neurology 1980;**30**:327–330.
35. Miller SM, Liu GB, Ngo TT et al. Interhemispheric switching mediates perceptual rivalry. Curr Biol 2000; **10**:383–392.

36. Lumer ED, Friston KJ, Rees, G. Neural correlates of perceptual rivalry in the human brain. Science 1998;**280**: 1930–1934.
37. Miller SM. Binocular rivalry and the cerebral hemispheres: with a note on the correlates and constitution of visual consciousness. Brain Mind 2001;**2**:119–149.
38. Díaz-Caneja E. Sur l'alternance binoculaire. Ann Ocul 1928;**165**:721–731.
39. Ngo TT, Miller SM, Liu GB, Pettigrew JD. Binocular rivalry and perceptual coherence. Curr Biol 2000; **10**:R134–R136.
40. Kovács I, Papathomas TV, Yang M, Feher A. When the brain changes its mind: interocular grouping during binocular rivalry. Proc Natl Acad Sci U S A 1996;**93**: 15508–15511.
41. Papathomas TV, Kovács I, Feher A, Julesz B. Visual dilemmas: competition between eyes and between percepts in binocular rivalry. In: Lepore E, Pylyshyn Z, eds. What is cognitive science? Malden: Blackwell Publishing, 1999: 263–294.
42. Pettigrew JD, Miller SM. A 'sticky' interhemispheric switch in bipolar disorder? Proc Roy Soc Lond B Biol Sci 1998;**265**:2141–2148.
43. Bench CJ, Frackowiak RSJ, Dolan RJ. Changes in regional cerebral blood flow on recovery from depression. Psychol Med 1995;**25**:247–251.
44. Martinot J, Hardy P, Feline A et al. Left prefrontal glucose hypometabolism in the depressed state: a confirmation. Am J Psychiatry 1990;**147**:1313–1317.
45. Migliorelli R, Starkstein SE, Teson A et al. SPECT findings in patients with primary mania. J Neuropsychiatry Clin Neurosci 1993;**5**:379–383.
46. Henriques JB, Davidson RJ. Left frontal hypoactivation in depression. J Abnorm Psychol 1991;**100**:535–545.
47. Robinson RG, Downhill JE. Lateralization of psychopathology in response to focal brain injury. In: Davidson RJ, Hugdahl K, eds. Brain asymmetry. Cambridge: MIT Press, 1995: 693–711.
48. Christianson S-Å, Säisä J, Garvill J, Silfvenius H. Hemisphere inactivation and mood-state changes. Brain Cogn 1993;**23**:127–144.
49. Lee GP, Loring DW, Meader KJ, Brooks BB. Hemispheric specialization for emotional expression: a reexamination of results from intracarotid administration of sodium amobarbitol. Brain Cogn 1990;**12**:267–280.
50. Grisaru N, Chudakov B, Yaroslavsky Y, Belmaker RH. Transcranial magnetic stimulation in mania: a controlled study. Am J Psychiatry 1998;**155**:1608–1610.
51. Pascual-Leone A, Rubio B, Pallardó F, Catalá MD. Rapid-rate transcranial magnetic stimulation of left dorsolateral prefrontal cortex in drug-resistant depression. Lancet 1996;**348**:233–237.
52. Bearden CE, Hoffman KM, Cannon TD. The neuropsychology and neuroanatomy of bipolar affective disorder: a critical review. Bipolar Disord 2001;**3**:106–150.
53. Haldane M, Frangou S. Functional neuroimaging studies in mood disorders. Acta Neuropsychiatr 2006; **18**:88–99.
54. Ramachandran VS. Phantom limbs, neglect syndromes and Freudian psychology. Int Rev Neurobiol 1994;**37**: 291–333.
55. Cappa S, Sterzi R, Vallar G, Bisiach E. Remission of hemineglect and anosognosia during vestibular stimulation. Neuropsychologia 1987;**25**:775–782.
56. Bisiach E, Vallar G, Perani D, Papagno C, Berti A. Unawareness of disease following lesions of the right hemisphere: anosognosia for hemiplegia and anosognosia for hemianopia. Neuropsychologia 1986;**24**:471–482.
57. McGlynn SM, Schacter DL. Unawareness of deficits in neuropsychological syndromes. J Clin Exp Neuropsych 1989;**11**:143–205.
58. Jehkonen M, Laihosalo M, Kettunen J. Anosognosia after stroke: assessment, occurrence, subtypes and impact on functional outcome reviewed. Acta Neurol Scand 2006;**114**:293–306.
59. Davidson RJ. Cerebral asymmetry, emotion, and affective style. In: Davidson RJ, Hugdahl K, eds. Brain asymmetry. Cambridge: MIT Press, 1995: 361–388.
60. Silberman EK, Weingartner H. Hemispheric lateralization of functions related to emotion. Brain Cogn 1986; **5**:322–353.
61. Demaree HA, Everhart DE, Youngstrom EA, Harrison DW. Brain lateralization of emotional processing: historical roots and a future incorporating "dominance". Behav Cogn Neurosci Rev 2005;**4**:3–20.
62. Bhogal SK, Teasell R, Foley N, Speechley M. Lesion location and post-stroke depression. Systematic review of the methodological limitations in the literature. Stroke 2004;**35**:794–802.
63. Celik Y, Erdogan E, Tuglu C, Utku U. Post-stroke mania in late life due to right temporoparietal infarction. Psychiatry Clin Neurosci 2004;**58**:446–447.
64. Cummings JL, Mendez MF. Secondary mania with focal cerebrovascular lesions. Am J Psychiatry 1984;**141**: 1084–1087.
65. Gainotti G. Emotional behavior and hemispheric side of lesion. Cortex 1972;**8**:41–55.
66. Jorge R, Robinson RG. Mood disorders following traumatic brain injury. Neurorehabilitation 2002;**17**:311–324.
67. Mimura M, Nakagome K, Hirashima N et al. Left frontotemporal hyperperfusion in a patient with post-stroke mania. Psychiatry Res 2005;**139**:263–267.
68. Robinson RG, Boston JD, Starkstein SE, Price TR. Comparison of mania and depression after brain injury: causal factors. Am J Psychiatry 1988;**145**:172–178.
69. Starkstein SE, Boston JD, Robinson RG. Mechanisms of mania after brain injury. 12 case reports and review of the literature. J Nerv Ment Dis 1988;**176**:87–100.
70. Starkstein SE, Mayberg HS, Berthier ML et al. Mania after brain injury: neuroradiological and metabolic findings. Ann Neurol 1990;**27**:652–659.
71. Vataja R, Leppävuori A, Pohjasvaara T et al. Post-stroke depression and lesion location revisited. J Neuropsychiatry Clin Neurosci 2004;**16**:156–162.
72. Miller SM, Gynther BD, Heslop KR et al. Slow binocular rivalry in bipolar disorder. Psychol Med 2003;**33**:683–692.
73. Ewen JH. The psychological estimation of the effects of certain drugs upon the syntonic and schizophrenic psychoses. With a brief enquiry into a physiological basis of temperament. J Ment Sci 1931;**77**:742–766.
74. Hunt J, Guilford JP. Fluctuation of an ambiguous figure in dementia praecox and in manic depressive patients. J Abnormal Soc Psychol 1933;**27**:443–452.
75. Blumberg HP, Stern E, Martinez D et al. Increased anterior cingulate and caudate activity in bipolar mania. Biol Psychiatry 2000;**48**:1045–1052.
76. Dodson MJ. Vestibular stimulation in mania: a case report. J Neurol Neurosurg Psychiatry 2004;**75**:168–169.
77. Benke Th, Kurzthaler I, Schmidauer Ch, Moncayo R, Donnemiller E. Mania caused by a diencephalic lesion. Neuropsychologia 2002;**40**:245–252.

78. Liebson E. Anosognosia and mania associated with right thalamic haemorrhage. J Neurol Neurosurg Psychiatry 2000;**68**:107–108.
79. Migliorelli R, Teson A, Sabe L et al. Anosognosia in Alzheimer's disease: a study of associated factors. J Neuropsychiatry Clin Neurosci 1995;**7**:338–344.
80. Soza Ried AM, Aviles M. Asymmetries of vestibular dysfunction in major depression. Neuroscience 2007; **144**:128–134.
81. Shiroyama T, Kayahara T, Yasui Y, Nomura J, Nakano K. Projections of the vestibular nuclei to the thalamus in the rat: a *Phaseolus vulgaris* leucoagglutinin study. J Comp Neurol 1999;**407**:318–332.
82. Barmack NH. Central vestibular system: vestibular nuclei and posterior cerebellum. Brain Res Bull 2003; **60**:511–541.
83. Halmagyi GM, Cremer PD, Anderson J, Murofushi T, Curthoys IS. Isolated directional preponderance of caloric nystagmus: I. Clinical significance. Am J Otol 2000;**21**:559–567.
84. De La Iglesia HO, Meyer J, Carpino A Jr, Schwartz WJ. Antiphase oscillation of the left and right suprachiasmatic nuclei. Science 2000;**290**:799–801.
85. Pettigrew JD. Searching for the switch: neural bases for perceptual rivalry alternations. Brain Mind 2001;**2**: 85–118.
86. Blanke O, Perrig S, Thut G, Landis T, Seeck M. Simple and complex vestibular responses induced by electrical cortical stimulation of the parietal cortex in humans. J Neurol Neurosurg Psychiatry 2000;**69**:553–556.
87. Duque-Parra JE. Perspective on the vestibular cortex throughout history. Anat Rec B New Anat 2004;**280**:15–19.
88. Eickhoff SB, Weiss PH, Amunts K, Fink GR, Zilles K. Identifying human parieto-insular vestibular cortex using fMRI and cytoarchitectonic mapping. Hum Brain Mapp 2006;**27**:611–621.
89. Kahane P, Hoffmann D, Minotti L, Berthoz A. Reappraisal of the human vestibular cortex by cortical electrical stimulation study. Ann Neurol 2003;**54**:615–624.
90. Petit L, Beauchamp MS. Neural basis of visually guided head movements studied with fMRI. J Neurophysiol 2003;**89**:2516–2527.
91. Guldin WO, Grüsser O-J. Is there a vestibular cortex? Trends Neurosci 1998;**21**:254–259.
92. Karnath H-O, Dieterich M. Spatial neglect – a vestibular disorder? Brain 2006;**129**:293–305.
93. Bense S, Stephan T, Yousry TA, Brandt T, Dieterich M. Multisensory cortical signal increases and decreases during vestibular galvanic stimulation (fMRI). J Neurophysiol 2001;**85**:886–899.
94. Fink GR, Marshall JC, Weiss PH et al. Performing allocentric visuospatial judgments with induced distortion of the egocentric reference frame: an fMRI study with clinical implications. Neuroimage 2003;**20**:1505–1517.
95. Lobel E, Kleine JF, Bihan DL, Leroy-Willig A, Berthoz A. Functional MRI of galvanic vestibular stimulation. J Neurophysiol 1998;**80**:2699–2709.
96. Bucher SF, Dieterich M, Seelos KC, Brandt T. Sensorimotor cerebral activation during optokinetic nystagmus: a functional MRI study. Neurology 1997;**49**: 1370–1377.
97. Bense S, Stephan T, Bartenstein P, Schwaiger M, Brandt T, Dieterich M. Fixation suppression of optokinetic nystagmus modulates cortical visual-vestibular interaction. Neuroreport 2005;**16**:887–890.
98. Bense S, Janusch B, Schlindwein P et al. Direction-dependent visual cortex activation during horizontal optokinetic stimulation (fMRI study). Hum Brain Mapp 2006;**27**:296–305.
99. Dieterich M, Bense S, Stephan T, Yousry TA, Brandt T. fMRI signal increases and decreases in cortical areas during small-field optokinetic stimulation and central fixation. Exp Brain Res 2003;**148**:117–127.
100. Brandt T, Bartenstein P, Janek A, Dieterich M. Reciprocal inhibitory visual-vestibular interaction. Visual motion stimulation deactivates the parietoinsular vestibular cortex. Brain 1998;**121**:1749–1758.
101. Deutschländer A, Bense S, Stephan T, Schwaiger M, Dieterich M, Brandt T. Rollvection versus linearvection: comparison of brain activations in PET. Hum Brain Mapp 2004;**21**:143–153.
102. Dieterich M, Brandt T. Brain activation studies on visual-vestibular and ocular motor interaction. Curr Opin Neurol 2000;**13**:13–18.
103. Stephan T, Deutschländer A, Nolte A et al. Functional MRI of galvanic vestibular stimulation with alternating currents at different frequencies. Neuroimage 2005; **26**:721–732.
104. Karnath H-O. Subjective body orientation in neglect and the interactive contribution of neck muscle proprioreception and vestibular stimulation. Brain 1994;**114**: 1001–1012.
105. Karnath H-O, Christ K, Hartje W. Decrease of contralateral neglect by neck muscle vibration and spatial orientation of trunk midline. Brain 1993;**116**:383–396.
106. Karnath H-O, Fetter M, Dichgans J. Ocular exploration of space as a function of neck proprioceptive and vestibular input: observations in normal subjects and patients with spatial neglect after parietal lesions. Exp Brain Res 1996;**109**:333–342.
107. Pizzamiglio L, Frasca R, Guariglia C, Incoccia C, Antonucci G. Effect of optokinetic stimulation in patients with visual neglect. Cortex 1990;**26**:534–540.
108. Mattingley JB, Bradshaw JL, Bradshaw JA. Horizontal visual motion modulates focal attention in left unilateral spatial neglect. J Neurol Neurosurg Psychiatry 1994;**57**:1228–1235.
109. Vallar G, Guariglia C, Magnotti L, Pizzamiglio L. Optokinetic stimulation affects both vertical and horizontal deficits of position sense in unilateral neglect. Cortex 1995;**31**:669–683.
110. Schindler I, Kerkhoff G. Convergent and divergent effects of neck proprioceptive and visual motion stimulation on visual space processing in neglect. Neuropsychologia. 2004;**42**:1149–1155.
111. Kerkhoff G, Keller I, Ritter V, Marquardt C. Repetitive optokinetic stimulation induces lasting recovery from visual neglect. Restor Neurol Neurosci 2006; **24**:357–369.
112. Rorsman I, Magnusson M, Johansson BB. Reduction of visuo-spatial neglect with vestibular galvanic stimulation. Scand J Rehabil Med 1999;**31**:117–124.
113. Dieterich M, Bucher SF, Seelos KC, Brandt T. Horizontal or vertical optokinetic stimulation activates visual motion-sensitive, ocular motor and vestibular cortex areas with right hemispheric dominance. An fMRI study. Brain 1998;**121**:1479–1495.
114. Galati G, Pappata S, Pantano P, Lenzi GL, Samson Y, Pizzamiglio L. Cortical control of optokinetic nystagmus in humans: a positron emission tomography study. Exp Brain Res 1999;**126**:149–159.

115. Bucher SF, Dieterich M, Wiesmann M et al. Cerebral functional magnetic resonance imaging of vestibular, auditory, and nociceptive areas during galvanic stimulation. Ann Neurol 1998;**44**:120–125.
116. Vogt BA, Finch DM, Olson CR. Functional heterogeneity in cingulate cortex: the anterior executive and posterior evaluative regions. Cereb Cortex 1992;**2**:435–443.
117. Devinsky O, Morrell MJ, Vogt BA. Contributions of anterior cingulate cortex to behaviour. Brain 1995; **118**:279–306.
118. Isomura Y, Takada M. Neural mechanisms of versatile functions in primate anterior cingulate cortex. Rev Neurosci 2004;**15**:279–291.
119. Mega MS, Cummings JL. The cingulate and cingulate syndromes. In: Trimble MR, Cummings JL, eds. Contemporary behavioral neurology. Boston: Butterworth-Heinemann, 1997: 189–214.
120. Weissman DH, Gopalakrishnan A, Hazlett CJ, Woldorff MG. Dorsal anterior cingulate cortex resolves conflict from distracting stimuli by boosting attention toward relevant events. Cereb Cortex 2005;**15**:229–237.
121. Yücel M, Harrison BJ, Wood SJ et al. State, trait and biochemical influences on human anterior cingulate function. Neuroimage 2007;**34**:1766–1773.
122. Holroyd CB, Nieuwenhuis S, Yeung N et al. Dorsal anterior cingulate cortex shows fMRI response to internal and external error signals. Nat Neurosci 2004;**7**:497–498.
123. Williams ZM, Bush G, Rauch SL, Cosgrove GR, Eskandar EN. Human anterior cingulate neurons and the integration of monetary reward with motor responses. Nat Neurosci 2004;**7**:1370–1375.
124. Bush G, Luu P, Posner MI. Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn Sci 2000;**4**:215–222.
125. Koski L, Paus T. Functional connectivity of the anterior cingulate cortex within the human frontal lobe: a brain-mapping meta-analysis. Exp Brain Res 2000;**133**:55–85.
126. Paus T. Primate anterior cingulate cortex: where motor control, drive and cognition interface. Nat Rev Neurosci 2001;**2**:417–424.
127. Picard N, Strick PL. Motor areas of the medial wall: a review of their location and functional activation. Cereb Cortex 1996;**6**:342–353.
128. Drevets WC. Functional neuroimaging studies of depression: the anatomy of melancholia. Annu Rev Med 1998; **49**:341–361.
129. Mayberg HS. Modulating dysfunctional limbic-cortical circuits in depression: towards development of brain-based algorithms for diagnosis and optimised treatment. Br Med Bull 2003;**65**:193–207.
130. Seminowicz DA, Mayberg HS, Mcintosh AR et al. Limbic-frontal circuitry in major depression: a path modeling metanalysis. Neuroimage 2004;**22**:409–418.
131. Malhi GS, Sachdev P. Novel physical treatments for the management of neuropsychiatric disorders. J Psychosom Res 2002;**53**:709–719.
132. Fitzgerald PB, Brown TL, Daskalakis ZJ. The application of transcranial magnetic stimulation in psychiatry and neurosciences research. Acta Psychiatr Scand 2002; **105**:324–340.
133. Simons W, Dierick M. Transcranial magnetic stimulation as a therapeutic tool in psychiatry. World J Biol Psychiatry 2005;**6**:6–25.
134. Bittar RG, Kar-Purkayastha I, Owen SL et al. Deep brain stimulation for pain relief: a meta-analysis. J Clin Neurosci 2005;**12**:515–519.
135. Bittar RG. Neuromodulation for movement disorders. J Clin Neurosci 2006;**13**:315–318.
136. Kopell BH, Greenberg B, Rezai AR. Deep brain stimulation in psychiatric disorders. J Clin Neurophysiol 2004;**21**:51–67.
137. Henry TR. Therapeutic mechanisms of vagus nerve stimulation. Neurology 2002;**59**:S3–S14.
138. Groves DA, Brown VJ. Vagal nerve stimulation: a review of its applications and potential mechanisms that mediate its clinical effects. Neurosci Biobehav Rev 2005;**29**: 493–500.
139. Rubens AB. Caloric stimulation and unilateral visual neglect. Neurology 1985;**35**:1019–1024.
140. Rode G, Tilikete C, Luauté J, Rossetti Y, Vighetto A, Boisson D. Bilateral vestibular stimulation does not improve visual hemineglect. Neuropsychologia 2002;**40**: 1104–1106.
141. André J-M, Martinet N, Paysant J, Beis J-M, Le Chapelain L. Temporary phantom limbs evoked by vestibular caloric stimulation in amputees. Neuropsychiatry Neuropsychol Behav Neurol 2001;**14**:190–196.
142. Dieterich M, Bense S, Lutz S et al. Dominance for vestibular cortical function in the non-dominant hemisphere. Cereb Cortex 2003;**13**:994–1007.
143. Schindler I, Kerkhoff G, Karnath H-O, Keller I, Goldenberg G. Neck muscle vibration induces lasting recovery in spatial neglect. J Neurol Neurosurg Psychiatry 2002;**73**:412–419.
144. Johannsen L, Akermann H, Karnath H-O. Lasting amelioration of spatial neglect by treatment with neck muscle vibration even without concurrent training. J Rehabil Med 2003;**35**:249–253.
145. Michel C. Simulating unilateral neglect in normals: myth or reality? Restor Neurol Neurosci 2006;**24**:419–430.
146. Kerkhoff G, Rossetti Y. Plasticity in spatial neglect – recovery and rehabilitation. Restor Neurol Neurosci 2006;**24**:201–206.
147. Luauté J, Halligan P, Rode G, Rossetti Y, Boisson D. Visuo-spatial neglect: a systematic review of current interventions and their effectiveness. Neurosci Biobehav Rev 2006;**30**:961–982.
148. Adair JC, Na DL, Schwartz RL, Heilman KM. Caloric stimulation in neglect: evaluation of response as a function of neglect type. J Int Neuropsychol Soc 2003;**9**: 983–988.
149. Geminiani G, Bottini G. Mental representation and temporary recovery from unilateral neglect after vestibular stimulation. J Neurol Neurosurg Psychiatry 1992;**55**: 332–333.
150. Rode G, Perenin MT. Temporary remission of representational hemineglect through vestibular stimulation. Neuroreport 1994;**5**:869–872.
151. Vallar G, Sterzi R, Bottini G, Cappa S, Rusconi ML. Temporary remission of left hemianesthesia after vestibular stimulation. A sensory neglect phenomenon. Cortex 1990;**26**:123–131.
152. Bottini G, Paulesu E, Gandola M et al. Left caloric vestibular stimulation ameliorates right hemianesthesia. Neurology 2005;**65**:1278–1283.
153. Rode G, Perenin M-T, Honoré J, Boisson D. Improvement of the motor deficit of neglect patients through vestibular stimulation: evidence for a motor neglect component. Cortex 1998;**34**:253–261.
154. Bisiach E, Rusconi ML, Vallar G. Remission of somatoparaphrenic delusion through vestibular stimulation. Neuropsychologia 1991;**29**:1029–1031.

155. Rode G, Charles N, Perenin M-T, Vighetto A, Trillet M, Aimard G. Partial remission of hemiplegia and somatoparaphrenia through vestibular stimulation in a case of unilateral neglect. Cortex 1992;**28**:203–208.
156. Pridmore S, Oberoi G, Marcolin M, George M. Transcranial magnetic stimulation and chronic pain: current status. Australas Psychiatry 2005;**13**:258–265.
157. Lefaucheur JP. The use of repetitive transcranial magnetic stimulation (rTMS) in chronic neuropathic pain. Neurophysiol Clin 2006;**36**:117–124.
158. Pleger B, Janssen F, Schwenkreis P, Völker B, Maier C, Tegenthoff M. Repetitive transcranial magnetic stimulation of the motor cortex attenuates pain perception in complex regional pain syndrome type I. Neurosci Lett 2004;**356**:87–90.
159. Bittar RG, Otero S, Carter H, Aziz TZ. Deep brain stimulation for phantom limb pain. J Clin Neurosci 2005;**12**:399–404.
160. Kirchner A, Birklein F, Stefan H, Handwerker HO. Vagusstimulation – Eine Behandlungsoption für chronische Schmerzen? Schmerz 2001;**15**:272–277.
161. Hord ED, Evans MS, Mueed S, Adamolekun B, Naritoku DK. The effect of vagus nerve stimulation on migraines. J Pain 2003;**4**:530–534.
162. Mauskop A. Vagus nerve stimulation relieves chronic refractory migraine and cluster headaches. Cephalalgia 2005;**25**:82–86.
163. Privitera MD, Welty TE, Ficker DM, Welge J. Vagus nerve stimulation for partial seizures. Cochrane Database Syst Rev 2002; CD002896.
164. Rush AJ, Sackeim HA, Marangell LB et al. Effects of 12 months of vagus nerve stimulation in treatment-resistant depression: a naturalistic study. Biol Psychiatry 2005;**58**:355–363.
165. Shih JJ, Devier D, Behr A. Late onset laryngeal and facial pain in previously asymptomatic vagus nerve stimulation patients. Neurology 2003;**60**:1214.
166. Le Chapelain L, Beis J-M, Paysant J, André J-M. Vestibular caloric stimulation evokes phantom limb illusions in patients with paraplegia. Spinal Cord 2001;**39**:85–87.
167. Ramachandran VS, McGeoch PD, Williams L. Can vestibular caloric stimulation be used to treat Dejerine-Roussy Syndrome? Med Hypotheses 2007 (in press).
168. Williams LE, Ramachandran VS. Novel experimental approaches to reflex sympathetic dystrophy/complex regional pain syndrome type 1 (RSD/CRPS -1) and obsessive-compulsive disorder (OCD). Program No. 49.8/J3. 2006 Neuroscience Meeting Planner. Atlanta: Society for Neuroscience 2006, Online.
169. Galer BS, Jensen M. Neglect-like symptoms in complex regional pain syndrome: results of a self-administered survey. J Pain Symptom Manage 1999;**18**:213–217.
170. Frettlöh J, Hüppe M, Maier C. Severity and specificity of neglect-like symptoms in patients with complex regional pain syndrome (CRPS) compared to chronic limb pain of other origins. Pain 2006;**124**:184–189.
171. Sumitani M, Rossetti Y, Shibata M et al. Prism adaptation to optical deviation alleviates pathologic pain. Neurology 2007;**68**:128–133.
172. Frassinetti F, Angeli V, Meneghello F, Avanzi S, Làdavas E. Long-lasting amelioration of visuospatial neglect by prism adaptation. Brain 2002;**125**:608–623.
173. Luauté J, Halligan P, Rode G, Jacquin-Courtois S, Boisson D. Prism adaptation first among equals in alleviating left neglect: a review. Restor Neurol Neurosci 2006;**24**:409–418.
174. Redding GM, Wallace B. Prism adaptation and unilateral neglect: review and analysis. Neuropsychologia 2006;**44**:1–20.
175. Rainville P, Duncan GH, Price DD, Carrier B, Bushnell MC. Pain affect encoded in human anterior cingulate but not somatosensory cortex. Science 1997;**277**:968–971.
176. Apkarian AV, Bushnell MC, Treede R-D, Zubieta J-K. Human brain mechanisms of pain perception and regulation in health and disease. Eur J Pain 2005;**9**:463–484.
177. Büchel C, Bornhövd K, Quante M, Glauche V, Bromm B, Weiller C. Dissociable neural responses related to pain intensity, stimulus intensity, and stimulus awareness within the anterior cingulate cortex: a parametric single-trial laser functional magnetic resonance imaging study. J Neurosci 2002;**22**:970–976.
178. Tolle TR, Kaufmann T, Siessmeier T et al. Region-specific encoding of sensory and affective components of pain in the human brain: a positron emission tomography correlation analysis. Ann Neurol 1999;**45**: 40–47.
179. Kwan CL, Crawley AP, Mikulis DJ, Davis KD. An fMRI study of the anterior cingulate cortex and surrounding medial wall activations evoked by noxious cutaneous heat and cold stimuli. Pain 2000;**85**:359–374.
180. Ballantine HT Jr, Cassidy WL, Flanagan NB, Marino R Jr. Stereotaxic anterior cingulotomy for neuropsychiatric illness and intractable pain. J Neurosurg 1967;**26**: 488–495.
181. Corkin S, Hebben N. Subjective estimates of chronic pain before and after psychosurgery or treatment in a pain unit. Pain 1981;**11**:S150.
182. Faillace LA, Allen RP, McQueen JD, Northrup B. Cognitive deficits from bilateral cingulotomy for intractable pain in man. Dis Nerv Syst 1971;**32**:171–175.
183. Foltz EL, White LE Jr. Pain ''relief'' by frontal cingulumotomy. J Neurosurg 1962;**19**:89–100.
184. Foltz EL, White LE. The role of rostral cingulumotomy in ''pain'' relief. Int J Neurol 1968;**6**:353–373.
185. Hassenbusch SJ, Pillay PK, Barnett GH. Radiofrequency cingulotomy for intractable cancer pain using stereotaxis guided by magnetic resonance imaging. Neurosurgery 1990;**27**:220–223.
186. Hurt RW, Ballantine HT Jr. Stereotactic anterior cingulate lesions for persistent pain: a report on 68 cases. Clin Neurosurg 1974;**21**:334–351.
187. Pillay PK, Hassenbusch SJ. Bilateral MRI-guided stereotactic cingulotomy for intractable pain. Stereotact Funct Neurosurg 1992;**59**:33–38.
188. Santo JL, Arias LM, Barolat G, Schwartzman RJ, Grossman K. Bilateral cingulumotomy in the treatment of reflex sympathetic dystrophy. Pain 1990;**41**:55–59.
189. Sharma T. Absence of cognitive deficits from bilateral cingulotomy for intractable pain in humans. Tex Med 1973;**69**:79–82.
190. Wilson DH, Chang AE. Bilateral anterior cingulectomy for the relief of intractable pain. Report of 23 patients. Confin Neurol 1974;**36**:61–68.
191. Wilkinson HA, Davidson KM, Davidson RI. Bilateral anterior cingulotomy for chronic noncancer pain. Neurosurgery 1999;**45**:1129–1136.
192. Yen CP, Kung SS, Su YF, Lin WC, Howng SL, Kwan AL. Stereotactic bilateral anterior cingulotomy for intractable pain. J Clin Neurosci 2005;**12**:886–890.
193. Ballantine Jr HT, Bouckoms AJ, Thomas EK, Giriunas IE. Treatment of psychiatric illness by stereotactic cingulotomy. Biol Psychiatry 1987;**22**:807–819.

194. Cosgrove GR, Rauch SL. Stereotactic cingulotomy. Neurosurg Clin N Am 2003;**14**:225–235.
195. Jung HH, Kim C-H, Chang JH, Park YG, Chung SS, Chang JW. Bilateral anterior cingulotomy for refractory obsessive-compulsive disorder: long-term follow-up results. Stereotact Funct Neurosurg 2006;**84**:184–189.
196. Sachdev P, Sachdev J. Sixty years of neurosurgery for psychiatric disorders: its present status and its future. Aust N Z J Psychiatry 1997;**31**:457–464.
197. Tow PM, Whitty CWM. Personality changes after operations on the cingulate gyrus in man. J Neurol Neurosurg Psychiatry 1953;**16**:186–193.
198. Gureje O. Psychiatric aspects of pain. Curr Opin Psychiatry 2007;**20**:42–46.
199. Rommel O, Willweber-Strumpf A, Wagner P, Surall D, Malin J-P, Zenz M. Psychische Veränderungen bei Patienten mit komplexem regionalem Schmerzsyndrom (CRPS). Schmerz 2005;**19**:272–284.
200. Williams LJ, Jacka FN, Pasco JA, Dodd S, Berk M. Depression and pain: an overview. Acta Neuropsychiatr 2006;**18**:79–87.
201. Benrud-Larson LM, Wegener ST. Chronic pain in neurorehabilitation populations: prevalence, severity and impact. Neurorehabilitation 2002;**14**:127–137.
202. Van Leeuwen MT, Blyth FM, March LM, Nicholas MK, Cousins MJ. Chronic pain and reduced work effectiveness: the hidden cost to Australian employers. Eur J Pain 2006;**10**:161–166.
203. Nikolajsen L, Jensen TS. Phantom limb. In: McMahon SB, Koltzenburg M, eds. Wall and Melzack's textbook of pain. Philadelphia: Elsevier, 2006: 961–971.
204. Siddall PJ, Loeser JD. Pain following spinal cord injury. Spinal Cord 2001;**39**:63–73.
205. Oaklander AL, North RB. Failed back surgery syndrome. In: Loeser JD, ed. Bonica's management of pain. Philadelphia: Lippincott Williams & Wilkins, 2001: 1540–1549.
206. Rasche D, Siebert S, Stippich C et al. Epidurale Rückenmarkstimulation bei Postnukleotomiesyndrom. Pilotstudie zur Therapieevaluation mit der funktionellen Magnetresonanztomographie (fMRT). Schmerz 2005; **19**:497–500,502–505.
207. Kim JS. Pattern of sensory abnormality in cortical stroke. Evidence for a dichotomized sensory system. Neurology 2007;**68**:174–180.
208. Maarrawi J, Peyron R, Mertens P et al. Differential brain opioid receptor availability in central and peripheral neuropathic pain. Pain 2007;**127**:183–194.
209. Brooks JCW, Tracey I. The insula: a multidimensional integration site for pain. Pain 2007;**128**:1–2.
210. Bauman ML, Kemper TL. The neurobiology of autism. Baltimore: Johns Hopkins University Press, 1994.
211. Gomot M, Bernard FA, Davis MH et al. Change detection in children with autism: an auditory event-related fMRI study. Neuroimage 2006;**29**:475–484.
212. Kana RK, Keller TA, Minshew NJ, Just MA. Inhibitory control in high-functioning autism: decreased activation and underconnectivity in inhibition networks. Biol Psychiatry 2007 (in press).
213. Levitt JG, O'Neill J, Blanton RE et al. Proton magnetic resonance spectroscopic imaging of the brain in childhood autism. Biol Psychiatry 2003;**54**:1355–1366.
214. Mundy P. Annotation: the neural basis of social impairments in autism: the role of the dorsal medial-frontal cortex and anterior cingulate system. J Child Psychol Psychiatry 2003;**44**:793–809.
215. Ornitz EM. The modulation of sensory input and motor output in autistic children. J Autism Child Schizophr 1974;**4**:197–215.
216. Ornitz EM, Atwell CW, Kaplan AR, Westlake JR. Brain-stem dysfunction in autism. Results of vestibular stimulation. Arch Gen Psychiatry 1985;**42**:1018–1025.
217. Goldberg MC, Landa R, Lasker A, Cooper L, Zee DS. Evidence of normal cerebellar control of the vestibulo-ocular reflex (VOR) in children with high-functioning autism. J Autism Dev Disord 2000;**30**:519–524.
218. Kaplan M, Edelson SM, Seip J-AL. Behavioral changes in autistic individuals as a result of wearing ambient transitional prism lenses. Child Psychiatry Hum Dev 1998;**29**:65–76.
219. Sachdev PS, Malhi GS. Obsessive-compulsive behaviour: a disorder of decision-making. Aust N Z J Psychiatry 2005;**39**:757–763.
220. Viard A, Flament MF, Artiges E et al. Cognitive control in childhood-onset obsessive-compulsive disorder: a functional MRI study. Psychol Med 2005;**35**:1007–1017.
221. Yücel M, Wood SJ, Fornito A, Riffkin J, Velakoulis D, Pantelis C. Anterior cingulate dysfunction: implications for psychiatric disorders? J Psychiatry Neurosci 2003;**28**:350–354.
222. López-Ibor JJ, López-Ibor M-I. Research on obsessive-compulsive disorder. Curr Opin Psychiatry 2003;**16**: S85–S91.
223. Sharma T. Abolition of opiate hunger in humans following bilateral anterior cingulotomy. Tex Med 1974;**70**:49–52.
224. Sewards TV, Sewards MA. Representations of motivational drives in mesial cortex, medial thalamus, hypothalamus and midbrain. Brain Res Bull 2003;**61**:25–49.
225. Bush G, Vogt BA, Holmes J et al. Dorsal anterior cingulate cortex: a role in reward-based decision making. Proc Natl Acad Sci U S A 2002;**99**:523–528.
226. Cohen MX, Heller AS, Ranganath C. Functional connectivity with anterior cingulate and orbitofrontal cortices during decision-making. Cogn Brain Res 2005; **23**:61–70.
227. Rogers RD, Ramnani N, Mackay C et al. Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. Biol Psychiatry 2004;**55**:594–602.
228. Cohen RA, Kaplan RF, Zuffante P et al. Alteration of intention and self-initiated action associated with bilateral anterior cingulotomy. J Neuropsychiatry Clin Neurosci 1999;**11**:444–453.
229. Nitschke JB, Mackiewicz KL. Prefrontal and anterior cingulate contributions to volition in depression. Int Rev Neurobiol 2005;**67**:73–94.
230. Tucker DM, Luu P, Pribram KH. Social and emotional self-regulation. Ann N Y Acad Sci 1995;**769**: 213–239.
231. Minassian A, Paulus MP, Perry W. Increased sensitivity to error during decision-making in bipolar disorder patients with acute mania. J Affect Disord 2004;**82**:203–208.
232. Mayberg HS, Lozano AM, Voon V et al. Deep brain stimulation for treatment-resistant depression. Neuron 2005;**45**:651–660.
233. Marin RS, Wilkosz PA. Disorders of diminished motivation. J Head Trauma Rehabil 2005;**20**:377–388.
234. Kalivas PW, Barnes CD, eds. Limbic motor circuits and neuropsychiatry. Boca Raton: CRC Press, 1993.
235. Aston-Jones GS, Desimone R, Driver J, Luck SJ, Posner MI. Attention. In: Zigmond MJ, Bloom FE,

Landis SC, Roberts JL, Squire LR, eds. Fundamental neuroscience. San Diego: Academic Press, 1999: 1385–1409.
236. Damasio AR, Anderson SW. The frontal lobes. In: Heilman KM, Valenstein E, eds. Clinical neuropsychology. New York: Oxford University Press, 1993: 409–460.
237. Damasio AR, Van Hoesen GW. Emotional disturbances associated with focal lesions of the limbic frontal lobe. In: Heilman KM, Satz P, eds. Neuropsychology of human emotion. New York: Guilford, 1983: 85–110.
238. Braun CMJ, Dumont M, Duval J, Hamel-Hébert I. Speech rate as a sticky switch: a multiple lesion case analysis of mutism and hyperlalia. Brain Lang 2004;**89**:243–252.
239. Berardelli A, Rothwell JC, Hallett M, Thompson PD, Manfredi M, Marsden CD. The pathophysiology of primary dystonia. Brain 1998;**121**:1195–1212.
240. Tarsy D, Simon DK. Dystonia. N Eng J Med 2006;**355**:818–829.
241. Bhatia KP, Bhatt MJ, Marsden CD. The causalgia-dystonia syndrome. Brain 1993;**116**:843–851.
242. Van Hilten JJ, Van De Beek WJT, Roep BO. Multifocal or generalised tonic dystonia of complex regional pain syndrome: a distinct clinical entity associated with HLA-DR13. Ann Neurol 2000;**48**:113–116.
243. Bittar RG, Yianni J, Wang S et al. Deep brain stimulation for generalised dystonia and spasmodic torticollis. J Clin Neurosci 2005;**12**:12–16.
244. Holloway KL, Baron MS, Brown R, Cifu DX, Carne W, Ramakrishnan V. Deep brain stimulation for dystonia: a meta-analysis. Neuromodulation 2006;**9**:253–261.
245. Rosengren SM, Colebatch JG. Cervical dystonia responsive to acoustic and galvanic vestibular stimulation. Mov Disord 2006;**21**:1495–1499.
246. Leis AA, Dimitrijevic MR, Delapasse JS, Sharkey PC. Modification of cervical dystonia by selective sensory stimulation. J Neurol Sci 1992;**110**:79–89.
247. Karnath H-O, Konczak J, Dichgans J. Effect of prolonged neck muscle vibration on lateral head tilt in severe spasmodic torticollis. J Neurol Neurosurg Psychiatry 2000;**69**:658–660.
248. Münchau A, Bronstein AM. Role of the vestibular system in the pathophysiology of spasmodic torticollis. J Neurol Neurosurg Psychiatry 2001;**71**:285–288.
249. Bove M, Brichetto G, Abbruzzese G, Marchese R, Schieppati M. Neck proprioception and spatial orientation in cervical dystonia. Brain 2004;**127**:2764–2778.
250. Bove M, Brichetto G, Abbruzzese G, Marchese R, Schieppati M. Postural responses to continuous unilateral neck muscle vibration in standing patients with cervical dystonia. Mov Disord 2007;**22**:498–503.
251. Taylor MA, Fink M. Catatonia in psychiatric classification: a home of its own. Am J Psychiatry 2003; **160**:1233–1241.
252. Northoff G. What catatonia can tell us about "top-down modulation": a neuropsychiatric hypothesis. Behav Brain Sci 2002;**25**:555–604.
253. Dhossche DM, Wing L, Ohta M, Neumärker K-L, eds. Catatonia in autism spectrum disorders. New York: Academic Press, 2006.
254. Bächtold D, Baumann T, Sándor PS, Kritos M, Regard M, Brugger P. Spatial- and verbal-memory improvement by cold-water caloric stimulation in healthy subjects. Exp Brain Res 2001;**136**:128–132.
255. Churchland PS. Neurophilosophy: toward a unified science of the mind-brain. Cambridge: MIT Press, 1986.
256. Bechara A, Damasio AR, Damasio H, Anderson SW. Insensitivity to future consequences following damage to human prefrontal cortex. Cognition 1994;**50**:7–15.
257. Knoch D, Gianotti LRR, Pascual-Leone A et al. Disruption of right prefrontal cortex by low-frequency repetitive transcranial magnetic stimulation induces risk-taking behavior. J Neurosci 2006;**26**:6469–6472.
258. Baron-Cohen S, Leslie AM, Frith U. Does the autistic child have a "theory of mind"? Cognition 1985;**21**:37–46.
259. Carruthers P, Smith PK, eds. Theories of mind. Cambridge: Cambridge University Press, 1996.
260. Frith U, De Vignemont F. Egocentrism, allocentrism, and Asperger syndrome. Conscious Cogn 2005;**14**:719–738.
261. Blanke O, Mohr C, Michel CM et al. Linking out-of-body experience and self processing to mental own-body imagery at the temporoparietal junction. J Neurosci 2005;**25**:550–557.
262. Mast FW, Merfeld DM, Kosslyn SM. Visual mental imagery during caloric vestibular stimulation. Neuropsychologia 2006;**44**:101–109.
263. Arzy S, Seeck M, Ortigue S, Spinelli L, Blanke O. Induction of an illusory shadow person. Nature 2006;**443**:287.
264. Lenggenhager B, Smith ST, Blanke O. Functional and neural mechanisms of embodiment: importance of the vestibular system and the temporal parietal junction. Rev Neurosci 2006;**17**:643–657.
265. Pia L, Tamietto M. Unawareness in schizophrenia: neuropsychological and neuroanatomical findings. Psychiatry Clin Neurosci 2006;**60**:531–537.
266. Rickelman BL. Anosognosia in individuals with schizophrenia: toward recovery of insight. Issues Ment Health Nurs 2004;**25**:227–242.
267. Shad MU, Tamminga CA, Cullum M, Haas GL, Keshavan MS. Insight and frontal cortical function in schizophrenia: a review. Schizophr Res 2006;**86**:54–70.
268. Price DD, Barrell JJ, Rainville P. Integrating experiential-phenomenological methods and neuroscience to study neural mechanisms of pain and consciousness. Conscious Cogn 2002;**11**:593–608.
269. Tibbetts PE. The anterior cingulate cortex, akinetic mutism, and human volition. Brain Mind 2001;**2**:323–341.
270. Burns K, Bechara A. Decision making and free will: a neuroscience perspective. Behav Sci Law 2007;**25**: 263–280.
271. Gomes G. Free will, the self, and the brain. Behav Sci Law 2007;**25**:221–234.
272. Tancredi LR. The neuroscience of "free will". Behav Sci Law 2007;**25**:295–308.