

Galvanic vestibular stimulation influences randomness of number generation

Elisa Raffaella Ferrè · Eleonora Vagnoni · Patrick Haggard

Received: 26 June 2012 / Accepted: 5 October 2012 / Published online: 31 October 2012
© Springer-Verlag Berlin Heidelberg 2012

Abstract Successful interaction with the external environment requires a balance between novel or exploratory and routine or exploitative behaviours. This distinction is often expressed in terms of location or orientation of the body relative to surrounding space: functions in which the vestibular system plays an important role. However, the distinction can also be applied to novel versus repetitive production of any behaviour or symbol. Here, we investigated whether vestibular inputs contribute to the balance between novel and routine behaviours, independently of their effects on spatial orienting, by assessing effects of galvanic vestibular stimulation (GVS) on a random number generation task. Right-anodal/left-cathodal GVS, which preferentially activates the left cerebral hemisphere decreased the randomness of the sequence, while left-anodal/right-cathodal GVS, which preferentially activates the right hemisphere increased it. GVS did not induce any spatial biases in locations chosen from the number line. Our results suggest that vestibular stimulation of each hemisphere has a specific effect on the balance between novel and routine actions. We found no evidence for effects of non-specific arousal due to GVS on random number generation, and no evidence for effects on number

generation consistent with modulation of spatial attention due to GVS.

Keywords Galvanic vestibular stimulation · Randomness · Exploration and exploitation · Neglect

Abbreviations

GVS Galvanic vestibular stimulation
R score Redundancy score
RNG-I Random number generation index
FODs First-order differences

Introduction

Adaptive behaviours in a changing world require the ability to balance exploration and exploitation (Cohen et al. 2007). Exploration involves discovering new possibilities and varying choices, while exploitation involves perseveration and stereotyped behaviour. Thus, every behaviour is based on a decision whether to exploit familiar but possibly sub-optimal alternatives or to explore potentially more profitable ones (Sugrue et al. 2004; Daw et al. 2006). Often, both exploration and exploitation are couched in terms of spatial location and orientation with respect to the external environment. From an evolutionary perspective, searching novel stimuli is a fundamental process motivating organisms to explore new environments. For example, balancing exploration and exploitation is essential to all foraging species: animals either explore the environment for new food sources or exploit sources in the current location.

The vestibular system responds to linear and angular acceleration providing continuous information to the brain to update body position and to maintain orientation in the

Electronic supplementary material The online version of this article (doi:10.1007/s00221-012-3302-6) contains supplementary material, which is available to authorized users.

E. R. Ferrè (✉) · P. Haggard
Institute of Cognitive Neuroscience (ICN),
University College London, Alexandra House,
17 Queen Square, London WC1N 3AR, UK
e-mail: e.ferre@ucl.ac.uk

E. Vagnoni
Department of Psychological Sciences, Birkbeck,
University of London, Malet Street, London WC1E 7HX, UK

surrounding space (Berthoz 1996). Hence, it is essential for all the interactions between the organism and the external environment. Therefore, one might expect vestibular inputs contribute to the balance between exploratory and exploitative orienting behaviours. However, a very general distinction, rather similar to the explore/exploit distinction in spatial foraging, can also be identified in strategic control of almost any behaviour. Almost any behaviour or choice can be changed in a novel way (akin to exploration) or repeated in a routine, perseverative or stereotyped way (akin to exploitation). The balance between innovation and perseveration is generally considered a feature of executive control by the frontal lobes (Norman and Shallice 1986). Perhaps surprisingly, it has rarely been linked with the explore/exploit distinction in foraging and reinforcement learning. It remains unclear whether the vestibular system could contribute to the balance of behaviour control in such non-spatial, non-navigational contexts. Here, we used galvanic vestibular stimulation (GVS) to investigate whether vestibular inputs to each hemisphere contribute to the balancing between novel and stereotyped responses in generating behaviour.

GVS is a non-invasive tool that directly stimulates the vestibular receptors (Fitzpatrick and Day 2004), producing complex oculomotor, perceptual and postural responses. It is thought to stimulate the entire vestibular nerve, including both otolith and semicircular canal afferents (Stephan et al. 2005). In the traditional bilateral bipolar GVS configuration, an anode and cathode are placed on the left and right mastoid or vice versa. Perilymphatic cathodal currents are thought to depolarize the trigger site and lead to excitation, whereas anodal currents hyperpolarize it resulting in inhibition (Goldberg et al. 1984). Neuroimaging studies using GVS have revealed widespread vestibular projections reaching many areas of the cerebral cortex. Interestingly, these areas are largely multisensory, such as the retroinsular cortex, the superior temporal gyrus, the temporo-parietal cortex, the basal ganglia and the anterior cingulate (Bense et al. 2001; Bucher et al. 1998). Further, left-anodal and right-cathodal GVS induced unilateral activation of the right-hemispheric vestibular system, while the opposite polarity, that is, left-cathodal and right-anodal GVS, led to a bilateral activation of both vestibular cortices (Fink et al. 2003). This may reflect right-hemisphere dominance for vestibular processing in humans (Dieterich et al. 2003). A recent review of lateralised effects of GVS on a battery of cognitive tasks showed several hemisphere-specific effects. Indeed, GVS was considered an important method for inducing hemisphere-specific activations, and thus for studying cerebral lateralisation (Utz et al. 2010a, b).

To investigate whether vestibular input could influence the balance between novel and routine behaviour, we used a standard random number generation paradigm in which

participants were asked to generate sequences of numbers as randomly as possible (Loetscher and Brugger 2007). The ability to generate random numbers has been defined as a *basic* cognitive function. Some authors suggested that the generation of random digits is characterized by a '*creativity mechanism, while not truly random, [that] provides novelty*' (Bains 2008). Therefore, the link between novelty and randomness may be unsurprising since randomness can be considered as a source of novelty, in contrast to the recurrent generation of '*obvious*' choices (Bains, 2008). Further, random number generation has been extensively used in neuropsychological and cognitive testing as a measure of executive function, and quantitative measures of the various aspects of executive function have been developed (Peters et al. 2007). Neuroimaging studies revealed that random number generation activates a distributed cortical network including the dorsolateral prefrontal cortex, the lateral premotor cortex, anterior cingulate and inferior and superior parietal cortex (Jahan-shahi et al. 1998, 2000). Many strategies might be used during the generation of random sequences (Strengge and Rogge 2010), but the inhibition of prepotent counting behaviour is recognized as particularly important (Spatt and Goldenberg 1993). Thus, random number generation requires efficient and flexible cognition, since it involves both suppressing stereotyped responses and generating non-stereotyped responses (Daniels et al. 2003).

Several studies have demonstrated that numerical representations are spatially coded into a non-verbal mental number line (Dehaene 1992; de Hevia et al. 2008). Spatial-numerical interactions in random number generation (Loetscher and Brugger 2007) revealed that small numbers are implicitly associated with the left side of the space, and larger numbers with the right side of the space, according to the mental number line concept (Dehaene 1992; Galfano et al. 2006). Results from random number generation tasks also suggested that numbers were spontaneously remapped to spatial locations along a number line (Strengge and Bohm 2004). In particular, participants may mentally visualize the order of digits to facilitate the process of generation (Towse 1998). Studies with right brain-damaged patients (Rubens 1985) have demonstrated a strong effect of vestibular stimulation on spatial attention (Rubens 1985; Utz et al. 2011). Recently, a contribution of vestibular information to allocation of attention has also been suggested in healthy volunteers. Passive whole-body rotation was found to influence the allocation of spatial attention toward the side of rotation (Figliozzi et al. 2005). Further, active head turning directed spatial attention to the corresponding side in mental number space (Loetscher et al. 2008). This study found that small numbers (i.e. located in the left side of the mental number space) were generated more often during leftward head turns as compared with

rightward head turns. Similar results have been observed using passive whole-body motion (Hartmann et al. 2011). In contrast, Rorden et al. (2001) did not find shifts of attention following caloric stimulation of the vestibular system. However, differences between the types of vestibular stimulation used (see Lopez et al. 2012), and therefore in the distribution of vestibular afferents stimulated, might explain the contrasting findings.

Based on the previous literature, we therefore had a strong hypothesis that GVS could have spatial-type effects in random number generation, and that these effects might also be specific to the hemisphere stimulated. In particular, vestibular stimulations that activated the right hemisphere are known to enhance orienting to the left side of space (Vallar et al. 1990). This stimulation might produce a bias towards generating small numbers in random number generation.

Materials and methods

Participants

Twenty-four naïve right-handed paid participants volunteered in the study (14 male, ages mean \pm SD: 24.7 \pm 4.91 years). Subjects with a history of vestibular or auditory disorders were excluded. Informed consent was obtained prior to participation in the experiment. The experimental protocol was approved by University College London research ethics committee. The study was designed according to ethical standards of the Declaration of Helsinki. Data from one participant were discarded due to an inability to correctly follow the instructions (see below).

Galvanic vestibular stimulation procedure

To reduce the postural consequences of vestibular input, the experiment was conducted in a comfortable sitting position. This also reduced the tendency to tilt towards the anodal side during GVS (Day et al. 1997). Bipolar GVS was used to deliver a boxcar pulse of 1 mA with 11 s of duration, via a commercial stimulator (Good Vibrations Engineering Ltd., Nobleton, Ontario, Canada). Carbon rubber electrodes (area 10 cm²) were placed binaurally over the mastoid processes and fixed in place with adhesive tape. The areas of application were first cleaned with surgical spirit-soaked cotton wool and electrode gel was applied to reduce the impedance. According to our convention, left-anodal and right-cathodal configuration is named ‘L-GVS’, and predominantly stimulates the right hemisphere. The inverse polarity, namely left-cathodal and right-anodal configuration is named ‘R-GVS’, and predominantly stimulates the left hemisphere. A ‘PSEUDO-

GVS’ stimulation, based on that used by Lopez et al. (2010), was applied using electrodes on the left and right side of the neck (about 5 cm below the GVS electrodes), with a left-anodal and right-cathodal configuration. This causes a similar tingling skin sensation to real GVS, and it functions as a control for non-specific alerting effects, and for the knowledge that an unusual stimulation is occurring. Other forms of sham GVS have also been proposed. These include onset-only sham stimulation (Utz et al. 2010a, b), in which all trials begin with GVS, but the stimulating current is then gradually reduced to zero in the sham condition. However, the advantages of this approach become less compelling when the stimulation period is relatively short, as in our study. We therefore preferred a sham stimulation that produces similar cutaneous effects to GVS, but does not affect the vestibular organ or afferents.

Random number generation task

Data from each participant were gathered in a single session. At the beginning of the session, participants received verbal and written instructions about the task. Participants were comfortably seated with a neutral head posture, that is, neither tilted nor flexed. Participants were asked to keep the eye opened during the task and direct the gaze to a fixation point, thus avoiding strong illusory motion perception induced by vestibular stimulation. Participants performed a random number generation task during L-GVS, R-GVS or PSEUDO-GVS. The random number generation task and analyses were based on standard methods (Loetscher and Brugger 2007; Towse and Neil 1998). This task requires participants to generate a sequence of 20 consecutive digits. In particular, participants were instructed to name the digits from 1 to 9 as random as possible. The generation was paced by a series of tones, at 2 Hz, lasting approximately 10 s. The beginning of each trial (i.e. each sequence) was signalled by a different sound. Here, participants were instructed to consider three different tones as a ‘ready-steady-go’ signal and to start the generation of digits after the last tone, that is, ‘go’ tone, but in concomitance to the first beat. Five hundred milliseconds after the ‘go’ tone, L-GVS, R-GVS or PSEUDO-GVS was administered for 500 ms and then the first beat was played. We considered the first 500 ms of GVS or PSEUDO-GVS as the onset phase of the stimulation: during this phase, participants could potentially feel a transient paraesthesia under the electrodes in all conditions, which could distract them from the RNG task. Therefore, the beats for pacing the RNG task began only after the sensations of GVS were stabilized. Accordingly, the generation of random digits started after this phase of stimulation accommodation. L-GVS, R-GVS or PSEUDO-GVS was delivered for 11 s. Three sequences lasting

approximately 14 s for each type of stimulation were repeated in a pseudo-randomized order. The order was different in each participant. A rest period of few minutes between different sequences was given to the participants to avoid any discomfort induced by the stimulation.

Data analysis

The data were analysed by using dependent variables previously established in the random number generation literature, and linked with specific hypothetical cognitive components of random number generation. Analysis of the spatial component in the random number generation task was assessed by calculating the percentage of large digits ('6', '7', '8' and '9') indicating preference for numbers at the right side of the mental number line (Loetscher and Brugger 2007). We also estimated the distribution of first-order differences (FODs) (Towse and Neil 1998; Loetscher and Brugger 2007), between successive numbers. FODs varied between -8 , that is, response '9' followed by response '1' and $+8$, that is, response '1' followed by response '9'. Positive values indicate ascending series, or following a mental number line rightwards, whereas negative values indicate descending series, or following a number line leftwards. Further, over-representation of $+1/-1$ responses indicates that participants tend to adopt a counting strategy during the generation of digits. Similarly, increased 0 responses reflect the tendency to repeat a number.

To calculate the quality of the randomness produced in the random number generation task, we calculated the redundancy score (*R* score) for each sequence. This reflects sampling bias, by calculating deviations from the equiprobability of response alternatives. *R* score ranges from 0 (all alternatives generated equally frequently) to 100 (one single alternative provided on all trials) (Towse and Neil 1998). We reasoned that low *R* score values would correspond to exploration or novel behaviour, and high values to exploitation or routine behaviour. Finally, the random number generation index (RNG-I) was applied to assess the degree of equiprobability of pairs of consecutive responses. RNG-I ranges from 0 (all sequential pairs equally frequent) to 1 (perfect predictability of a digit from the preceding digit) (Towse and Neil 1998). Both repetition and counting, for example, would produce high values of RNG-I. An open-source program was used to calculate *R* score and RNG-I (<http://www.lancs.ac.uk/staff/towse/rngpage.html>).

Percentages of large digits, FODs, *R* scores and RNG-I indexes were estimated for each sequence and averaged within each experimental condition, that is, L-GVS, R-GVS and PSEUDO-GVS. We hypothesized that vestibular stimulation might influence random number generation in either of two distinct ways, and we accordingly

expressed these hypotheses as planned contrasts. First, any activation of the vestibular system might have a general effect on cognitive processes underlying random number generation, independent of the polarity of the stimulation, and of any specific hemispheric effects. To test this *generic* hypothesis, we compared the average of the L-GVS and R-GVS conditions with the PSEUDO-GVS condition, for each dependent variable. Second, we also tested the hypothesis, according to which the effects of vestibular stimulation on random number generation might be specific to the hemisphere primarily activated by the vestibular stimulation. This *specific* hypothesis was tested by comparing L-GVS and R-GVS directly, for each dependent variable. Hemisphere-specific effects might arise because of potential hemispheric lateralization of specific cognitive processes underlying random number generation, or because one polarity of GVS might be stronger than the other, or because of a combination of these factors (Table 1).

Results

The mean data in each condition are shown in Table 2.

Generic vestibular effects on random number generation

To directly investigate whether vestibular stimulation influences random number generation, we computed a *generic* vestibular effect, defined as $(L-GVS + R-GVS)/2$, and compared this with the PSEUDO-GVS condition, for each dependent variable. Investigation of spatial effects in random number generation did not reveal any differences between vestibular stimulation and pseudo-stimulation. The percentage of 'large' digits generated did not differ

Table 1 Hypotheses for the effects of vestibular stimulation on random number generation and their corresponding contrast coefficients

	Stimulation condition		
	L-GVS	R-GVS	PSEUDO-GVS
<i>Generic hypothesis</i> (Vestibular system activation influences random number generation)	1	1	-2
<i>Specific hypothesis</i> (Activating the vestibular projections in the two hemispheres has different effects on random number generation)	1	-1	0

Table 2 Mean scores in each stimulation condition

	Stimulation condition		
	L-GVS	R-GVS	PSEUDO-GVS
<i>Measures of spatial bias</i>			
Large digits (%)	38.22 (5.41)	38.76 (4.43)	39.51 (4.72)
Negative first-order differences (FODs)	9.07 (1.27)	9.01 (1.20)	9.01 (1.78)
Positive first-order differences (FODs)	8.92 (1.36)	9.13 (1.42)	8.93 (1.87)
<i>Measures of randomness</i>			
Redundancy score (<i>R</i> score)	4.27 (2.07)	5.31 (2.52)	4.85 (2.19)
Random number generation index (RNG-I)	0.20 (0.07)	0.19 (0.08)	0.19 (0.07)

Measures of spatial bias and randomness (mean scores, SD) in L-GVS, R-GVS and PSEUDO-GVS

between experimental conditions ($t_{(22)} = -0.935$, $p = 0.36$) (Fig. 1a). These results indicate that vestibular activation did not elicit any general leftward or rightward preference in the generation of number. Similarly, neither the sum of negative FODs (Fig. 1b) nor the sum of positive FODs (Fig. 1c) differed significantly between experimental conditions (respectively, $t_{(22)} = 0.103$, $p = 0.919$ and $t_{(22)} = 0.311$, $p = 0.759$). However, we note that due to the inability of some participants to produce a sequence of exactly 20 digits, the mathematical sum of FODs in our data is not 19 as expected in the generation of 20 digits sequence, but slightly below (see Table 2).

Testing the hypothesis of a generic vestibular effect on measures of randomness did not reveal differences. No generic vestibular effect was found in the redundancy score (*R* score) ($t_{(22)} = -0.188$, $p = 0.853$) (Fig. 1d) or RNG-I index ($t_{(22)} = 0.354$, $p = 0.726$) (Fig. 1e).

Specific polarity/hemisphere-dependent vestibular effects on random number generation

According to our hemisphere-specific hypothesis, scores on each variable were directly compared between L-GVS and R-GVS conditions, to investigate differences in how vestibular projections in each hemisphere might influence the cognitive processes involved in random number generation. No differences were found between experimental conditions in the dependent variables used to investigate spatial effects in random number generation. The percentage of ‘large’ digits generated did not differ between L-GVS and R-GVS ($t_{(22)} = -0.583$, $p = 0.566$), indicating the absence of a leftward or rightward preference related to the experimental stimulation (Fig. 1a). In particular, R-GVS did not decrease the leftward bias, nor did L-GVS decrease the rightward bias, as a hypothesis of spatial-attentional shifts induced by GVS might predict.

Similarly, the use of ascending and descending strategies, as assessed by FODs, did not differ between experimental conditions (Fig. 1b, c). The sum of negative FODs did not show any difference between L-GVS and R-GVS ($t_{(22)} = 0.213$, $p = 0.833$). Similar results were found for the sum of positive FOD values ($t_{(22)} = -0.69$, $p = 0.497$). There were no obvious differences between conditions in the frequency of any particular value of the FODs variable (supplementary figure 1).

In contrast, measures of randomness revealed specific differences between GVS polarities. The redundancy score (*R* score) significantly differed between the two polarities of stimulation ($t_{(22)} = -2.25$, $p = 0.035$), because R-GVS increased redundancy relative to L-GVS (Fig. 1d). To investigate whether this effect reflected a benefit or a cost, we additionally compared each individual stimulation condition with PSEUDO-GVS. We found that neither mean was significantly different from zero ($p > 0.05$), suggesting that the effect lay fundamentally in the balance between the two experimental stimulations, rather than an effect of just one polarity on redundancy. Finally, RNG-I did not show a significant difference between L-GVS and R-GVS ($t_{(22)} = 0.098$, $p = 0.923$) (Fig. 1e).

Discussion

The balance between exploratory or novel behaviour and exploitative or routine behaviour is fundamental to successfully interact with the surrounding environment. Here, we show that vestibular input, in general, did not interfere with the cognitive processes involved in random number generation. In contrast, specific polarities of vestibular input, associated with activation of vestibular projections in each hemisphere separately, had differential effects on specific aspects of random number generation behaviour. In particular, our data revealed hemisphere-specific modulation in the redundancy of behaviour: L-GVS specifically decreased redundancy, or increased randomness, compared with R-GVS which increased redundancy, or decreased randomness. Other dependent variables showed no significant modulation by GVS condition. The redundancy measure reflects the breadth of sampling from the entire response space, while the RNG-I reflects predictable sequential progression through the response space, due to dependence of each number on the preceding number. We found hemisphere-specific effects of GVS on the former, but not the latter. Thus, hemispheric GVS appears to influence the degree of novelty and variation in sampling from the range of alternative responses, rather than the use of transition rules, such as repetition or counting, between successive actions.

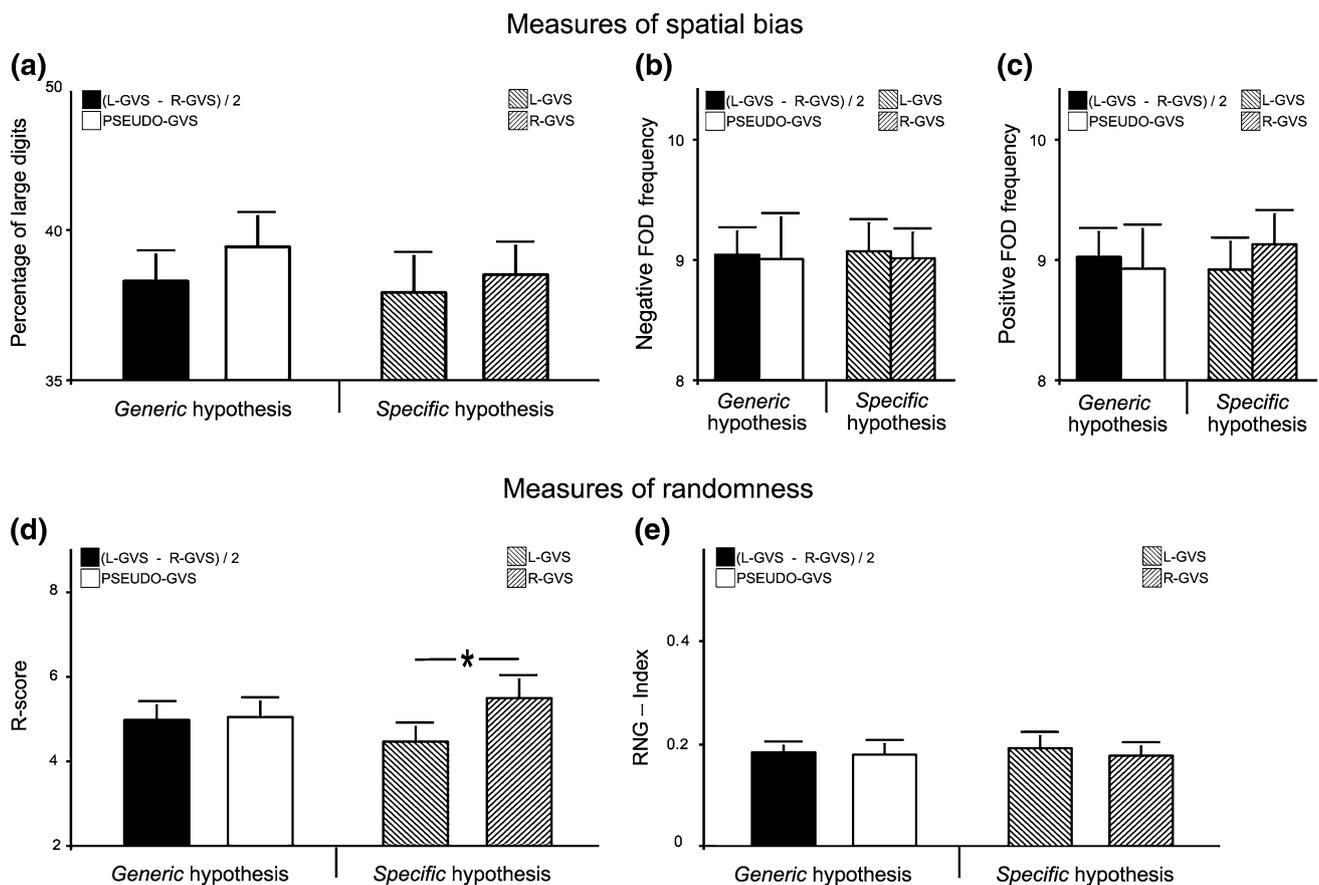


Fig. 1 Effects of GVS on spatial bias and randomness. **a** Preference for large digits as a function of experimental condition. **b** Sum of negative values indicating descending bias and **c** sum of positive

values indicating ascending bias in each experimental condition. **d** Redundancy scores in each experimental condition. **e** RNG-I scores in each experimental condition

In a previous study, TMS over left dorsolateral prefrontal cortex interfered with the normal tendency to avoid a counting strategy (e.g. 1–2–3) in random number generation tasks (Jahanshahi et al. 1998). Our FODs and RNG-I measures did not provide any evidence in this direction. It is noteworthy that repetition and counting strategies are more likely to be associated with the generation of longer sequences of digits. The sequences we used were short (20 digits) relative to those used in other random number generation studies (between 66 and 100 generated numbers, Jahanshahi et al. 1998; Towse and Neil 1998; Loetscher and Brugger 2007). These short sequences were used because administering GVS or PSEUDO-GVS for long periods can cause uncomfortable tingling or pinpricking sensation in the skin surface below the attached electrodes.

Binaural galvanic vestibular stimulation produces polarity-dependent differences in a percept described as a “virtual rotation vector” (Day and Fitzpatrick 2005) as well as sensory and cognitive functions in both healthy volunteers and brain-damaged patients (Utz et al. 2010a, b). L-GVS mimics an inhibition of the left ear and an activation of the right ear vestibular systems, decreasing

the firing rate of the vestibular nerve on the left side and increasing it on the right side (Fitzpatrick and Day 2004; Goldberg et al. 1984). Neuroimaging studies have revealed asymmetrical cortical vestibular projections, suggesting that the core region of the vestibular network is primarily located in the non-dominant right hemisphere in right-handed subjects (Dieterich et al. 2003). However, these conclusions were based mostly on monaural stimulation methods. Fink et al. (2003) used fMRI to study the effects of bipolar GVS. They found that left-anodal and right-cathodal stimulation, corresponding to our L-GVS, produced unilateral activation of the right-hemispheric vestibular projections, while the opposite polarity, that is, left-cathodal and right-anodal GVS, corresponding to our R-GVS, activated both left and right hemispheres (Fink et al. 2003).

Two alternative mechanisms could explain the vestibular modulation of random number generation. First, R-GVS and L-GVS might diffusely activate an entire cerebral hemisphere by vestibular input. Vestibular stimulation can produce non-specific increases in cortical excitability of the contralateral hemisphere (Utz et al. 2010a, b). If the two

hemispheres further differ in their contributions to exploratory and exploitative behaviour, then this might account for the effects we observe. Crucially, the right hemisphere was shown to dominate in suppressing repetitive behaviours (Sandson and Albert 1987), since right brain-damaged patients show more repetitive behaviour than patients with comparable lesions in the left hemisphere. Goldberg et al. (1994) proposed a principle of hemispheric lateralization based on cognitive novelty and cognitive routine: the right hemisphere is critical for the generation and exploratory processing of novel cognitive situations, while the left hemisphere is critical for processing based on pre-existing representations and routine cognitive strategy (Goldberg et al. 1994). In their series, patients with left frontal lobe lesions showed generative and exploratory reasoning in ambiguous cognitive tasks, while patients with right frontal lobe lesions showed perseverative and routine responses (Goldberg et al. 1994). Our results are consistent with the idea that hemispheric GVS similarly influences the balance between generative and repetitive behaviours. Thus, in the random number generation task, L-GVS would promote randomness by facilitating novel, generative or exploratory behaviour controlled by the right hemisphere, while R-GVS would reduce randomness by facilitating routine, stereotyped behaviour controlled by the left hemisphere.

Alternatively, vestibular input might specifically project to cortical areas within each hemisphere that are involved in random number generation. Vestibular modulation of cognitive control of behaviour has not been discussed previously, as far as we are aware. In fact, one comprehensive study of cognitive effects of vestibular stimulation reported “*some evidence of a small adverse effect of GVS on the Stroop test*” (Dilda et al., 2012, p 281), but offered no interpretation. However, perceptual studies show that vestibular stimulation directly influences alternation patterns of binocular rivalry (Miller et al. 2000). Miller et al. (2000) hypothesized that each hemisphere is responsible for one of the competing percepts in binocular rivalry situations, and that the alternations induced in the perceptual level correspond to the hemispheric alternations (Miller et al. 2000). Furthermore, neuroimaging studies identified the right fronto-parietal cortex as the core area involved in binocular transitions experienced during rivalry (Lumer et al. 1998). Similarly, the generation of random numbers activated the dorsolateral prefrontal cortex, the lateral premotor cortex, the anterior cingulate and the inferior and superior parietal cortex (Daniels et al. 2003; Jahanshahi et al. 1998, 2000). Given the unique multimodal nature of the vestibular system and its strong projections in the right hemisphere, we cannot exclude the possibility that vestibular signals reach specific cortical areas involved in the generation of explorative behaviours in the right fronto-parietal cortex.

Our data do not provide any evidence of a purely spatial effect. However, previous reports suggested that vestibular stimulation causes strong modulations of spatial attention in right brain-damaged patients (Rubens 1985; Utz et al. 2011). Additionally, GVS was shown to interfere with spatial processing on two spatial tasks: a spatial match-to-sample memory task and a perspective transformation task (Dilda et al. 2012). Similarly, Figliozzi et al. (2005) showed that vestibular inputs could produce spatiotopic shifts of attention, even under central fixation in vestibular-ocular reflex suppression conditions. The random number generation task has been applied to explore the properties of number space because of its strong relation with the mental number line (Loetscher and Brugger 2007). A spatial component in the generation of random number has been suggested, with spatial-attentional asymmetries in numerical processing supporting the presence of pseudo-neglect in number space in healthy volunteers (Loetscher and Brugger 2007). This account would predict orientation towards left hemi-space, that is, an increased generation of small numbers, during L-GVS, and towards right hemi-space, that is, an increased generation of larger numbers, during R-GVS.

In line with this prediction, active head turns (Loetscher et al. 2008) and also passive body motion (Hartmann et al. 2011) were reported to influence numerical cognition. The influence was interpreted as a shift in spatial attention along the mental number line. In particular, this evidence showed that leftward head/body motion facilitated the generation of small digits, whereas rightward head/body motion facilitated the generation of large digits. In contrast, we found no evidence concerning drifts of spatial attention to the side of the mental number line contralateral to the hemisphere activated by the GVS. Since vestibular cortical activations induced by whole head–body rotatory accelerations and GVS are quite different, it is difficult to directly compare the previous results with those we report here. Although GVS produces mild illusory self-motion (Lobel et al. 1998; Barnett-Cowan and Harris, 2009; Trainor et al. 2009), a strong “*virtual rotation vector*” has been described (Day and Fitzpatrick 2005). This suggests that purely vestibular activation is not sufficient to interact with spatial representation in healthy participants does not have strong spatial effects. This suggestion is also supported by a lack of vestibular-induced modulation of visual spatial attention in healthy participants (Rorden et al. 2001). Alternatively, the strength of our stimulation might have been insufficient to shift spatial attention. However, there is evidence that even low-intensity GVS can modulate neglect and tactile extinction (Utz et al. 2011; Kerkhoff et al. 2011). In fact, we employed a low-intensity galvanic vestibular stimulation (1 mA) as it circumvents merely cueing effects that occur with high-intensity stimulation: we did not want

strong tactile sensation under one or both electrodes to cue participants to the left or right side. Further, a clear balance response is evoked by GVS at 1 mA, as used here. Such balance responses confirm that our levels of GVS were sufficient to activate vestibular afferents (Day and Fitzpatrick 2005). Finally, the lack of spatial effect in our data could arise if our participants used a non-spatial method of random number generation. Further studies are needed to clarify the role of vestibular inputs in higher order spatial and attentional representation.

Interestingly, the present findings are fully in agreement with data recently observed in neurological patients. A speculation based on prior literature would predict that patients affected by hemispatial neglect after right parietal lesions might evidence a large-number bias in random number generation, thereby neglecting digits from the left side of the mental number line (Loetscher and Brugger 2009). However, Loetscher and Brugger (2009) showed that there were no differences between hemispatial neglect patients and healthy control participants in the generation of small numbers, that is, digits located in the left side of the mental number line. Importantly, left hemispatial neglect patients reported a drastic stereotyped behaviour compared with controls. In particular, the observed stereotyped behaviour was not reflecting an excessive counting strategy, but an enhanced redundancy (Loetscher and Brugger 2009).

Finally, our data suggest novel interpretations of effects induced by vestibular stimulation in neglect patients. Traditionally, the dramatic transitory improvement in visuo-spatial exploration following vestibular stimulation described in neglect patients had been interpreted as a reallocation of the spatial attention toward the neglected side of space (Utz et al. 2010a, b). The present findings suggest that vestibular stimulation might not merely produce displacement in spatial attention, but also generation of more novel behaviours. Since we did not test neglect patients, we can only speculate on this point. However, exploratory behaviour induced by L-GVS might include more visuo-spatial scanning, that is, increasing the overall number of saccades, both in the left and right hemi-space. Thus, the increased leftward exploratory behaviour would simulate a reallocation of the attention in the left hemi-space inducing a remission of visuo-spatial neglect, while any increased rightward behaviour would be unremarked, perhaps because of ceiling effects. We believe future studies could address this hypothesis by measuring the direction of spontaneous saccades following vestibular stimulation in neglect patients. Any component of the vestibular effect due to modulation of exploratory behaviour could be measured as an increase in orienting behaviour towards both left and right space, while any spatial component could be measured as an increase in leftward

saccades over and above rightward saccades. We speculate that both components may be present, but that different lesion sites may affect primarily the exploratory or the spatial components.

To conclude, we have shown that galvanic vestibular stimulation interacts with the generation of novel/exploratory versus routine/exploitative responses. The vestibular system plays a fundamental role in the active relation with external environment, but it remains unclear whether our results reflect a specific vestibular influence on those areas involved in cognitive control, or a more diffuse hemispheric activation caused by vestibular stimulation.

Acknowledgments This work was supported by a BIAL Foundation Bursary (215/10) awarded to PH. PH was further supported by EU FP7 project VERE and by a Leverhulme Trust Major Research Fellowship.

References

- Bains W (2008) Random number generation and creativity. *Med Hypotheses* 70(1):186–190
- Barnett-Cowan M, Harris LR (2009) Perceived timing of vestibular stimulation relative to touch, light and sound. *Exp Brain Res* 198(2–3):221–231
- Bense S, Stephan T, Yousry TA, Brandt T, Dieterich M (2001) Multisensory cortical signal increases and decreases during vestibular galvanic stimulation (fMRI). *J Neurophysiol* 85(2): 886–899
- Berthoz A (1996) How does the cerebral cortex process and utilize vestibular signals. In: Halmagyi GM, Baloh RW (eds) *Disorders of the vestibular system*. Oxford University Press, Oxford, pp 113–125
- Bucher SF, Dieterich M, Wiesmann M, Weiss A, Zink R, Yousry TA et al (1998) Cerebral functional magnetic resonance imaging of vestibular, auditory, and nociceptive areas during galvanic stimulation. *Ann Neurol* 44(1):120–125
- Cohen JD, McClure SM, Yu AJ (2007) Should I stay or should I go? How the human brain manages the trade-off between exploitation and exploration. *Philos Trans R Soc Lond B Biol Sci* 362(1481):933–942
- Daniels C, Witt K, Wolff S, Jansen O, Deuschl G (2003) Rate dependency of the human cortical network subserving executive functions during generation of random number series: a functional magnetic resonance imaging study. *Neurosci Lett* 345(1): 25–28
- Daw ND, O’Doherty JP, Seymour B, Dayan P, Dolan RJ (2006) Cortical substrates for exploratory decisions in humans. *Nature* 441:876–879
- Day BL, Fitzpatrick RC (2005) Virtual head rotation reveals a process of route reconstruction from human vestibular signals. *J Physiol* 567(Pt 2):591–597
- Day BL, Séverac Cauquil A, Bartolomei L, Pastor MA, Lyon IN (1997) Human body-segment tilts induced by galvanic stimulation: a vestibularly driven balance protection mechanism. *J Physiol* 500(Pt 3):661–672
- de Hevia MD, Vallar G, Girelli L (2008) Visualizing numbers in the mind’s eye: the role of visuo-spatial processes in numerical abilities. *Neurosci Biobehav Rev* 32(8):1361–1372
- Dehaene S (1992) Varieties of numerical abilities. *Cognition* 44(1–2): 1–42

- Dieterich M, Bense S, Lutz S, Drzezga A, Stephan T, Bartenstein P, Brandt T (2003) Dominance for vestibular cortical function in the non-dominant hemisphere. *Cereb Cortex* 13(9):994–1007
- Dilda V, MacDougall HG, Curthoys IS, Moore ST (2012) Effects of galvanic vestibular stimulation on cognitive function. *Exp Brain Res* 216(2):275–285
- Figliozzi F, Guariglia P, Silvetti M, Siegler I, Doricchi F (2005) Effects of vestibular rotatory accelerations on covert attentional orienting in vision and touch. *J Cogn Neurosci* 17(10):1638–1651
- Fink GR, Marshall JC, Weiss PH, Stephan T, Grefkes C, Shah NJ et al (2003) Performing allocentric visuospatial judgments with induced distortion of the egocentric reference frame: an fMRI study with clinical implications. *Neuroimage* 20(3):1505–1517
- Fitzpatrick RC, Day BL (2004) Probing the human vestibular system with galvanic stimulation. *J Appl Physiol* 96(6):2301–2316
- Galfano G, Rusconi E, Umiltà C (2006) Number magnitude orients attention, but not against one's will. *Psychon Bull Rev* 13(5):869–874
- Goldberg JM, Smith CE, Fernandez C (1984) Relation between discharge regularity and responses to externally applied galvanic currents in vestibular nerve afferents of the squirrel monkey. *J Neurophysiol* 51(6):1236–1256
- Goldberg E, Podell K, Lovell M (1994) Lateralization of frontal lobe functions and cognitive novelty. *J Neuropsychiatry Clin Neurosci* 6(4):371–378
- Hartmann M, Grabherr L, Mast FW (2011) Moving along the mental number line: Interactions between whole-body motion and numerical cognition. *J Exp Psychol Hum Percept Perform*. doi: [10.1037/a0026706](https://doi.org/10.1037/a0026706)
- Jahanshahi M, Profice P, Brown RG, Ridding MC, Dirnberger G, Rothwell JC (1998) The effects of transcranial magnetic stimulation over the dorsolateral prefrontal cortex on suppression of habitual counting during random number generation. *Brain* 121(Pt 8):1533–1544
- Jahanshahi M, Dirnberger G, Fuller R, Frith CD (2000) The role of the dorsolateral prefrontal cortex in random number generation: a study with positron emission tomography. *Neuroimage* 12(6):713–725
- Kerkhoff G, Hildebrandt H, Reinhart S, Kardinal M, Dimova V, Utz KS (2011) A long-lasting improvement of tactile extinction after galvanic vestibular stimulation: two Sham-stimulation controlled case studies. *Neuropsychologia* 49(2):186–195
- Lobel E, Kleine JF, Bihan DL, Leroy-Willig A, Berthoz A (1998) Functional MRI of galvanic vestibular stimulation. *J Neurophysiol* 80(5):2699–2709
- Loetscher T, Brugger P (2007) Exploring number space by random digit generation. *Exp Brain Res* 180(4):655–665
- Loetscher T, Brugger P (2009) Random number generation in neglect patients reveals enhanced response stereotypy, but no neglect in number space. *Neuropsychologia* 47(1):276–279
- Loetscher T, Schwarz U, Schubiger M, Brugger P (2008) Head turns bias the brain's internal random generator. *Curr Biol* 22(18(2)):R60–R62
- Lopez C, Lenggenhager B, Blanke O (2010) How vestibular stimulation interacts with illusory hand ownership. *Conscious Cogn* 19(1):33–47
- Lopez C, Blanke O, Mast FW (2012) The human vestibular cortex revealed by coordinate-based activation likelihood estimation meta-analysis. *Neuroscience* 212:159–179
- Lumer ED, Friston KJ, Rees G (1998) Neural correlates of perceptual rivalry in the human brain. *Science* 280(5371):1930–1934
- Miller SM, Liu GB, Ngo TT, Hooper G, Riek S, Carson RG et al (2000) Interhemispheric switching mediates perceptual rivalry. *Curr Biol* 10(7):383–392
- Norman W, Shallice T (1986) Attention to action. In: Davidson RJ, Schwartz GE, Shapiro D (eds) *Consciousness and self regulation: advances in research and theory*, vol 4. Plenum, New York, pp 1–18
- Peters M, Giesbrecht T, Jelicic M, Merckelbach H (2007) The random number generation task: psychometric properties and normative data of an executive function task in a mixed sample. *J Int Neuropsychol Soc* 13(4):626–634
- Rorden C, Karnath HO, Driver J (2001) Do neck-proprioceptive and caloric-vestibular stimulation influence covert visual attention in normals, as they influence visual neglect? *Neuropsychologia* 39(4):364–375
- Rubens AB (1985) Caloric stimulation and unilateral visual neglect. *Neurology* 35(7):1019–1024
- Sandson J, Albert ML (1987) Perseveration in behavioral neurology. *Neurology* 37(11):1736–1741
- Spatt J, Goldenberg G (1993) Components of random generation by normal subjects and patients with dysexecutive syndrome. *Brain Cogn* 23(2):231–242
- Stephan T, Deutschlander A, Nolte A, Schneider E, Wiesmann M, Brandt T et al (2005) Functional MRI of galvanic vestibular stimulation with alternating currents at different frequencies. *Neuroimage* 26(3):721–732
- Streng H, Bohm J (2004) Random number generation in native and foreign languages. *Percept Mot Skills* 98(3 Pt 2):1153–1161
- Streng H, Rogge C (2010) Strategic use of number representation is independent of test instruction in random number generation. *Percept Mot Skills* 110(2):453–462
- Sugrue LP, Corrado G, Newsome WT (2004) Matching behavior and the representation of value in the parietal cortex. *Science* 304:1782–1787
- Towse JN (1998) On random generation and the central executive of working memory. *Br J Psychol* 89(Pt 1):77–101
- Towse J, Neil D (1998) Analyzing human random generation behavior: a review of methods used and a computer program for describing performance. *Behav Res Methods Instrum Comput* 30(4):583–591
- Trainor LJ, Gao X, Lei JJ, Lehtovaara K, Harris LR (2009) The primal role of the vestibular system in determining musical rhythm. *Cortex* 45(1):35–43
- Utz KS, Dimova V, Oppenlander K, Kerkhoff G (2010a) Electrified minds: transcranial direct current stimulation (tDCS) and galvanic vestibular stimulation (GVS) as methods of non-invasive brain stimulation in neuropsychology—a review of current data and future implications. *Neuropsychologia* 48(10):2789–2810
- Utz KS, Korluss K, Schmidt L, Rosenthal A, Oppenlander K, Keller I et al (2010b) Minor adverse effects of galvanic vestibular stimulation in persons with stroke and healthy individuals. *Brain Inj* 25(11):1058–1069
- Utz KS, Keller I, Kardinal M, Kerkhoff G (2011) Galvanic vestibular stimulation reduces the pathological rightward line bisection error in neglect—a sham stimulation-controlled study. *Neuropsychologia* 49(5):1219–1225
- Vallar G, Sterzi R, Bottini G, Cappa S, Rusconi ML (1990) Temporary remission of left hemianesthesia after vestibular stimulation. A sensory neglect phenomenon. *Cortex* 26(1):123–131