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RESEARCH ARTICLE

Effects of Galvanic vestibular stimulation on cognitive function

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Abstract Although imaging studies suggest activation of cortical areas by vestibular input, there is little evidence of an adverse effect of non-veridical vestibular input on cognitive function. To test the hypothesis that degraded vestibular afferent input adversely affects cognition, we compared performance on a cognitive test battery in a group undergoing suprathreshold bilateral bipolar Galvanic vestibular stimulation (GVS) with a control group receiving no GVS or subthreshold stimulation. The battery consisted of six cognitive tests as follows: reaction time, dual tasking, Stroop, mental rotation, perspective-taking and matching-to-sample, as well as a simple visuomotor (manual tracking) task. Subjects performed the test battery before, during and after suprathreshold GVS exposure or subthreshold stimulation. Suprathreshold GVS significantly increased error rate for the match-to-sample and perspective-taking tasks relative to the subthreshold group, demonstrating a negative effect of non-veridical vestibular input in these specific cognitive tasks. Reaction time, dual tasking, mental rotation and manual tracking were unaffected by GVS exposure. The adverse effect of suprathreshold GVS on perspective taking but not mental rotation is consistent with imaging studies, which have demonstrated that egocentric mental transformations (perspective taking) occur primarily in cortical areas that receive vestibular input (the parietal–temporal junction and superior parietal lobule), whereas object-based transformations (mental rotation) occur in the frontoparietal region. The increased error rate during the match-to-sample task is likely due to interference with hippocampal processing related to spatial memory, as suggested by imaging studies on vestibular patients.

Keywords Egocentric mental transformation · Spatial memory · Hippocampus · Perspective taking · Microgravity

Introduction

There is little direct evidence of an adverse effect of non-veridical vestibular input on cognitive function. Patients with vestibular impairment have demonstrated difficulty in counting backwards by twos (Risey and Briner 1990) and sevens (Andersson et al. 2002; Andersson et al. 2003) and exhibit deficits in short-term and working memory on standard psychological tests such as the Digit Span and Mini Mental State Exam (Hanes and McCollum 2006). Imaging studies have provided more substantial (albeit indirect) evidence for a role of vestibular input in cognition by demonstrating cerebral cortex activation by afferent vestibular signals. Application of Galvanic vestibular stimulation (GVS) during fMRI induced activity in the intraparietal sulcus (Lobel et al. 1998; Lobel et al. 1999; Fink et al. 2003), the parietal–temporal junction and central sulcus (Lobel et al. 1998; Lobel et al. 1999), the superior temporal gyrus and insula (Fink et al. 2003), ventral premotor areas (Fink et al. 2003) and the cingulate gyrus (Lobel et al. 1998). Similar activation has been observed in fMRI (Suzuki et al. 2001) and PET (Bottini et al. 2001; Deutschlander et al. 2002) studies during caloric vestibular stimulation; the intraparietal sulcus (Suzuki et al. 2001), superior temporal gyrus and insula (Bottini et al. 2001;

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Suzuki et al. 2001; Deutschlander et al. 2002), parietal–temporal junction (Bottini et al. 2001), cingulate gyrus (Bottini et al. 2001; Suzuki et al. 2001) and the superior parietal lobule and basal ganglia (Deutschlander et al. 2002). Activation of the hippocampus by vestibular input is well established in humans (Vitte et al. 1996; Smith et al. 2010). Significant atrophy in hippocampal volume (with concomitant spatial memory deficit) has been observed in patients with chronic bilateral vestibular loss (Brandt et al. 2005).

Bilateral bipolar GVS, in which a small current is passed between surface electrodes placed on the mastoid processes, is a potential tool to elucidate the effects of vestibular input on cognitive function [see (Fitzpatrick and Day 2004) for review]. Animal studies have established the site of action of Galvanic current at the spike trigger zone of primary vestibular afferents, using electrodes in direct contact with perilymph (Goldberg et al. 1984). Perilymphatic cathodal currents depolarize the trigger site and lead to excitation, whereas anodal currents hyperpolarize resulting in inhibition (Goldberg et al. 1984). Application of suprathreshold stochastic Galvanic current (above the human sensory threshold of $\sim$1 mA) induces behavioral effects analogous to mild vestibular deficit, such as postural instability (MacDougall et al. 2006) and reduced dynamic visual acuity (Moore et al. 2006). In contrast, subthreshold ($\leq$1 mA) noisy Galvanic stimulation can improve motor performance (Yamamoto et al. 2005; Pal et al. 2009) and cognition (Wilkinson et al. 2008), most likely via the phenomenon of stochastic resonance.

We have leveraged the destabilizing effect of suprathreshold GVS on sensorimotor function to replicate in healthy subjects the decrements in postural (MacDougall et al. 2006), locomotor (Moore et al. 2006), oculomotor (Moore et al. 2006) and fine motor (Moore et al. 2011) performance observed in astronauts after spaceflight. We propose that the GVS analog superposes the pseudorandom current waveform on the veridical vestibular afferent signal at the spike trigger zone, and this experiment was designed to test the hypothesis that degraded vestibular input adversely affects cognitive function. We selected a range of attentional (reaction time, dual tasking, Stroop), spatial (mental rotation, perspective taking), memory (matching to sample) and visuomotor coordination (manual tracking) tasks, to be performed with and without GVS. These tests were based on the Spaceflight Cognitive Assessment Test for Windows (WinSCAT), a subset of the ANAM (Automated Neuropsychological Assessment Metrics) (Kane et al. 2005) used by the US military. An ancillary aim was to compare cognitive effects of the GVS analog to the results from studies on cognition in astronauts during and immediately after spaceflight.

Methods

Subjects

A total of 120 healthy subjects were randomly assigned into 4 groups: 0, 1, 3.5 and 5 mA peak GVS current (Table 1). Participants had no prior experience with GVS. Mount Sinai School of Medicine's Institutional Review Board approved the experiments, and subjects gave their informed consent and were free to withdraw at any time.

Experimental paradigm and apparatus

A battery of cognitive tests was administered to each participant under three conditions: pre-GVS baseline, during intermittent GVS and 15 min after GVS exposure. The pseudorandom bilateral–bipolar Galvanic stimulus consisted of a sum of sines (0.16, 0.33, 0.43, 0.61 Hz) with peak amplitude of either 0, 1, 3.5 or 5 mA (MacDougall et al. 2006; Moore et al. 2006). The 0- and 1-mA groups were considered subthreshold controls, with stimuli of no GVS current (0 mA) or at an amplitude below the threshold of vestibular-mediated behavioral effects (1 mA peak). The latter group was intended to control for cutaneous tingling or itching experienced at the electrode sites at suprathreshold (3.5 and 5 mA) current amplitudes, without generating significant behavioral effects or perception of motion. Although direct current GVS of 0.5 mA has been found to generate small (<0.5°) torsional eye movements in a pilot study ($N = 6$) (Severac Cauquil et al. 2003), these

Table 1 Subject demographics for 120 starting subjects and 115 subjects who completed the experiment

Current (mA)	Started			Completed		
	Number	Age	Gender (M/F)	Number	Age	Gender (M/F)
0.0	30	27.0 (CI 2.3)	14/16	30	27.0 (CI 2.3)	14/16
1.0	30	26.8 (CI 1.3)	15/15	30	26.8 (CI 1.3)	15/15
3.5	30	30.3 (CI 3.2)	17/13	28	29.9 (CI 3.1)	16/12
5.0	30	28.7 (CI 2.5)	15/15	27	28.5 (CI 2.8)	15/12
Total	120		61/59	115		60/55

movements are considerably smaller than the low-frequency drift in cycloversion (over 2° peak-to-peak) observed in the resting state (Ott et al. 1992; Van Rijn et al. 1994) and likely to be negligible in a behavioral sense. To support this conclusion, we recently compared performance in 10 subjects on computerized dynamic posturography during 1- and 0-mA GVS in an ongoing study. There was no difference in the composite equilibrium score (1 mA 84.3 [CI 3.3]; 0 mA 83.0 [CI 3.3]; $P = 0.52$) or in the vestibular score (1 mA 69.4 [CI 11.5]; 0 mA 70.6 [CI 10.8]; $P = 0.89$) from the sensory organization test (Nashner 1993), demonstrating that 1-mA GVS did not affect postural performance (in contrast to 3.5- and 5-mA GVS, which significantly lowered the composite and vestibular scores (MacDougall et al. 2006; Wood et al. 2009)). In addition, none of the 30 subjects exposed to 1-mA GVS reported a sensation of movement induced by Galvanic current.

An optically isolated constant current generator delivered the current to the surface of the subject's skin via leads and large electrodes placed over the mastoid processes, cut from electrosurgical split grounding plate electrodes (7180, 3 M Health Care, St. Paul, MN). The electrodes were coated with an additional layer of EMG electrode gel and then applied to the surface of the subject's skin using the electrode's adhesive surround, and a piece of insulated tape was added to the skin underneath the bare metal tag. A soft pad was placed over each electrode and held firmly in place by an elasticized strap. The electrodes and strap did not produce discomfort or restrict head movement. Prior to testing, subjects were briefly exposed to the Galvanic stimulus to ensure that there was no adverse cutaneous effects, such as a sensation of burning at the electrode site. We have previously demonstrated that the GVS analog is well tolerated in the vast majority of subjects during extended exposure (up to 20 min) at amplitudes of 3.5 and 5 mA (Dilda et al. 2011).

The cognitive test battery, written in Matlab (Mathworks, Natick, MA), was presented on a computer screen 1 m distant from the subject. Each subject sat at a desk with the head unrestrained and practiced the test battery once after receiving verbal instructions. The order of cognitive tests was randomized within each stimulation condition (pre, per, post). During the GVS task, the stimulus was turned on at the beginning of each cognitive test and off at task completion (for current amplitudes of 1, 3.5 and 5 mA). Duration of each GVS exposure was dependent on the time taken to perform the particular cognitive test, averaging 89 s (CI 1.3) per task and 641 s (CI 9.3) total for subjects completing the test battery. The experiment was terminated if severe nausea was reported (a feeling that vomiting was imminent) or at any time at the subject's request.

Cognitive test battery

Reaction time

A solid black dot was presented on a white background after a randomized delay of 1–3 s. Subjects were required to respond by pressing the left mouse button as soon as they saw the stimulus. Forty trials were performed.

Dual tasking

Subjects performed the reaction time task described above while counting backwards by three from a randomly generated number ranging between 160 and 200.

Stroop

A series of colored words appeared on the screen. The color of the font was either congruent (e.g., the word "red" written in red color) or incongruent (e.g., "red" written in yellow). Subjects were asked to indicate whether the word stimulus was congruent or incongruent by pressing the appropriate key on the keyboard (right arrow for incongruent and left arrow for congruent). Eighty words were presented.

Mental rotation

A computerized version of the Shepard and Metzler mental rotation task (Shepard and Metzler 1971) was developed using 3D cube images from the Peters and Battista stimulus library (Peters and Battista 2008) (Fig. 1a). Subjects were presented with an image of two identical objects. The object on the right was either a matching or mirror image of the left-hand object, rotated to one of four orientations, ±45° and ±135°, in roll, pitch and yaw (24 trials, repeated for a total of 48 trials). Subjects were asked to imagine turning of the image on the right (an object-based mental transformation) to determine whether it was a rotated version of the object on the left or its mirror image and press the appropriate key (left arrow for "same" and right arrow for "mirror").

Perspective taking

A computerized perspective-taking task was developed (Fig. 1b) based on the Directional Orientation Test from the Test of Basic Aviation Skills (TBAS) used by the US Air Force to assess potential pilot recruits (Carretta 2005). A topographical map was shown on the left of the screen with an aircraft icon at the center (Fig. 1b). The aircraft was heading in one of four cardinal directions (north, south, east or west). On the right side of the screen was an

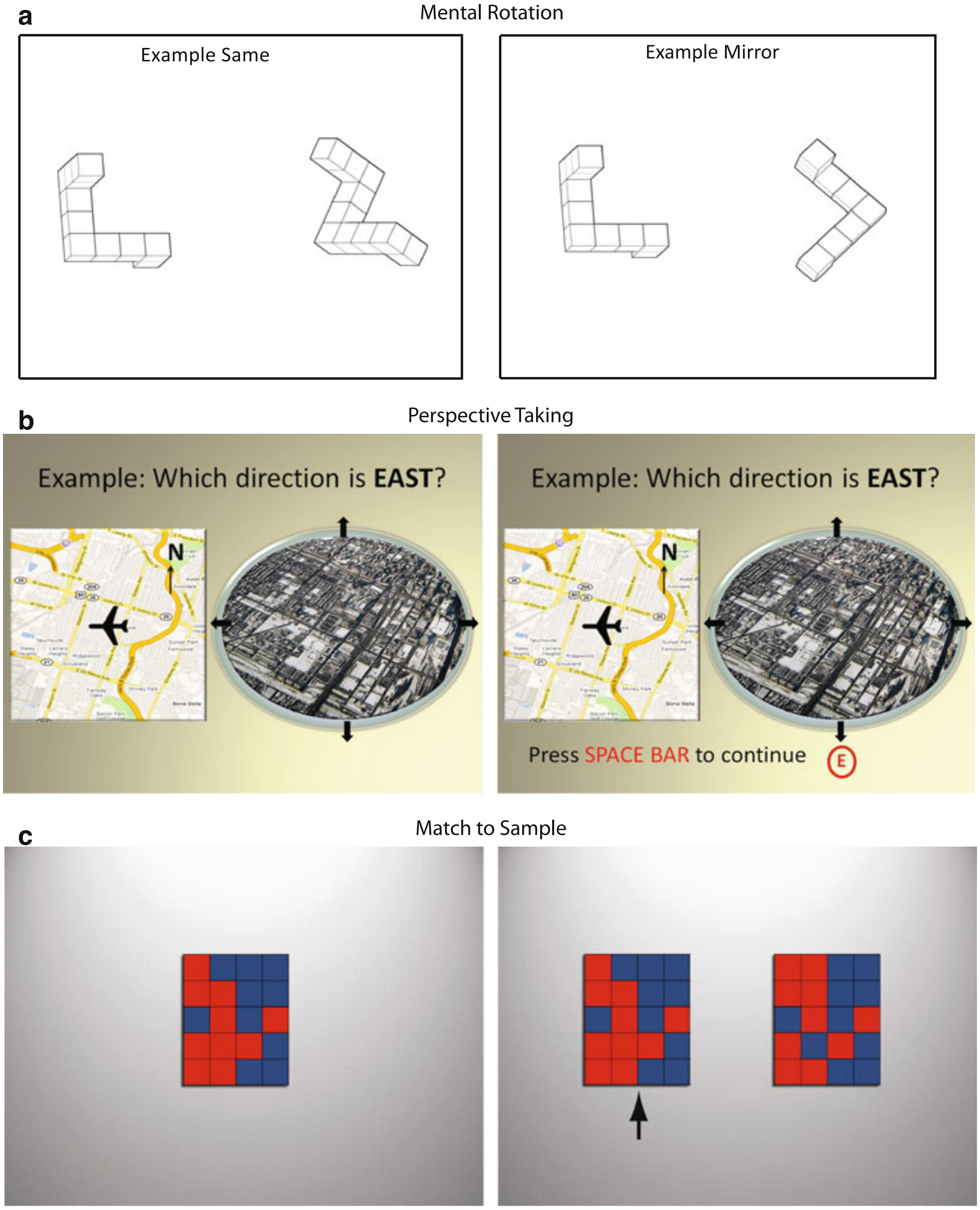

Fig. 1 Example slides from **a** the mental rotation task showing rotated and mirror image object pairs; **b** the perspective-taking task; **c** the match-to-sample task

image looking forward out of a cockpit window, and subjects were instructed to imagine they were piloting the aircraft. They were asked to indicate a cardinal direction (e.g., "Which direction is East?") relative to the cockpit window using one of four arrow keys. Participants performed 32 trials.

Matching to sample

Subjects were instructed to memorize a single 3 × 3 array of blue and red squares presented for 2 s. After a 2-second delay, two 3 × 3 patterns appeared on the screen, one of which matched the previously viewed array (Fig. 1c). Subjects were instructed to identify the matching pattern by pressing the corresponding right or left arrow key on the computer keyboard. The task consisted of 20 trials.

Manual tracking

In addition to the cognitive tests, we also assessed visuomotor coordination. Subjects were required to use the computer mouse to maintain a cross-hair target inside a 15-mm-diameter circle moving randomly on the computer screen. The circle moved at two speeds: slow (10 mm/s) for 30 s and then fast (20 mm/s) for another 30 s.

Data analysis

Data were analyzed using SPSS 19.0 software. Mean error rate (percentage of incorrect responses) and mean response time (time to complete each trial) were computed for each task (error rate and reaction time for matching to sample, Stroop, mental rotation and perspective taking, response time only for reaction time and dual tasking), current (0, 1, 3.5 and 5 mA) and condition (pre, during sub- or suprathreshold GVS, and post). For manual tracking, the error rate was calculated as the percentage of time the cross-hair was outside the target circle. Response times greater than 2.5 times the standard deviation from the mean were discarded as outliers.

The first analysis step was to demonstrate that there were no significant differences in error rates between 0- and 1-mA groups using a mixed design ANOVA (3 conditions [pre, per, post] × 2 current amplitudes [0, 1 mA]) with current as a between-subject factor; thus, results from these subjects could be pooled into a subthreshold GVS group. A similar analysis was performed for subjects receiving 3.5- and 5-mA GVS to form a suprathreshold group. Error rate and response times were subsequently analyzed for each task using 3 condition (pre, per, post) × 2 current amplitude (subthreshold or suprathreshold GVS) mixed design ANOVA with current as a between-subject factor. In both cases, post hoc paired *t* tests were utilized to further analyze any significant effects of GVS current and condition on error rates or response times; results were considered significant for $P < 0.05$. Variance is stated as 95% confidence interval (CI) of the mean.

Results

Five subjects requested termination of the Galvanic stimulus due to nausea and withdrew from the experiment; two subjects (one man and one woman) in the 3.5 mA group and three (all women) in the 5-mA group (Table 1). The demographics of 115 subjects who completed the experiment (age, gender balance) were not significantly different ($P > 0.5$) to the starting sample of 120 (Table 1).

Subthreshold GVS error rate

A 3 condition (pre, per, post) × 2 current (0 and 1 mA) mixed design ANOVA with current as a between-subject factor demonstrated no significant condition by current interaction between 0- and 1-mA groups (mental rotation $P = 0.25$; match to sample $P = 0.81$; perspective taking $P = 0.68$; Stroop $P = 0.86$). Error rates were substantially higher across all three conditions for the mental rotation task in the 0-mA group when compared to subjects receiving 1-mA GVS (pre $P = 0.0001$; per $P = 0.006$; post $P = 0.003$) (Fig. 2a, b). Performance on the mental rotation, match to sample, perspective taking and Stroop tests improved during subthreshold GVS relative to baseline for both 0- and 1-mA groups; error rate decreased across all four tasks by an average of −12 to −29% suggesting a practice effect (Fig. 2c), with no significant difference between 0- and 1-mA groups.

Suprathreshold GVS error rate

A 3 condition (pre, per, post) × 2 current (3.5 and 5 mA) mixed design ANOVA with current as the between-subject factor demonstrated no significant condition by current interaction between 3.5- and 5-mA groups (match to sample $P = 0.38$, mental rotation $P = 0.07$; Stroop $P = 0.87$; perspective taking $P = 0.86$) (Fig. 3a, b). The mean percent change in error rate between baseline and application of suprathreshold GVS tended to increase for match to sample, perspective taking and Stroop by +4–+31%, indicative of an adverse effect of Galvanic stimulation on performance, with no significant differences between 3.5- or 5-mA groups (Fig. 3c). Mental rotation exhibited a similar pattern to the subthreshold (0 and 1 mA) groups, with mean error decreasing by −17% in the 3.5-mA group and by −1% at 5-mA GVS (NS).

Subthreshold versus suprathreshold error rate

On the basis of the statistical analyses above, 0- and 1-mA data were pooled into a subthreshold GVS group ($N = 60$) and the 3.5- and 5-mA data were combined to form a suprathreshold GVS group ($N = 55$) for subsequent analysis (Table 2; Fig. 4). A 3 condition (pre, per, post) × 2 current (subthreshold, suprathreshold) mixed design ANOVA with current as a between-subject factor suggested a current by condition interaction for mental rotation [$F(2, 226) = 3.04$, $P = 0.05$], matching to sample [$F(2, 226) = 3.3$, $P < 0.05$] and perspective taking [$F(2, 226) = 2.96$, $P = 0.05$]. There was no significant difference in error rate in the baseline condition between subthreshold and suprathreshold groups on any task; similarly, no difference was found in error rate for the post-stimulation condition (Fig. 4a, b; Table 2). Error rates during suprathreshold GVS exposure were significantly higher than during subthreshold stimulation for the match-to-sample ($P = 0.005$), perspective-taking ($P = 0.022$) and Stroop ($P = 0.009$) tasks (Fig. 4b; Table 2).

For the match-to-sample task, the mean error rate decreased by 13% during subthreshold GVS relative to baseline, whereas error rate increased by 26% relative to baseline during suprathreshold GVS; this difference in

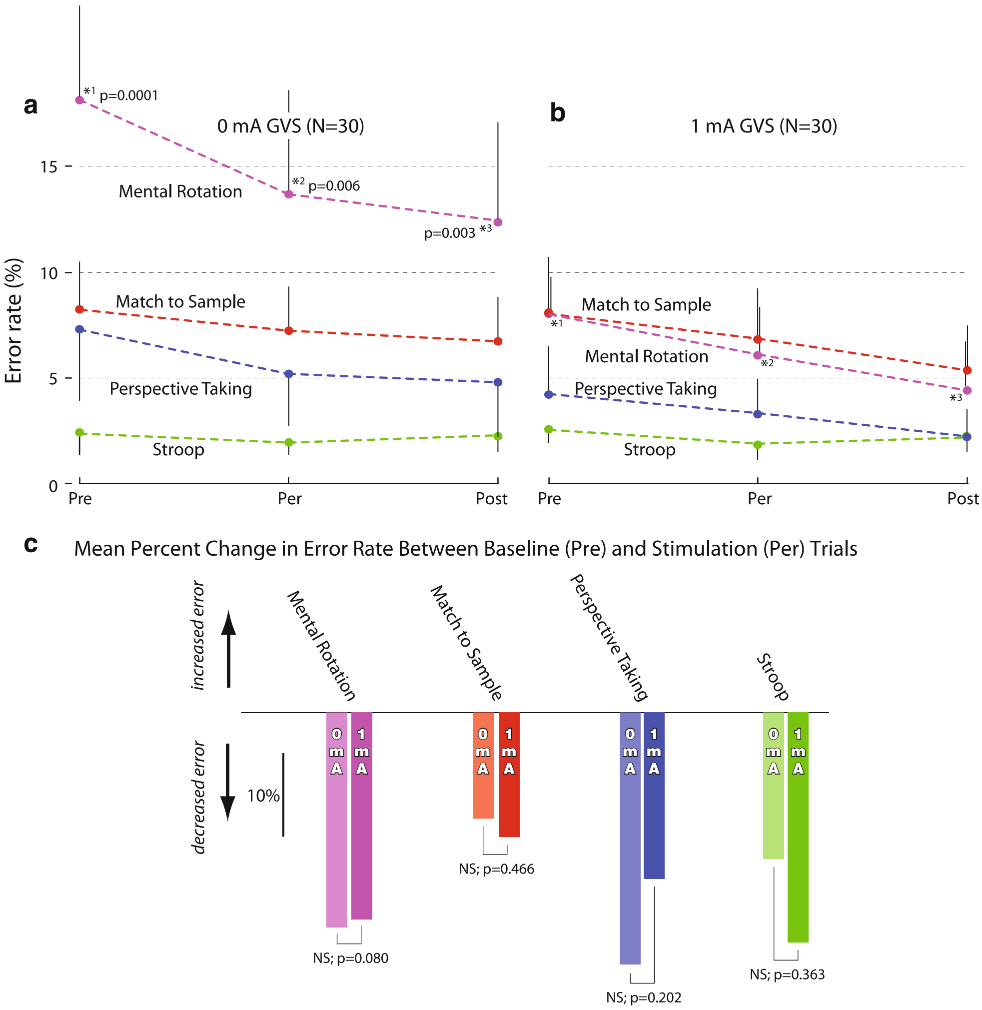

Fig. 2 Error rates (mean and 95% CI) at baseline (pre), during subthreshold (0 or 1 mA) GVS stimulation and 15-min post-stimulation for mental rotation, match-to-sample, perspective-taking and Stroop tasks at **a** 0 mA (no GVS) and **b** 1 mA GVS peak current. Numbered asterix pairs represent significant differences between groups for a particular task and condition (e.g., $*^{1}$–$*^{1}$ → 0-mA versus 1-mA baseline mental rotation error). **c** Mean percent change in error rate between baseline and subthreshold (0 or 1 mA peak) Galvanic stimulation conditions for mental rotation, match-to-sample, perspective-taking and Stroop tasks

relative error rate between subthreshold and suprathreshold groups was significant (Fig. 4c; $P = 0.01$). For the perspective-taking task, error rate decreased by 26% during subthreshold GVS and increased by 18% during suprathreshold GVS (both relative to baseline), and again, this difference was significant (Fig. 4c; $P = 0.01$). A similar pattern was observed in the Stroop task, with a 22% reduction in error rate during subthreshold GVS and a 10% increase in error rate during suprathreshold GVS, which did not reach significance (Fig. 4c; $P = 0.06$). These results suggest that performance improved with practice on these three tasks in the subthreshold group but was adversely affected by suprathreshold GVS exposure. Performance on the mental rotation task improved during both sub (25%) and suprathreshold (10%) GVS relative to baseline (Fig. 4c; $P = 0.05$). There was no significant difference in error during the manual tracking task across three conditions (pre, per, post) for both subthreshold and suprathreshold GVS groups (Table 2).

Time to respond

A 3 condition (pre, per, post) × 2 current (subthreshold, suprathreshold) mixed design ANOVA with current as a between-subject factor demonstrated no significant condition by current interaction between subthreshold and suprathreshold GVS groups for match to sample $P = 0.82$, mental rotation $P = 0.07$, perspective taking $P = 0.13$, dual tasking $P = 0.96$ and reaction time $P = 0.36$ (Fig. 5a, b). There was a significant condition by current effect on the Stroop task [$F(2, 226) = 6.92$, $P = 0.001$]. There was a tendency for the time to respond to decrease during GVS stimulation relative to baseline, which was unrelated to the level of current for mental rotation, match to sample, perspective tasking and dual tasking (NS; Fig. 5c). Response time decreased by 6% for the Stroop task during subthreshold GVS relative to baseline but was unchanged during suprathreshold GVS ($P = 0.0008$) (Fig. 5c).

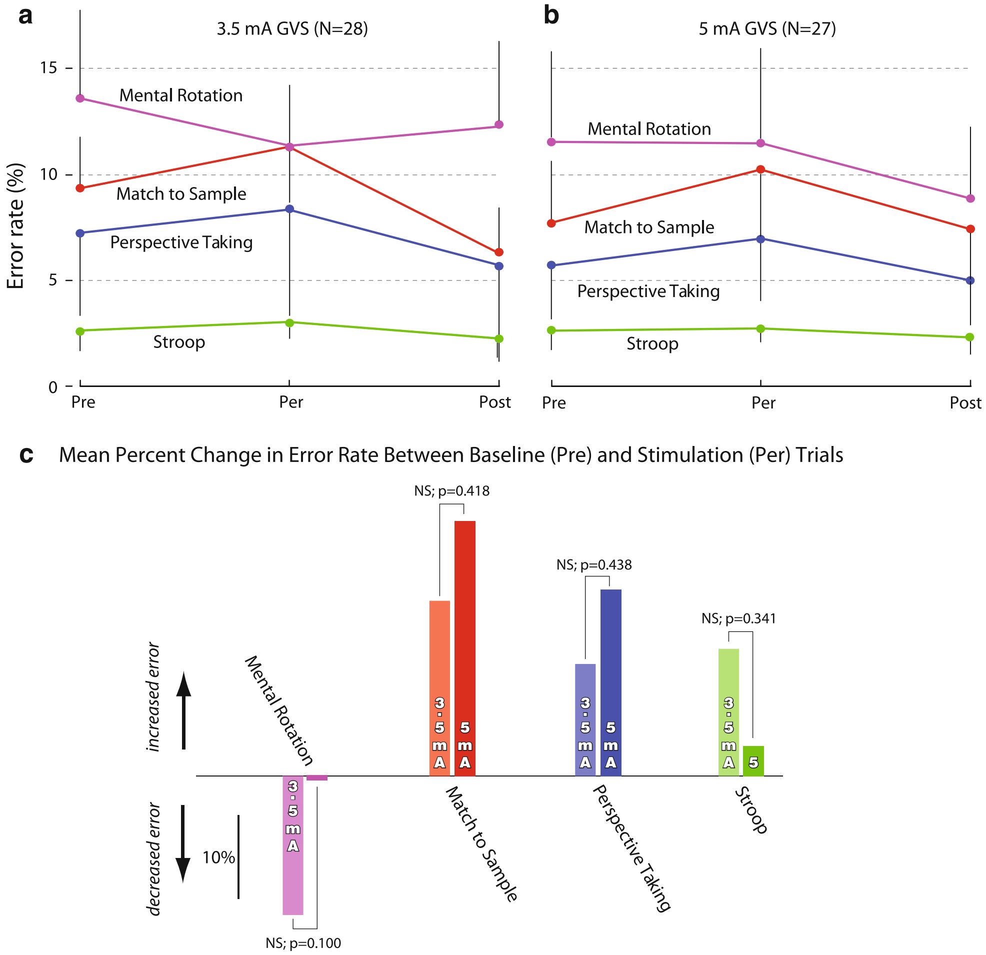

Fig. 3 Error rates (mean and 95% CI) at baseline (pre), during suprathreshold (3.5 or 5 mA) GVS and 15-min post-stimulation for mental rotation, match-to-sample, perspective-taking and Stroop tasks at **a** 3.5 mA and **b** 5 mA GVS peak current. **c** Mean percent change in error rate between baseline and suprathreshold GVS (3.5 or 5 mA peak) conditions for mental rotation, match-to-sample, perspective-taking and Stroop tasks

Discussion

The results of this study demonstrate that application of suprathreshold pseudorandom bilateral bipolar GVS significantly degraded performance on short-term spatial memory (match to sample) and egocentric mental rotation (perspective taking), which demonstrates a negative effect of non-veridical vestibular input in these specific cognitive tasks. There was also some evidence of a small adverse effect of GVS on the Stroop test. Reaction time, dual tasking, mental rotation and manual tracking were unaffected by GVS exposure. The adverse effects of suprathreshold pseudorandom GVS on cognition are consistent with neuro-anatomical findings. It is clearly established that the hippocampus receives afferent input from the vestibular cortex and plays a prominent role in spatial memory (Vitte et al. 1996; Brandt et al. 2005). This may underlie the increase in error rate during GVS in the match-to-sample task, which required the subject to retain a 2D shape in short-term memory. Perspective taking requires an egocentric mental transformation, which has been shown to rely on activation of the parietal–temporal junction and superior parietal lobule (Zacks and Michelon 2005). These areas receive vestibular input (Lobel et al. 1998; Lobel et al. 1999; Bottini et al. 2001; Deutschlander et al. 2002), thus it is reasonable to expect that GVS would adversely affect perspective taking. Object-based transformations utilized during the mental rotation task occur primarily in the frontoparietal lobe (although activation of some parietal–temporal areas may be common to both tasks) (Zacks and Michelon 2005), which was not activated by GVS in functional imaging studies (Lobel et al. 1998; Fink et al. 2003). This may explain why GVS negatively impacted one spatial task (perspective taking) but not another (mental rotation). Our results are consistent with a previous study (Lenggenhager et al. 2008) in which an interfering effect of right-anode GVS was observed in 5 subjects employing an egocentric mental transformation when making right/left judgments of pictures of a human body, relative to 6 subjects utilizing an object-based mental transformation.

There are several alternative explanations for the observed effects of suprathreshold GVS on cognitive function. Galvanic stimulation produces reflex eye

Table 2 Error rates and time to respond (mean and 95% CI) from cognitive testing at baseline (pre), during subthreshold (0, 1 mA) or suprathreshold (3.5, 5 mA) GVS (per) and post-stimulation

	Subthreshold GVS ($N = 60$)						Suprathreshold GVS ($N = 55$)					
	Pre		Per		Post		Pre		Per		Post	
	Mean	CI	Mean	CI	Mean	CI	Mean	CI	Mean	CI	Mean	CI
Error rate (%)												
Match to sample	8.08	1.82	7.00*[1]	1.65	6.00	1.63	8.55	1.85	10.73*[1]	2.32	6.82	1.84
Perspective taking	5.68	2.15	4.22*[2]	1.57	3.44	1.23	6.48	2.45	7.61*[2]	2.96	5.34	2.56
Mental rotation	13.08	2.82	9.87	2.99	8.41	2.88	12.52	3.00	11.33	2.61	10.56	2.59
Stroop	2.46	0.64	1.92*[3]	0.50	2.25	0.56	2.59	0.73	2.84*[3]	0.57	2.25	0.55
Manual tracking[a]												
Fast	23.29	1.85	21.18	1.75	20.14	1.57	27.20	2.52	25.60	2.27	25.65	2.21
Slow	6.38	0.70	6.34	0.74	7.12	0.88	8.50	1.27	8.91	1.10	9.09	1.18
Time to respond (ms)												
Match to sample	1,653.5	108.5	1,538.8	103.2	1,472.9	94.5	1,722.1	117.9	1,593.5	89.7	1,558.3	95.5
Perspective taking	2,540.2	350.5	2,117.5	261.4	1,848.2	206.6	2,530.4	402.8	2,046.2	240.4	1,999.0	265.4
Mental rotation	3,027.2	277.0	2,425.7	250.6	2,114.2	225.6	2,979.6	331.9	2,265.2	210.7	2,211.2	206.0
Stroop	914.2	41.0	858.6	38.1	822.8	33.7	874.7	37.3	871.0	38.7	820.5	31.4
Dual tasking	622.6	85.1	593.1	72.8	557.0	61.1	678.6	80.3	652.7	68.6	621.8	60.2
Reaction time	297.9	8.4	300.7*[4]	9.0	299.3	8.7	308.1	10.3	316.1*[4]	11.1	307.1	9.7

Numbered asterisk pairs indicate significant differences between subthreshold and suprathreshold groups for a particular task and condition

[a] Error rate defined as percentage of time cursor is outside of target circle

movements, which may have degraded vision during the match-to-sample and perspective-taking tasks. However, bilateral bipolar GVS induces a primarily torsional eye response (MacDougall et al. 2002) and was therefore unlikely to have significantly affected visual acuity (foveal acuity is relatively independent of rotation about the line of sight (Leigh and Zee 1999)). Moreover, all seven cognitive tasks required vision but only two were significantly affected by GVS. There was no relationship between GVS-induced autonomic symptoms and increased error rate; only 5 of 85 subjects who completed the cognitive test battery while experiencing transmastoidal current reported more than mild nausea (Dilda et al. 2011). It is also possible that non-vestibular effects of Galvanic stimulation, such as cutaneous tingling or itching sensations at the electrode site and dysgeusia (a metallic taste in the mouth due to activation of taste buds by GVS), may have had a distracting effect that decreased performance. This explanation is unlikely; if this was the case, it would be reasonable to expect GVS to have degraded performance on other complex tasks such as mental rotation. The 1-mA group also experienced these electrophysiological effects (albeit at a lower intensity than the suprathreshold group) with no change in performance during Galvanic stimulation relative to the 0-mA (no GVS) group. Moreover, habituation to these cutaneous sensations is rapid. Subjects could not differentiate between long-duration (20-min) 1.5 mA direct current GVS and a sham stimulation in which the current was ramped down to zero after 10 s (Utz et al. 2011). Similarly, patients could not distinguish a 20-min 1 mA transcranial direct current stimulation from a sham stimulation ramped down to zero within 30 s (Gandiga et al. 2006). There was also no evidence that subjects "rushed" to complete the cognitive test battery when exposed to suprathreshold GVS; the pattern of time to respond across conditions was similar for both sub and suprathreshold current amplitudes.

There were significant differences in baseline performance on the mental rotation task between 0- and 1-mA groups. We propose that this discrepancy in error rate during mental rotation reflects the difficult nature of the task and high inter-subject variability in the population at large, resulting in significant differences when sampling small groups. This is supported by the finding that the relative change in performance from the first (baseline) to second (no or subthreshold GVS) condition did not differ between 0- and 1-mA groups (each group's performance was internally consistent) and that when group size was doubled by combining 0- and 1-mA (subthreshold) and 3.5- and 5-mA (suprathreshold) groups the discrepancy in baseline mental rotation performance was resolved. We have described a similar phenomenon during another

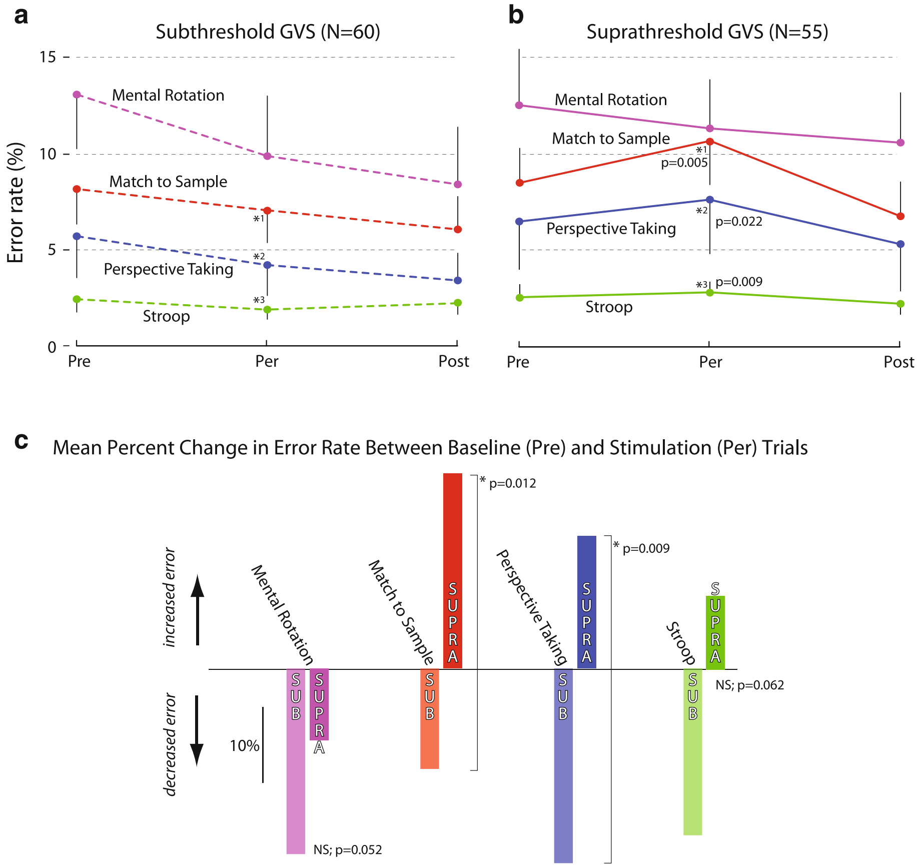

Fig. 4 Error rates (mean and 95% CI) at baseline (pre), during subthreshold or suprathreshold GVS stimulation and 15-min post-stimulation for mental rotation, match-to-sample, perspective-taking and Stroop tasks for **a** the subthreshold group (combined 0 and 1 mA GVS peak current) and **b** the suprathreshold group (combined 3.5 and 5 mA GVS peak current). Error rates for match-to-sample, perspective-taking and Stroop tasks were significantly greater during suprathreshold stimulation than during subthreshold GVS (indicated by numbered asterisk pairs). **c** Mean percent change in error rate between baseline and subthreshold and baseline and suprathreshold GVS conditions, for mental rotation, match-to-sample, perspective-taking and Stroop tasks. Error rate decreased (improved performance) on all tasks in the subthreshold group. In contrast, error rate increased in the suprathreshold GVS group for match-to-sample, perspective-taking and Stroop tasks. This relative change in performance between suprathreshold (degraded performance) and subthreshold (improved performance) groups was significant for match to sample and perspective taking

complex task: the subjective visual vertical (SVV) test (Moore et al. 2010). Analogous to baseline mental rotation performance in the current study, significant differences in error rates were observed between two groups that were internally consistent across repeated SVV test sessions; similar inter-group discrepancies in mean baseline SVV error rates were observed by Yakovleva et al. (1976).

We developed the GVS analog to replicate the sensorimotor effects of neuro-vestibular readaptation to terrestrial gravity after an extended period in microgravity (MacDougall et al. 2006; Moore et al. 2006; Moore et al. 2011); thus, it is of interest to compare the cognitive effects of GVS with the studies on cognition during and after spaceflight. Mental rotation was unaffected by microgravity exposure in eight cosmonaut subjects (Leone et al. 1995). A single-subject study found no change during or after flight in reaction time and Stroop task performance (Benke et al. 1993). Dual tasking ($N = 4$) was also unaffected by spaceflight on the Neurolab shuttle mission (STS-90) (Bock et al. 2001). Performance on the match-to-sample task was not significantly affected by spaceflight; however, considerable variance was observed in the performance of four shuttle astronaut subjects (Eddy et al. 1998).

Although there is a general agreement in the lack of an effect of microgravity and GVS exposure on attention and mental rotation, it is not feasible to draw conclusions about the effects of spaceflight on cognitive function due to the limited amount of data currently available. The results from this study suggest that when vestibular input is degraded, cognitive functions relevant to mission critical operations such as piloting (spatial memory and perspective taking) may be adversely affected. Whether this holds true for long-duration spaceflight is worthy of further

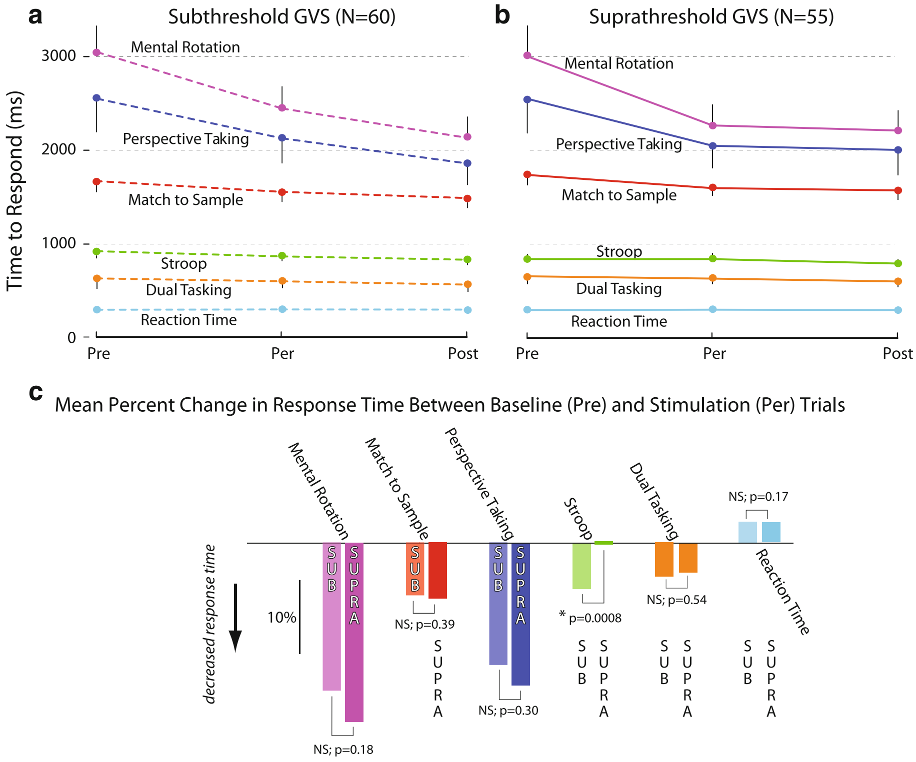

Fig. 5 Time to respond to each trial (mean and 95% CI) during mental rotation, perspective-taking, match-to-sample, Stroop, dual tasking and reaction time tasks for **a** the subthreshold and **b** the suprathreshold GVS groups. **c** Mean percent change in time to respond between baseline and subthreshold and baseline and suprathreshold conditions. Response time tended to decrease with practice in both groups and was not affected by the level of Galvanic current

study. In particular, there has been no formal investigation of egocentric mental transformation on orbit. Indirect evidence for impaired perspective taking is found in the collision of the unmanned Progress 234 spacecraft with the Mir space station in 1997. The commander was tasked to remotely pilot the Progress from a distance of 6,000 m to dock with Mir using hand controllers and a video display from the point of view of the approaching Progress. The primary cognitive issue was the difficulty in estimating the relative velocity of Progress from the video display (Ellis 2004), which required an egocentric mental transformation.

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