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Research report

The balance of feelings: Vestibular modulation of bodily sensations

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ABSTRACT

The vestibular system processes information about head movement and orientation. No unimodal vestibular cortex has been identified in the mammalian brain. Rather, vestibular inputs are combined with many other sensory signals in the cortex. This arrangement suggests that vestibular input could influence processing in other sensory modalities. Here we show that vestibular stimulation differentially modulates two submodalities of the somatosensory system, increasing sensitivity to tactile input, and independently reducing sensitivity to nociceptive input. These modulations of touch and pain can clearly be distinguished from supramodal attentional effects of vestibular stimulation, because they are bilateral and operate in different directions. Outside the artificial conditions of laboratory stimulation, the vestibular system codes movements of the head, indicating a new relation between the body and the external world. We suggest the vestibular system participates in a form of sensory signal management, changing the balance between the various sensory systems as the relation between the body and the external environment changes. This sensory rebalancing may be a crucial element in the brain's capacity to reorient towards novel or salient features in the environment.

1. Introduction

The vestibular system remains enigmatic among the human senses. Signals from the vestibular balance organs of the inner ear make a crucial contribution to most everyday behaviours, yet produce no conscious sensations of their own (Angelaki and Cullen, 2008). Further, this evolutionary primitive system is neuroanatomically different from other sensory pathways, since its cortical projections are widely distributed in the brain and are always shared with other sensory modalities (Lopez and Blanke, 2011). Electrophysiological studies have identified multimodal neurons responding to both vestibular inputs and other sensory modalities (Guldin and Grüsser, 1998). Guldin and Grüsser (1998) identified the parieto-insular vestibular cortex (PIVC) as the core region of the vestibular cortical network. The PIVC is strongly interconnected with other cortical areas receiving vestibular and multimodal projections, such as the somatosensory cortex and the ventral intraparietal area (Guldin and Grüsser, 1998). The human homologue of the monkey PIVC has been identified in a distributed pattern of

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activations in the posterior and anterior insula, the superior temporal gyrus and the inferior parietal lobule (Angelaki and Cullen, 2008; Bense et al., 2001; Bottini et al., 1994, 1995; Fasold et al., 2002). Moreover, human neuroimaging studies have also revealed other cortical vestibular projections in the primary and secondary somatosensory cortex (Fasold et al., 2002; Bottini et al., 1994; Emri et al., 2003), primary motor cortex and premotor cortex (Bense et al., 2001; Fasold et al., 2002). Traditionally, this convergence was thought to combine vestibular information with that from other sensory modalities, to generate optimal descriptions of the animal's relation to its external environment (Bremmer et al., 2001).

Clinical evidence suggests a functional link between vestibular and somatosensory systems. In particular, left cold caloric vestibular stimulation (CVS) produces dramatic transitory perceptual changes in tactile perception. A temporary remission of tactile hemianaesthesia in right (Vallar et al., 1990, 1993) and left brain-damaged patients (Bottini et al., 2005) has been observed immediately after left cold CVS. However, such data cannot distinguish between direct vestibular effects on tactile sensation, and indirect effects based on the hypothesised shift in spatial attention towards the left side induced by left cold CVS (Vallar et al., 1990, 1993). Evidence in right brain-damaged patients also suggests abnormal vestibular control of eye movements. Thus, Doricchi et al. (2002) found reduced leftward slow-phase nystagmus and Ventre-Dominey et al. (2003) found a rightward vestibulo-ocular reflex (VOR) bias in right brain-damaged patients affected by neglect. Both these results suggest some cortical involvement in vestibular control of gaze. On this basis, one might predict that left cold CVS could facilitate right-hemisphere neural circuits for gaze control disrupted by right brain damage, rather then simply reallocating spatial attention towards the neglected left space (Doricchi et al., 2002; Ventre-Dominey et al., 2003). However, Figliozzi et al. (2005) showed that vestibular inputs could produce spatiotopic shifts of attention, even under central fixation in VOR suppression conditions. Therefore, vestibular stimulation may independently affect both oculomotor and attentional processes.

Moreover, vestibular stimulation interacts with other somatosensory submodalities. For example, a reduction of chronic pain has been recently demonstrated in patients affected by right brain damage (McGeoch et al., 2009, 2008; Ramachandran et al., 2007). At least two alternative mechanisms have been suggested to explain these effects (McGeoch et al., 2009, 2008). First, pain relief may be caused by activation of the thermosensory cortex in the dorsal posterior insula adjacent to PIVC stimulated by CVS. Alternatively, the PIVC itself may be part of the interoceptive system and have a direct role in pain control. However, a systematic investigation of the basis of this modulation has not been yet conducted.

Surprisingly, the hypothesis of a direct vestibular modulation of somatosensory perception has barely been studied functionally in the healthy brain. We previously reported that left cold CVS increased tactile sensitivity on the left (Ferrè et al., 2011), and also the right (Ferrè et al., 2011) hand. Thus, these findings suggest that the anatomical overlap between vestibular and somatosensory brain projections reported previously (Bottini et al., 1995) may produce a functional cross-modal perceptual interaction between vestibular and mechanoreceptive systems.

Here we explore whether vestibular signals also influence processing in other specific sensory submodalities in healthy participants, focussing on touch and acute pain perception. We used an established cold left CVS paradigm for vestibular stimulation. This restriction is justified by the finding that left vestibular stimulation has stronger results than right vestibular stimulation in healthy volunteers, presumably reflecting the known right-hemisphere dominance of the cortical vestibular projections (Brandt and Dieterich, 1999). Additionally, previous studies with hemianaesthesic patients indicated that cold right CVS had no effects on somatosensory detection (Vallar et al., 1993).

2. Experiment 1: Vestibular modulation of somatosensory pathways

2.1. Materials and methods

2.1.1. Participants

Eleven participants [six males, mean age ± standard deviation (SD): 24.5 ± 4.4 years] took part in the study with ethical committee approval, and on the basis of written informed consent. All participants were right-handed as assessed using the Edinburgh handedness inventory (mean index ± SD: 90 ± 18). Exclusion criteria included any history of motor, somatosensory, vestibular or auditory disorders. The experimental protocol was approved by the research ethics committee of University College London, and the study adhered to the ethical standards of the Declaration of Helsinki. Data from one subject was discarded due to an inability to obtain a stable measure of cutaneous detection threshold prior to CVS (see below).

2.1.2. Design and CVS procedure

Participants were tested in a single session. Verbal and written instructions about the task were given to participants at the beginning of the session. We tested sensitivity to touch and pain stimuli before CVS (Pre-CVS condition) and immediately after CVS (Post-CVS condition). Although CVS is mildly unpleasant, and produces a brief vertigo, no participant reported experiencing any particular discomfort and no participant withdrew from the study.

CVS elicits the movement of the endolymphatic fluid in the semicircular canal, and this leads to an afferent signal in the vestibular nerve to the vestibular nuclei. This in turn predominantly activates subcortical and cortical structures in the hemisphere contralateral to the stimulation. CVS was performed positioning the participant's head 30° backward from the horizontal plane, so as to place the lateral semicircular canal in the vertical plane (Coats and Smith, 1967), and 30° towards the right. 30 ml of cold (iced) water was slowly introduced using a syringe (Schmal et al., 2005) for 30 sec with a short piece of tubing attached and placed in the external auditory canal, close to the tympanic membrane but without touching it, allowing any additional iced water to run out (Fig. 1A). Participants were asked to close their eyes during the stimulation to reduce discomfort. After CVS, the participant's head was positioned in the upright position to check the effectiveness of the vestibular stimulation and to perform the

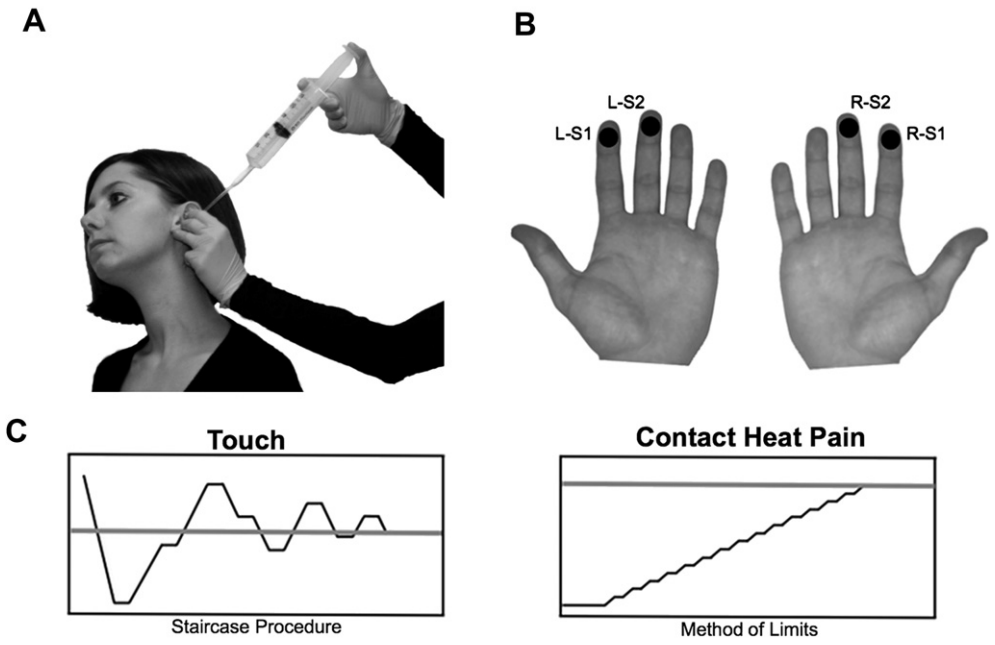

Fig. 1 – CVS, tactile and contact heat-pain thresholds.
(A) CVS required the positioning of the participant's head 30° backward from the horizontal plane to place the lateral semicircular canal in the vertical plane, and 30° towards the right to easily irrigate the outer ear, adjacent to the tymphanic membrane. (B) Sites for tactile and contact heat-pain stimulation. Tactile stimuli were delivered to the tips of the left and right index fingers (sites L-S1 and R-S1) and contact heat-pain was delivered to the tips of the left and right middle fingers (sites L-S2 and R-S2). This assignment of stimuli to fingers was reversed for half the participants. (C) To estimate tactile detection thresholds, a staircase procedure was used to estimate the lowest shock intensity at which a tactile stimulus could be reliably detected. Contact heat-pain threshold was estimated by the method of limits to find the value at which the heat generated by a thermode was first perceived as being painful.

somatosensory detection tasks. Effectiveness of the vestibular stimulation was confirmed by three established measures (Table 1). First, straight-ahead pointing showed significant leftward displacement immediately after CVS compared to before ($p < .001$). Second, electrooculogram (EOG) during eccentric fixation to the right was recorded in all experimental conditions, and the presence of oculomotor nystagmus characterized by leftward slow-phase and rightward fast-phase

Table 1 – Measures of CVS effectiveness.

	(a) Straight-ahead pointing error (cm)		(b) Mean number of fast-phase		(c) Velocity of slow-phase nystagmus (degrees/second)	
	Pre-CVS	Post-CVS	Pre-CVS	Post-CVS	Pre-CVS	Post-CVS
s1	1.8	−8.8	.800	1.200	.331	.534
s2	−3.3	−9.8	.533	.133	.434	1.109
s3	−2.6	−3.1	.467	.467	.238	.356
s4	−.2	−14.1	.400	.800	.574	.833
s5	−.4	−10.2	.333	.400	.372	.704
s6	1.8	−4.6	.067	.400	.374	.466
s7	−1.5	−5.1	.133	.933	.224	.391
s8	2.7	−7.7	.000	.467	.383	.677
s9	−.1	−4.5	.133	.667	.472	.669
s10	4.9	−.4	.067	1.000	.071	.563
s11	−1.2	−4.3	.400	.667	.696	.647
Mean	.173	−6.600	.303	.648	.379	.631
(SD)	2.429	3.901	.247	.314	.170	.213

Data from each participant in each experimental condition for (a) straight-ahead pointing. A positive value indicates a displacement to the right of the objective midline, and a negative value indicates a displacement to the left (b) number of fast-phase per second during eccentric fixation and (c) velocity of slow-phase nystagmus during an eccentric fixation. Each value is an average of five trials during 3 sec each. Mean and SD of the group are reported.

was confirmed immediately after the irrigation. Specifically, each value obtained was based on an average of five 3 sec epochs. We then measured the velocity in degrees/second from the peak of the saccade to its end and the number of microsaccades occurring in the slow-phase. We found both increased slow-phase eye velocity ($p < .001$) and increased frequency of fast-phase saccades ($p < .02$) immediately after CVS compared to before.

The time taken for irrigation, reported cessation of vertigo, pointing and oculomotor recording was up to 3 min. At this point, Post-CVS somatosensory testing was begun. Because CVS effects have limited duration, care was taken to ensure the Post-CVS condition was completed within 15 min following CVS, which corresponds to the window of maximal effect (Bottini et al., 1995; Ngo et al., 2007).

2.1.3. *Somatosensory detection tasks*

Six subjects received tactile (electrocutaneous) stimuli to the left and right index fingers, and contact heat-pain stimuli to the tips of the left and right middle fingers (see Fig. 1B). In the remaining subjects, the assignment of stimuli to fingers was reversed. Data from one participant were discarded due to an inability to measure stable cutaneous thresholds prior to CVS. Participants were blindfolded during somatosensory testing to avoid the influence of confounding visual inputs or tonic gaze deviation (Figliozzi et al., 2005).

Tactile detection and contact heat-pain thresholds were measured before (Pre-CVS condition) and immediately after CVS (Post-CVS condition), performed by irrigating the left ear with iced water. Five tactile threshold estimates, and five heat-pain threshold estimates were obtained from each hand, and the five estimates were averaged to give threshold values for touch and pain (Fig. 1B and C) in five blocks. Within each block, tactile and contact heat-pain stimuli were delivered at random to the left or right hand, and separate threshold estimates were collected for each submodality and each hand.

Electrocutaneous stimuli were delivered via 4 mm concentric electrodes (Katsarava et al., 2006), and a medically-isolated electrical stimulator (University College London Institute of Neurology, Sobell Research Department) to the tip of the finger. Pulse amplitude was held at 10 mA and pulse duration was varied to adjust the charge transferred to the skin, and thus the perceived shock intensity. To estimate tactile detection thresholds, a staircase procedure (Levitt, 1971) was used to determine the lowest shock intensity at which a tactile stimulus could be reliably detected. Pulses of increasing width were applied until participants reported a sensation. Pulse width was successively decreased and then increased again until exactly five of 10 stimuli were detected. This level was considered as a working estimate of each subject's tactile threshold.

Contact heat-pain stimuli were delivered to the tip of the index or middle finger using a 13 mm circular diameter Peltier-type thermode (NTE-2A, Physitemp Instruments Inc). Contact heat-pain threshold was estimated by the method of limits (Yarnitsky et al., 1995), a reliable procedure for measuring thermal pain perception thresholds (Heldestad et al., 2010). The probe temperature was fixed for 20 sec an initial level of 32 °C and gradually increased by 2 °C/sec. For safety, maximum temperature was limited to 50 °C. Participants pressed a foot pedal with their right foot when they first perceived the heat as being painful. Data for each threshold were recorded and analysed later. The method of limits was preferred for pain testing, rather than staircase methods, because it minimises actual pain. It is therefore better tolerated by participants, and more consistent with ethical principles. Our main aim was comparison of Pre-CVS and Post-CVS for each task. Therefore, use of different threshold estimation procedures between modalities should not affect our statistical inferences.

2.2. *Results*

Tactile threshold estimates were analysed using 2 × 2 univariate ANOVA with factors of CVS condition (Pre-CVS *vs* Post-CVS) and Side (Left hand *vs* Right hand). Tactile thresholds were significantly lower immediately after CVS than before [$F_{(1,10)} = 22.429$, $p = .001$]. Significant reductions were found for both the left hand, i.e., contralateral to the stimulated hemisphere, and for the right hand, and there was no interaction between stimulation condition and hand [$F_{(1,10)} = 2.261$, $p = .164$] (Fig. 2A). On average, vestibular stimulation reduced tactile thresholds by 25%.

In contrast, a similar univariate ANOVA applied to contact heat-pain data showed that thresholds were significantly *higher* immediately after CVS compared to before [$F_{(1,10)} = 94.581$, $p < .0001$]. Again, the effect was found for both hands, and the interaction between stimulation condition and hand was again not significant [$F_{(1,10)} = .464$, $p = .511$] (Fig. 2A). The average increase in contact heat-pain threshold was 1.96 °C.

If vestibular signals are able to modulate multiple somatosensory submodalities, then CVS-induced changes in tactile and pain thresholds should be positively correlated with each other, despite being opposite in sign. This correlation would arise because of the common vestibular input both to tactile and nociceptive areas. We therefore investigated correlations across individuals between our established measures of vestibular stimulation effectiveness and modulations of touch and pain thresholds. Specifically, we correlated the CVS-induced changes in tactile and pain thresholds with the corresponding changes in the straight-ahead pointing error, slow-phase velocity and number of fast-phase (Table 2). We found a significant association across individuals between touch and pain modulations ($r = -.631$, $p = .038$, two-tailed) (Fig. 2B). Previous results (Ferrè et al., 2011) allowed us to predict the direction of correlations between vestibular effectiveness measures and changes in touch thresholds, but not between vestibular measures and changes in pain thresholds. We found an association between number of fast-phase and modulation of touch ($r = -.549$, $p = .040$, one-tailed), and a trend towards an association between slow-phase velocity and modulation of touch ($r = .466$, $p = .074$, one-tailed), for which we had prior hypotheses (Ferrè et al., 2011). We found no associations between vestibular measures and pain modulation using two-tailed testing.

A small study such as ours has only low statistical power to detect associations, and individual correlation coefficients should be treated with caution. Therefore, to avoid both Type 1 and Type 2 errors we took an aggregation approach. Because anatomical and physiological studies show common vestibular and multisensory cortical projections, we had a strong

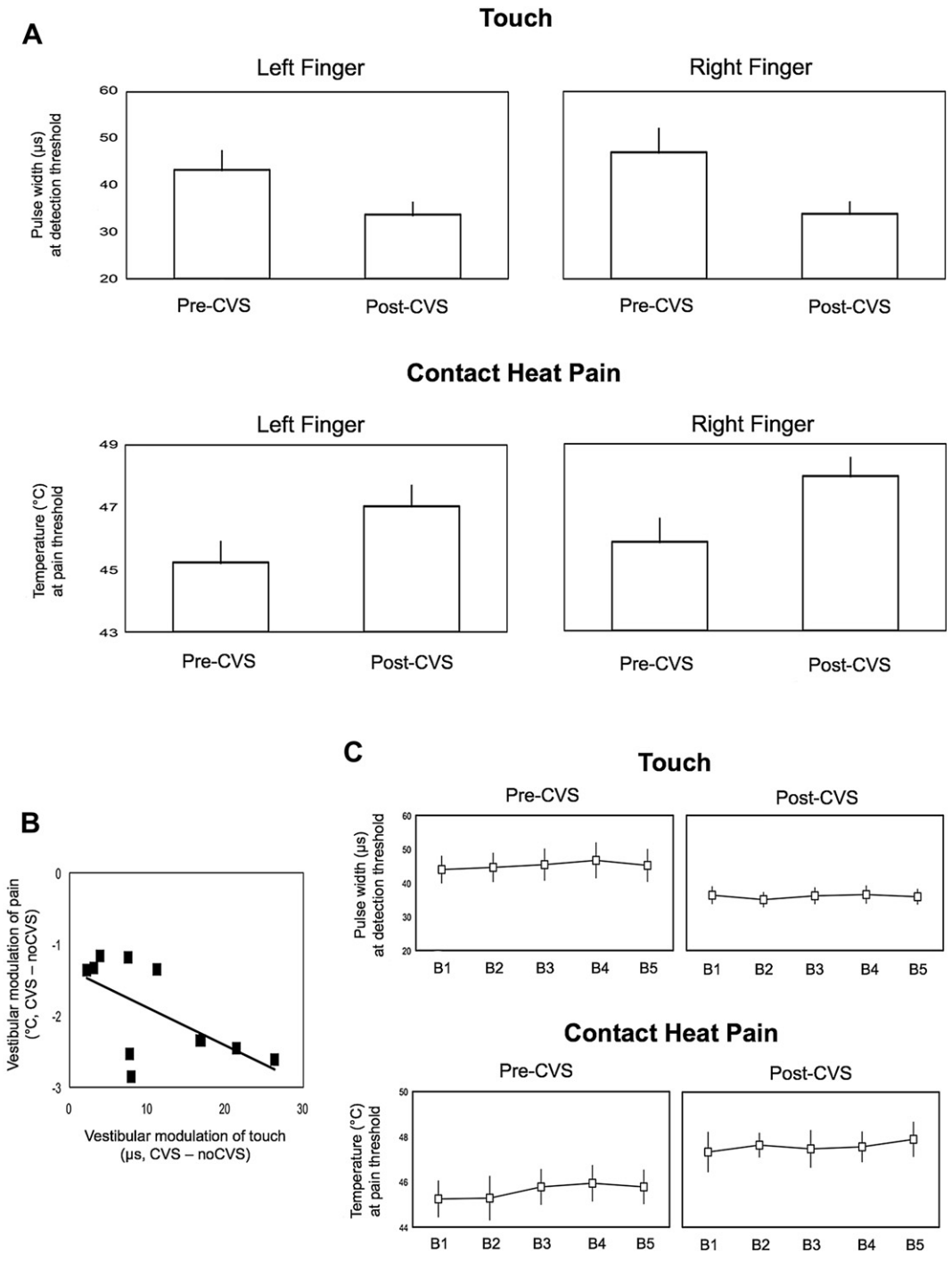

Fig. 2 – Tactile and contact heat-pain threshold results.
(A) Tactile threshold and contact heat-pain threshold values in each condition. Note reduced tactile thresholds and increased pain thresholds immediately after CVS compared to before. (B) Correlation across participants between the effects of vestibular stimulation on tactile and pain thresholds. (C) No order effects were found comparing threshold estimate blocks.

prior hypothesis of a single common source of variance affecting both vestibular and multisensory measures. We therefore used principal components analysis to summarise the variance structure underlying the correlation matrix. The first component (eigenvalue 2.33, explaining 45% of the variance) loaded somewhat homogeneously on vestibulo-ocular and somatosensory measures, but not on pointing. The second component (eigenvalue 1.19, explaining only 24%) loaded almost exclusively on the pointing measure. We interpret these components as, first, a common vestibular drive to both oculomotor and somatosensory processes, and a secondary independent effect restricted to spatial orientation.

Table 2 – Correlation matrix and principal components results.

	Touch	Pain	Straight-ahead pointing	Number of fast-phases	slow-phase velocity
Touch		−.631	.102	−.549	.466
Pain			−.162	.097	−.406
Straight-ahead pointing				−.007	−.278
Number of fast-phases					−.234
Principal components (PCs)					
PC1	.611	−.499	.013	−.400	.467
PC2	.132	−.223	.861	.005	−.435

Pearson correlations between CVS-induced changes in somatosensory and vestibular measures. Values exceeding ±.602 are significant at $p = .05$ two-tailed, and values exceeding ±.521 are significant at $p = .05$ one-tailed. Loadings from principal components analysis are also shown.

Thus, the main source of individual differences between our participants appeared to be sensitivity to CVS. This dimension had quite general effects on both oculomotor and somatosensory measures together.

The number of participants in our study is too small to *explore* the factors underlying these correlations, though it does allow us to test specific models of vestibular-somatosensory interaction suggested by the aggregation approach, using *confirmatory*, as opposed to *exploratory* analyses. To test alternative models of this interaction, we next created structural equation models of specific patterns of vestibular-somatosensory interaction using SAS PROC CALIS. In such modelling, better-fitting models have higher probability values associated with chi-squared statistics (inability to show difference of data from model predictions). They also have lower values of Akaike's Information Criterion (AIC), which is adjusted for parsimony. A first model with a single latent factor influencing all somatosensory and all vestibular measures provided the best fit [$\chi^2_{(5)}$=3.32, $p = .67$, AIC = −6.77]. Interestingly, this latent factor had much lower loading for pointing (standardised weight .11) than for either oculomotor (slow-phase .33, fast-phase −.48) or somatosensory measures (touch 1.22, pain −.43). Goodness of fit was reduced for a two factor model in which touch and pain measures were linked to one latent factor and the three vestibular measures to another [$\chi^2_{(4)} = 3.22$, $p = .52$, AIC = −4.78]. Finally, a model in which touch, pain and vestibular measures reflected three separate factors failed to converge. Thus, these methods confirmed a direct link between vestibular system activation and somatosensory perception.

Since the CVS procedure itself could induce changes in general arousal levels, which might in turn influence perception, we performed an additional time-course analyses, considering the interval between irrigation and touch or pain threshold measures. We reasoned that these arousal effects would most probably be linked to the unusual sensations of irrigation itself, and any brief subsequent experience of vertigo, and would therefore be short-lived. Any arousal effects would decrease over the five successive blocks of touch or pain threshold estimation. A linear trend analysis showed no time-related changes across the five blocks of the Post-CVS condition in any of the dependent variables (touch left hand: $p = .991$; touch right hand: $p = .900$; pain left hand: $p = .804$ and pain right hand: $p = .699$) (Fig. 2C). Moreover, a further ANOVA using block number as an additional factor showed no significant differences between any of the five blocks after Bonferroni correction for multiple comparisons (all $p > .05$ corrected).

2.3. Discussion

Vestibular input reduces the detection threshold of faint tactile stimuli delivered to either hand. Intriguingly, CVS also dramatically increases the threshold for detecting pain. Again, the modulation affects both the ipsilateral and contralateral hand. The bilateral modulations, and opposite effects on touch and pain perception contrast with explanations based on changes in arousal or in spatial attention (Vallar et al., 1990, 1993; Bisiach et al., 1991). Arousal effects due to the subjective feelings induced by vestibular stimulation, such as vertigo and dizziness, would be expected to be short-lived, and to generalise across modalities, while spatial effects would be expected to predominantly influence processing of stimuli to the left hand. Our results instead suggest that the vestibular system directly, and differentially modulates the activity in individual sensory submodality pathways for a period of at least several minutes.

Variability in CVS effects across individuals probably reflects differences in effectiveness of irrigation. Our correlation results are consistent with the view that vestibular stimulation, though more successful in some participants than in others, had linked effects on both touch and pain. Inference from these correlations should be cautious, given the small size of our sample, hence low statistical power. However, the pattern of correlations suggested a single underlying factor loading both on standard oculomotor measures of vestibular stimulation, and on both touch and pain measures. Future research with larger samples might usefully investigate whether vestibular inputs have dissociable effects on spatial representation and on somatic sensation.

However, these results are consistent with either of two possible *neural* models of vestibular-somatosensory interaction (Fig. 3A). In the first model, a common vestibular input has effects on *independent* systems coding for touch and pain. Crucially, on this model there is no direct interaction between touch and pain: they are simply driven by a single input. In a second model, vestibular input has a direct effect on touch,

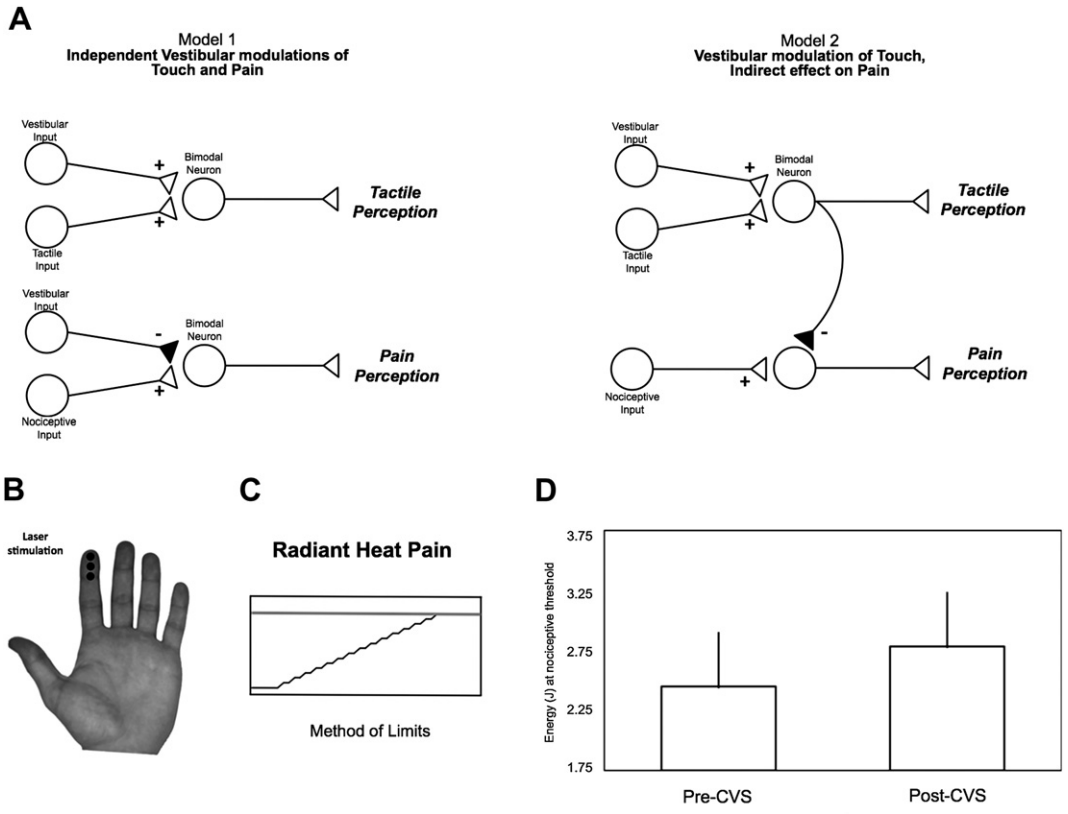

Fig. 3 – Two alternative models of vestibular effects on touch and pain.
(A) In Model 1, a common vestibular input independently influences touch and pain perception through distinct cortical projections. In Model 2, vestibular input has a primary and direct effect on touch, but only an indirect effect on pain due to the interdependence of touch and pain systems. (B) Skin sites where laser stimuli were delivered, on the left index finger. (C) Radiant heat-pain threshold was estimated by the method of limits. (D) Nociceptive-specific, radiant pain threshold values in each condition. Note the increased pain threshold immediately after CVS.

but only an indirect effect on pain. The indirect effect could be due to inhibitory links between cortical areas coding for touch and pain. In particular, increased activation of somatosensory areas due to vestibular input could, in turn, cause decreased afferent transmission in pain pathways, because of the known tactile 'gating' of pain (Melzack and Wall, 1965). We also considered a third model with reverse causality, in which vestibular inputs would directly influence pain, with only indirect effects on touch through a pain–touch link. However, we have found little evidence in the literature for such pain–touch interactions (Ploner et al., 2004). Moreover, our results demonstrated a CVS-induced inhibition of pain. Inhibition of pain would predict reduced influence of a pain–touch link after CVS, implying reduced facilitation of tactile perception. In fact, vestibular enhancement of touch was found, ruling out this third model.

To compare the first and second models, we performed a further experiment to measure CVS effects on thresholds for detecting radiant heat-pain, evoked by laser stimulation of Aδ afferents, without touching the skin. The first model predicts that vestibular stimulation should increase radiant pain thresholds, while the second model predicts no increase in pain threshold, because of the absence of tactile input.

3. Experiment 2: Vestibular modulation of nociception

3.1. Materials and methods

3.1.1. Participants

Three right-handed participants (one male, mean age ± SD: 26.7 ± 6.4 years) who took part in the previous experimental session volunteered for this second experiment. Procedures were approved by the University College London ethics committee.

3.1.2. Design and CVS procedure

At the beginning of the testing session verbal and written instructions were given to participants. Testing was performed Pre-CVS and Post-CVS, as in Experiment 1. The same CVS procedure adopted in the Experiment 1 was used, irrigating the left auditory canal for 30 sec with cold iced water. The participant's head was positioned 30° backward from the horizontal plane and 30° towards the right. The somatosensory task started only when participant had reported that vertigo had ceased.

3.1.3. *Nociceptive-specific laser stimulation*

Thresholds for the painful pinprick sensation elicited by selective activation of the nociceptive Aδ pathway were measured using Nd:YAP laser stimulation (Iannetti et al., 2006). Laser stimuli were delivered in blindfolded participants without any tactile contact immediately before (Pre-CVS condition) and after CVS (Post-CVS condition) (Fig. 3B and C).

Each trial consists of a method of limits search to identify the threshold for the painful pinprick sensation characteristic of Aδ firing. The general procedure was as for the first experiment. A laser pulse of 4 msec of duration was directed to the index fingertip of the left hand. It was transmitted via an optic fibre and delivered with a spot diameter of 8 mm (50 mm^2) at the target site. After each stimulus, to avoid nociceptor fatigue and sensitization, the spot location was shifted to another site of stimulation (Fig. 2B), in randomized order. Laser intensity was initially set at 1.75 J, and increased in steps of .25 J until the subject first felt the 'pinprick' sensation related to the activation of Aδ nociceptors (Bromm and Treede, 1984). Data from five different thresholding runs were collected and then averaged. Because variations in baseline skin temperature could influence the temperature achieved by laser stimulation (Baumgartner et al., 2005), an infrared thermometer was used to monitor whether baseline skin temperatures were affected by CVS stimulation. Skin temperature was measured before each trial.

3.2. *Results*

CVS significantly increased nociceptive thresholds on average by .33 J [$F_{(1,2)} = 30.769$, $p = .031$], even in the absence of touch (Fig. 3D). Including baseline skin temperature as a covariate showed that CVS effect remained significant, and the estimated pain threshold increase remained unchanged at .33 J, even after correction for baseline skin temperature [$F_{(1,2)} = 4.332$, $p = .047$]. Further, baseline temperature itself was not significantly related to nociception ($p > .05$).

3.3. *Discussion*

Vestibular input increased the detection threshold of pure nociceptive thermal stimuli, without any tactile component. Thus, this additional experiment rules out explanations of vestibular-induced analgesia based on tactile gating of pain (Model 2), and confirms Model 1 (see Fig. 3A). This experiment further suggests that a common vestibular signal has projections to multiple independent somatic sensory systems, enhancing tactile perception and directly reducing acute pain perception.

4. General discussion

Although vestibular inputs produce no overt, recognizable conscious sensations, the vestibular system provides continuous information to the brain to maintain orientation in space (Angelaki and Cullen, 2008). A common vestibular input projects to multiple independent somatic sensory systems, directly increasing tactile perceptual processing, and directly decreasing perceptual processing of nociceptive stimuli. This finding provides new insights into the role of the vestibular system in multisensory interactions, and in bodily awareness.

Several multimodal sensory areas are known to receive both vestibular information and information from other modalities, notably vision and somatosensation (Faugier-Grimaud and Ventre, 1989). For example, functional imaging studies highlighted an anatomical overlap of vestibular and somatosensory projections in primary and secondary somatosensory cortices bilaterally (Bottini et al., 1994; Fasold et al., 2002; Emri et al., 2003). The bilateral modulations of touch and pain that we observed are consistent with this neuroimaging evidence. Our bilateral effects further suggest that the vestibular modulation of somatosensation may particularly involve cortical areas whose neurons have bilateral somatosensory receptive fields, or strong transcallosal connections. The secondary somatosensory cortex is one such area (Iwamura et al., 1994). Interestingly, this area plays a major role in both touch and pain perception (Ploner et al., 1999).

A striking feature of vestibular multisensory interactions, therefore, is the specific independent modulation of distinct somatosensory submodalities. Decreases in tactile threshold demonstrate an up-regulation of tactile processing, while increases in pain threshold demonstrate a down-regulation of nociceptive processing. The pattern of correlation across participants between touch and pain effects suggests that both these modulations result from a common vestibular drive. Oculomotor and somatosensory effects of vestibular stimulation appeared to reflect a single latent factor. This view is also supported by a control experiment with nociceptive-specific laser stimulation. The vestibular system thus modulates connections with different somatosensory submodalities, regulating the activity in multiple sensory systems independently. Interestingly, human neuroimaging studies support this model, showing that vestibular stimulation both increases somatosensory cortex activations (Bottini et al., 1994, 1995; Bense et al., 2001; Fasold et al., 2002; Emri et al., 2003), but deactivates visual cortex (Bense et al., 2001). However, this is the first demonstration, to our knowledge, of how the vestibular system affects perceptual thresholds in various somatosensory submodalities, and also the first demonstration of vestibular modulation of experimental pain.

Clinical reports have shown a range of effects of vestibular stimulation on somatic sensory systems. Recently, it has been demonstrated that left cold CVS interacts not only with tactile perception (Vallar et al., 1990, 1993) but also with chronic pain in brain-damaged patients (Ramachandran et al., 2007; McGeoch et al., 2008), and with higher-order body representation (Bisiach et al., 1991). However, to our knowledge, no clinical study has studied effects of vestibular stimulation on diverse aspects of somatic processing in the same individuals. Here we extend previous clinical findings to healthy volunteers, and show that vestibular inputs have widespread functional effects on different somatosensory submodalities.

Because CVS has strong effects on spatial attention, particularly in right brain-damaged patients (Rubens, 1985), many previous clinical studies interpreted effects of CVS on tactile perception in terms of general arousal or shifts of supramodal attention towards the side of the space contralateral to the vestibular organs stimulated (Vallar et al., 1990, 1993). However, several lines of evidence suggest that our data

may reflect a direct vestibular-somatosensory interaction, and not just indirect effects mediated by attention. First, some clinical reports demonstrated an impairment of the VOR with reduced leftward slow-phase and rightward fast-phase in neglect patients (Doricchi et al., 2002; Ventre-Dominey et al., 2003). These results highlight the inter-relation between eye movements, attention, and the vestibular system. Oculomotor effects of vestibular stimulation suggest a direct influence of vestibular signals in the neural activity of brain-damaged areas in the right hemisphere (Ventre-Dominey et al., 2003). Moreover, evidence from healthy volunteers found no modulation of covert visuo-spatial attention following vestibular stimulation (Rorden et al., 2001). Additionally, CVS selectively affected somatosensory detection but not visual detection in a previous study (Ferrè et al., 2011). Finally, neuroanatomical overlap between vestibular and somatosensory cortical projections is widespread, and not confined to 'attentional' brain areas. The present results provide further evidence for a direct vestibular-somatosensory interaction, in addition to any attentional aspect. Our results cannot easily be reconciled with the attentional interpretation of CVS derived from patient studies. First we found that vestibular modulation of both touch and pain was bilateral, and not unilateral as a spatial attentional account would predict. Second, accounts based either on spatial attention, or on the general arousing effect of vestibular stimulation, predict facilitatory effects of vestibular stimulation on other modalities (Vallar et al., 1990). In particular, an attentional account predicts the reallocation of attentional resources to the side of space and body ipsilateral to the stimulated peripheral vestibular organs (Vallar et al., 1990, 1993). Moreover, recent studies in healthy participants showed vestibular activation induced by whole body rotatory accelerations produces spatiotopic shifts of attention in the direction of rotation (Figliozzi et al., 2005), even when VOR is suppressed by central fixation. These results suggested that the vestibular modulation of tactile attention was not merely mediated by vestibular effects on gaze direction. Since vestibular cortical activations induced by whole head-body rotatory accelerations and CVS are quite distinct (i.e., bilateral, and dynamic for rotations, unilateral and low-frequency for CVS), it is difficult to compare Figliozzi et al's (2005) results directly with ours. The effects induced by our CVS were found in a low-level perceptual task, suggesting that vestibular-induced modulation affected early perceptual mechanisms, and not just response biases (Figliozzi et al., 2005). However, further studies are needed to clarify the role of attentional effects occurring at later stages of somatosensory processing, such as tactile extinction or interhemispheric competition.

Attention can certainly modulate pain. For example, attention produces hyperalgesia for acute pain, while distraction is mildly analgesic (Scharein and Bromm, 1998; Liu et al., 2011). Our analgesic effects of CVS are clearly in contrast with such attentional interpretations. Additionally, since thresholds were modulated in opposite directions for touch and pain, and remained stable throughout the period of testing after CVS, our results cannot simply reflect CVS-induced response bias, or non-specific effects such as arousal, habituation, or perceptual learning. Thus, we conclude that vestibular-somatosensory links are not merely the result of a vestibular driving of a supramodal attentional system (Macaluso and Driver, 2005).

Could gaze deviation and eye movements induced by CVS influence our effects? We consider this unlikely. First, somatosensory detection was administered not during CVS itself, but approximately 3 min after irrigation when nystagmus fast components and vertigo have typically reduced or disappeared (Miller et al., 2000; Ngo et al., 2007, 2008). Secondly, we obtained somatosensory threshold estimates in blindfolded participants to avoid any confounding influence of visual signals. Finally, effects induced merely by ocular movements cannot simply explain the opposite modulation found in touch and pain.

In principle, our results could be subject to order effects. CVS and order were confounded, because our Post-CVS condition always followed the Pre-CVS condition. However, we think it unlikely that order effects play a major part in our results for several reasons. First, order effect is a general concept, which may include perceptual learning, sensitisation, habituation, fatigue and other factors. Any explanation of our results based on order effects, rather than direct vestibular-somatosensory interactions, would need to explain why tactile perception improved, while pain perception diminished. It is hard to explain why different submodalities would show different order effects, without ad hoc assumptions. Second, a previous study (Ferrè et al., 2011) included a follow-up condition after effects of CVS had worn off. In those data, tactile perception was enhanced immediately after CVS but returned to baseline levels in the follow-up condition, ruling out simple order effects. Third, our results showed no statistical evidence for any order effects across the five blocks of our Post-CVS conditions.

Recent computational theories of multisensory perception emphasise feed-forward optimal integration of different sources of sensory information, by weighting each source according to reliability (Fetsch et al., 2010). Feed-forward integration aims at combining information about a single spatiotemporal object (Helbig and Ernst, 2007). However, the vestibular system does not describe an external perceptual object in the same way that visual or haptic exteroception do. Further, our vestibular stimulation was spatially and temporally distinct from our somatosensory stimuli. Therefore, vestibular influences on somatosensation do not seem to act as an additional informative input contributing to multisensory integration (Fetsch et al., 2010). We suggest, instead, that vestibular input may serve as additional modulating inputs to multiple sensory systems.

Interestingly, no primary vestibular cortex has been identified in the primate brain (Lopez and Blanke, 2011). Rather, vestibular inputs share the cortical projections of other somatosensory pathways (Odkvist et al., 1974; Grüsser et al., 1990; Guldin et al., 1992), making it unsurprising that these systems interact. However, the mechanism of interaction remains unclear. Bimodal neurons that respond to both vestibular input and other modalities have been reported in different parietal areas (Odkvist et al., 1974; Grüsser et al., 1990; Guldin et al., 1992; Guldin and Grüsser, 1998). We speculate that vestibular modulation of somatosensation may occur because the vestibular input to such neurons modulates their sensitivity to somatic input. In principle, the strong vestibular

input generated by CVS may produce slow post-synaptic potentials (PSPs) in bimodal neurons, thus modulating their sensitivity to somatosensory inputs. Recent recordings in area ventral intraparietal area (VIP) show that bimodal neurons exhibit both mutually facilitatory and mutually inhibitory interactions between modalities, in similar proportions (Avillac et al., 2007). Thus, CVS-induced excitatory post-synaptic potentials (EPSPs) in bimodal neurons also coding for touch, and CVS-induced inhibitory post-synaptic potentials (IPSPs) in bimodal neurons also coding for pain could explain the observed decreases in tactile thresholds and increases in pain thresholds respectively. However, such post-synaptic effects are short-lived, so this explanation would require that CVS produces prolonged firing in vestibular afferents, and thus prolonged excitatory or inhibitory influence on bimodal neurons, throughout the time course of our experiment.

An alternative explanation would involve a longer-lasting effect of the transient stimulation of vestibular peripheral organs on the cortical targets of somatosensory pathways. Such enduring interactions are suggested by the lack of reduction of the modulatory effect observed across our five blocks of testing. CVS might perhaps produce long-lasting modulation of somatosensory synaptic strength by long term potentiation (LTP) of tactile pathways, and long term depression (LTD) of pain pathways. Further research is necessary to investigate these possible mechanisms of vestibular-somatosensory interaction.

What could be the adaptive function of these vestibular modulations of touch and pain? CVS is a very unnatural stimulus, so we can only speculate on this point. Outside the laboratory, vestibular canal input normally occurs during head rotation, as when an animal re-orients towards a new part of the external environment (Klam and Graf, 2006). We suggest that such reorienting may involve a rebalancing of sensory processing to provide an appropriate new balance of inputs. For example, pickup of information from novel environments may become urgently important following reorienting (Fecteau et al., 2004). Thus, vestibular signalling of head rotation during orienting movements could trigger increased sensitivity to tactile stimuli. Interestingly, our data suggest that vestibular input causes a complementary tweaking of the sensitivity of the two main submodalities of somatosensation, rather than a general reduction or increase in sensitivity of them. Interestingly, the observation that vestibular input has an analgesic effect is reminiscent of the notion that novel environments are themselves mildly analgesic (Siegfried et al., 1987). The observed tweaking of the sensitivity of the two somatosensory submodalities may reflect a multisensory mechanism for adjusting sensory processing following reorientation to novel environments, thus ensuring efficient perception and motivating exploratory behaviour (Cohen et al., 2007).

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