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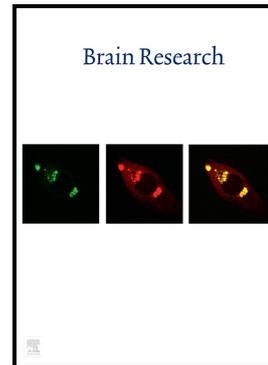
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Synchronised vestibular signals increase the P300 event-related potential elicited by auditory
oddballs

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Abstract

The perception of beat within an auditory rhythm can be facilitated when accompanied by synchronised movements. Electrophysiological investigation shows that this facilitatory effect is associated with a larger P300 amplitude. It has remained unclear, however, which movement-related processes drive this P300 effect. To investigate whether vestibular signals play a role, we administered alternating, sub-sensory (mean =.3mA) galvanic current to the vestibular nerves of participants while they counted the number of oddballs presented in a stream of tones played at a rate of 1Hz. Consistent with a vestibular effect, the P300 elicited by the oddballs was increased during stimulation relative to a sham condition, but only when the frequency of the alternating current matched that at which the tones were played. This finding supports the general idea that the vestibular system is involved in audio-motor synchronisation and is the first to show by electrophysiological means that it influences cognitive processes involved in beat perception.

Keywords: auditory-motor synchronization, attention, ERP, balance, neuro-modulation

1. Introduction

We are all familiar with the urge to nod our head, drum our fingers, tap our foot or even dance to music. This coordination of a repeated physical movement with an auditory rhythm makes it easier to both detect the beat and changes to it (see Todd and Lee, 2015). The present study investigates one mechanism by which this facilitatory effect might occur.

In a previous study we found that auditory-motor synchronization enhances the P300 response to pitch deviants (Schmidt-Kassow, Heinemann, Abel and Kaiser, 2013). Participants listened to periodic and aperiodic continuous tone sequences and were asked to silently count deviant tones that differed in sound frequency from the standard tones. While performing this task, they either sat still or pedalled on a stationary exercise bike at a rate that matched the frequency of the periodic tones. The detection of pitch deviants in periodic tone sequences while pedalling, compared to sitting still, elicited a larger P300. More so, this amplitude was greater and its latency shorter when the time taken to complete a revolution of the pedals more closely matched the frequency (1Hz) at which the deviant tones were presented. By contrast, electrophysiological responses to pitch deviants in aperiodic tone sequences were not influenced by whether participants were cycling or stationary. Precise interpretations of the P300 continue to be debated (see Patal and Azzam, 2005; Polich, 2007) but the observed effect was taken as support for the idea that synchronised limb movements improve attentionally-mediated aspects of auditory perception and may affect the way we encode and interpret beat (i.e., the basic ‘pulse’ of music) (see Butler and Trainor, 2015; Cirelli et al., 2014; Grahn and McAuley, 2009; Manning and Schutz, 2013, 2015; Morillon et al., 2013) and metre (i.e., the recurring pattern of stresses and accents in beat over time; see Tan, Pfordresher and Harré, 2012; Chemin, Mouraux and Nozaraden, 2014; Phillips-Silver and Trainor, 2005, 2007 and see also Repp and Su, 2013).

Recent studies have begun to cast light on the source of these facilitatory motor effects, and in particular, on the role of the vestibular system. The vestibular system detects

linear, angular and gravitational acceleration of the head and plays an important role in the autonomic control of eye movement, posture, gait and egocentric perception (see Smith and Zheng, 2013). Convergent sources of evidence suggest that vestibular signals may mediate audio-visual synchronisation in humans. At a biological level, the vestibular end-organs are known to respond to specific intensities and frequencies of sound (Colebatch et al., 1994) that, in turn, contribute to both short- (i.e., 10ms-30ms) and long- (i.e., 50ms-250ms) latency auditory cortical evoked potentials (Todd et al., 2014a, 2014b). Anatomical investigations indicate that the ascending vestibular afferents are closely entwined with those implicated in rhythm perception and tend to terminate in the same cortical association and motor areas (see Bense et al., 2001; Bucher et al., 1998; Todd and Lee, 2015). At the psychological level, infants' perceptions of metric structure are altered when they are bounced (i.e., subject to vestibular stimulation) in time with music (Phillips-Silver and Trainor, 2005). In adults, Phillips-Silver and Trainor (2008) demonstrated that while the interpretation of an ambiguous musical metre as a triple or duple metre is not affected by synchronous movement of the lower body (legs and feet), it is affected by the passive, synchronised rocking induced by lying on a moving seesaw. Given that these two forms of movement can be distinguished by the degree to which they activate the vestibular system, the authors tested whether head movements performed while the rest of the body remained stationary that were synchronised to either the second (duple) or third (triple) beat of a metre were sufficient to bias subsequent judgements of auditory tempo. Consistent with a vestibular-based effect, head movements alone were sufficient to bias these judgements.

To address the possibility raised by the studies above (e.g., Phillips-Silver and Trainor, 2005, 2008) that the beneficial effects of head movement on auditory perception may reflect increased proprioceptive and visual, rather than vestibular, stimulation, Trainor and colleagues tested the effect of galvanic vestibular stimulation (GVS) on auditory disambiguation. GVS involves the delivery of transcranial current to the mastoid processes

which are situated near the underlying vestibular nerve and peripheral organs (see Fitzpatrick and Day, 2004). Importantly, GVS modulates the firing rates of the vestibular (but not proprioceptive, visual or cochlear) afferents in a manner similar to natural head movement, and thereby elicits a comparable range of compensatory cortical and sub-cortical responses (Cevette et al., 2012; Lobel et al, 1998; Stephan et al., 2005). Trainor et al. (2009) asked their participants to listen to an ambiguous metric pattern (an auditory sequence that could be interpreted as duple or triple metre), while they were stimulated with super-sensory alternating current (AC) galvanic vestibular stimulation (GVS). At super-sensory levels, AC GVS induces an illusory perception of side-to-side rocking which, by manipulating the AC frequency, enabled Trainor and colleagues to match the illusory rocking sensations to the tempo (duple or triple time) of an auditory beat. As predicted, participants' interpretation of the ambiguous metre as either duple or triple was strongly determined by the frequency of the coincident vestibular stimulus; if the GVS frequency corresponded to the temporal structure of a duple metre then participants interpreted the ambiguous sequence as duple metre, while the same held for the triple metre condition. This outcome was taken as further evidence that the vestibular component of bodily movement exerts an independent influence on the perception of auditory sequences.

The outcome of the Trainor et al. (2009) study is compelling. In the current study we went a step further by investigating how sub-sensory, rather than super-sensory, GVS affects electrophysiological markers of auditory cognition. By applying a sub-sensory GVS signal we could test whether activation of the vestibular system without an experimentally-induced movement illusion is sufficient to influence auditory processing. One drawback of such an illusion is the corresponding activation of premotor regions and the supplementary motor area (Lobel et al., 1998; Stephan et al., 2005). A second problem with super-sensory currents is that they usually elicit itching/tingling underneath the electrodes. This can make it difficult to disentangle vestibular influences from those that are somatosensory in origin. Trainor and

colleagues sought to mitigate this problem by employing a control condition in which the stimulating electrodes were fastened to the elbows. Although this helped confirm that the observed effects could not be attributed to non-specific alerting, it could not address whether they might arise from cutaneous sensations emanating from the mastoid processes. By contrast, sub-sensory currents do not elicit illusory rocking or cutaneous sensations and therefore constitute a purer vestibular stimulus.

To gain insight into how the vestibular system might be affecting detection of pitch deviants, we employed an auditory oddball paradigm that enabled measurement of the P300. As discussed later, controversy surrounds the precise functional significance of the P300 waveform although there is general agreement that it is mostly driven by infrequent or unexpected stimulus change and reflects context-updating (Polich, 2007). Our specific aim was to build on the earlier finding that pedalling in time to a beat enhances the P300 response to pitch deviants (Schmidt-Kassow et al., 2013). If this effect is at least partly vestibular in origin then it should still be evident when, instead of pedalling, sub-sensory GVS is administered in time with pitch deviants.

We administered a 2-tone oddball auditory paradigm similar to that used by others to investigate the influence of stimulus timing on pitch perception (Kim and McAuley, 2013; Schmidt-Kassow et al., 2009; Schmidt-Kassow et al., 2013; Schwartz et al., 2011). Participants were seated and asked to silently count deviant tones that appeared within strings of non-deviant tones while receiving either active or sham stimulation. There were three stimulation conditions, all of which featured tones that were temporally spaced apart at a frequency of 1 Hz: (1) a sham condition in which subjects wore inactive GVS electrodes, 2) a condition in which the frequency of sub-sensory AC-GVS (1Hz) matched the temporal frequency at which the tones were presented (stim1 condition), and 3) a condition in which the frequency of sub-sensory AC-GVS (0.8Hz) did not match the temporal frequency at which the tones were presented (stim08 condition).

We reasoned that if the detection of pitch deviants is facilitated by coincident vestibular activation then the P300 elicited by auditory deviants should be amplified when the GVS signal is synchronised to the frequency at which the auditory stimuli are presented. By contrast, neither asynchronous nor sham stimulation should exert a comparable effect. Alternatively, if the mere co-presence of vestibular activity, regardless of its temporal frequency, is sufficient to influence processes concerned with deviant detection then, relative to the sham condition, the P300 amplitude should be affected by both asynchronous and synchronous GVS. Such an outcome might be predicted given that general movement of the head up-regulates metabolic activity across auditory, motor and multi-modal cortices and may therefore sharpen neural response (see Lopez et al., 2012).

Finally, we should point out that the auditory tones were presented at a frequency (600/700Hz and 75dB A) that fall outside the range typically associated with the induction of vestibular evoked myogenic potentials (Todd et al., 2014a). This is relevant because, under certain conditions, VEMPs can modulate short- and long- (i.e., N1 and P2) latency auditory cortical potentials. In the present experiment, even if (contrary to expectation) auditory tones constituted vestibular stimuli then there should be no net effect on the P300 because the tones are common to all three experimental conditions.

2. Results

2.1. Behavioural data

On average, participants made fewer than four errors in deviant tone counting per stimulation block (sham: 2.9 errors, SE = 0.6; stim08: 2.5 errors, SE = 0.6; stim1: 2.4 errors, SE = 0.7), indicating that they paid attention to the pitch changes. A one-way ANOVA revealed no significant difference between blocks, $F(2,16) = 0.29$, $p = 0.75$, $\eta_p = 0.02$.

2.2. ERP data

Grand average ERP waveforms are presented for each stimulation block and tone in Figure 1. It can be seen that, compared to standard tones, deviant tones elicited more negative-going deflections of the N1 and N2 peaks over frontal scalp areas, followed by a more positive P3 peak. This pattern appears to be enhanced on the P3 component in the stim1 stimulation block. ERP difference waves and scalp topographies for these standard/deviant tone effects in each stimulation block are shown in Figure 2.

N1 amplitude Analysis of the N1 peak revealed a main effect of region, $F(2,16) = 9.28, p = 0.002, \eta_p = 0.54$, showing that the N1 reached a greater peak amplitude over central (mean = $-2.36\mu\text{V}$, SE = 0.39) electrode sites compared to anterior (mean = $-2.02\mu\text{V}$, SE = 0.38; $t(17) = 2.67, p = 0.016$) and posterior (mean = $-1.88\mu\text{V}$, SE = 0.31; $t(17) = 2.66, p = 0.017$) electrode sites, which did not significantly differ from each other ($t < 0.6$). The main effect of laterality was also significant, $F(2,16) = 14.21, p < 0.001, \eta_p = 0.64$, showing that the N1 was maximal over midline electrodes (mean = $-2.25\mu\text{V}$, SE = 0.37) compared to electrodes over the left (mean = $-2.02\mu\text{V}$, SE = 0.35; $t(17) = 5.97, p < 0.001$) or right (mean = $-1.85\mu\text{V}$, SE = 0.29; $t(17) = 3.45, p = 0.003$) hemispheres. In addition, we found significant interactions between tone and region, $F(2,16) = 13.1, p < 0.001, \eta_p = .62$, and tone, region and laterality, $F(2, 16) = 3.14, p = 0.012, \eta_p = .4$, showing that N1 peak amplitude was larger for deviants than for standards over all frontal electrode sites, and over central and posterior lateral electrode sites. None of the interactions involving stimulation block were significant, all $F_s < 2.3, p_s > 0.12$, and crucially none of the interactions involving stimulation block and tone were significant, all $F_s < 1.8, p_s > 0.18$.

N2 amplitude The main effect of tone was significant, $F(1, 17) = 17.05, p < 0.001, \eta_p = 0.5$, reflecting a larger N2 peak amplitude for deviant tones (mean = $-1.6\mu\text{V}$, SE = 0.27)

compared to standard tones (mean = $-0.66\mu\text{V}$, SE = 0.25). This effect was qualified by interactions between tone and region, $F(2, 16) = 7.28$, $p = 0.006$, $\eta_p = 0.48$, and between tone, region and laterality, $F(4, 14) = 9.1$, $p < .001$, $\eta_p^2 = .72$, showing that the tone effect on N2 peak amplitude was largest over frontal lateral electrode sites. None of the interactions involving stimulation block were significant, and crucially none of the interactions involving stimulation block and tone were significant, all $F_s < 2.4$, $p_s > 0.13$.

P3 amplitude As predicted, the main effect of tone was significant, $F(1,17) = 7.51$, $p = 0.014$, $\eta_p = 0.31$, reflecting higher peak amplitudes for deviant (mean = $2.82\mu\text{V}$, SE = 0.6) versus standard tones (mean = $1.32\mu\text{V}$, SE = 0.18). The analysis also revealed a main effect of region, $F(2,16) = 10.79$, $p < 0.001$, $\eta_p = 0.57$, reflecting the typical distribution of maximal P3 peak amplitude over central (mean = $2.21\mu\text{V}$, SE = 0.36; $t(17) = 4.25$, $p < 0.001$) and posterior (mean = $2.14\mu\text{V}$, SE = 0.36; $t(17) = 1.98$, $p = 0.06$) electrode sites compared to anterior sites (mean = $1.86\mu\text{V}$, SE = 0.35). The main effect of laterality was also significant, $F(2,16) = 36.57$, $p < 0.001$, $\eta_p = 0.82$, showing that the P3 was maximal over midline electrodes (mean = $2.42\mu\text{V}$, SE = 0.38) compared to electrodes over the left (mean = $1.91\mu\text{V}$, SE = 0.37; $t(17) = 7.88$, $p < 0.001$) or right (mean = $1.88\mu\text{V}$, SE = 0.3; $t(17) = 4.9$, $p < 0.001$) hemispheres. In addition, a significant three-way interaction between between tone, region and laterality, $F(4,14) = 4.75$, $p = 0.012$, $\eta_p = .58$, showed that the tone effect on P3 peak amplitude was largest over central and posterior midline electrode sites.

Most importantly, the interaction between tone and stimulation was significant, $F(2,16) = 4.63$, $p = 0.026$, $\eta_p = 0.37$. Bonferroni-corrected one-tailed t-tests were used to compare the P3 peak amplitude for the deviant tones in the stim1 stimulation block with the P3 peak amplitude for the deviant tones in the sham and stim08 stimulation blocks due to our strong a-priori prediction that P3 would be amplified in the stim1 block where GVS was applied at the same frequency as tone presentation. These tests revealed a larger P3 peak in

the stim1 block (mean = 3.41 μ V, SE = 0.67) compared to both the sham block (mean = 2.52 μ V, SE = 0.64; $t(17) = 2.15$, $p = 0.047$) and the stim08 block (mean = 2.52 μ V, SE = 0.67; $t(17) = 2.03$, $p = 0.058$). None of the P3 amplitudes differed between stimulation blocks in the standard tone condition (all $t_s < 1.6$, $p_s > .1$).

3. Discussion

A previous study (Schmidt-Kassow et al., 2013) indicated that when movements are synchronised with incoming auditory stimuli, the P300 response to deviant tones within that auditory stream is amplified. However, it has remained unclear which movement-related signals drive this ERP effect. To address this question, participants performed an auditory oddball task in which they silently counted the deviant tones within a string of standard tones. Throughout this task, sub-sensory GVS was administered at a frequency that either matched (1Hz) or mismatched (0.8Hz) the rate at which the auditory stimuli were played (1Hz). The sub-sensory nature of the signal, coupled with the requirement for participants to sit still, minimized synchronous inputs from other peripheral receptors and central motor efference copies. An increase in P300 amplitude to deviant tones was observed but only when the frequency of vestibular stimulation and tones matched. This result supports the idea highlighted by Phillips-Silver and Trainor (2008) and Trainor et al. (2009) that the vestibular system is involved in audio-motor synchronisation and, more specifically, is the first to show by electrophysiological means that it influences processes related to beat perception.

Our result fits nicely with the sensory-motor theory of rhythm perception that has been proposed recently by Todd and Lee (2015). The authors argue that the vestibular system plays a key, perhaps privileged, role in rhythm perception by producing a dynamic, internal representation of the body in motion. Todd and Lee (2015) identify a diverse pattern of vestibular-thalamic connections that allow this information to influence sensory-motor circuits involved in beat detection and beat maintenance, as well as limbic circuits that

associate the movement with positive or negative affect. Of particular relevance is a proposed subcortical-cortical loop involving the cerebellum and basal ganglia that detects temporal regularities in sensory input and predicts the future course of events, essentially performing as a pacemaker (Schwartz & Kotz, 2013). Components of this loop may be especially important for analysing temporal structure when incongruent or unfamiliar stimuli are encountered (Kotz and Schwartz, 2010) and then rapidly transmitting, via cerebellum, updates to other sensory-motor areas involved in rhythm perception and, as in the present case, the detection of pitch deviants.

Inspection of the difference waves and scalp topographies in Figure 2 reveals subtle differences in the time-course and location of the P3 peak between stimulation conditions. Specifically, in the Stim1 condition the P3 begins from 300ms over central areas then spreads posteriorly and over most of the scalp. In contrast, the P3 begins from 350ms in the Sham and Stim08 conditions and maintains a central-posterior activation. These patterns suggest that synchronous vestibular and auditory stimulation elicit earlier P3 activation.

The more diffuse pattern of activation observed in the synchronous condition is consistent with the involvement of sub-cortical P300 generators, although our methodology makes it difficult to precisely localise signal source. Another generator that may also merit future investigation is the parietal lobe. The posterior parietal area is active during auditory stimulation (Miyamoto et al., 2007; Schlindwein et al., 2008) and seems especially important for the spatial (i.e. where) element of hearing. It is robustly activated during paradigms that show a response selectivity to auditory oddballs (Yoshiura et al., 1999), and when damaged elicits a temporal auditory attentional deficit (Cusack et al., 2000). Importantly, the posterior parietal lobe is also active during experimental vestibular stimulation (Lobel et al., 1998; Fasold et al., 2002, Stephan et al., 2005), and receives ascending inputs from, inter alia, the ventral posterior inferior thalamic nucleus (Akbarian et al., 1992) which includes neurons activated by rotatory vestibular cues (Büttner and Henn, 1976), and from the medial

geniculate nucleus in which many neurons respond to both vestibular and auditory nuclei (Blum et al., 1979). Within this region, the supramarginal gyrus may especially merit investigation given that it serves as both a vestibular hub (Lopez et al., 2012) and site for sensory-motor integration (Hickok and Pöppel, 2007; Linden, 2005).

Neither our experimental design nor the published literature tells us with any certainty which psychological processes within these sensory-motor circuits are likely indexed by the observed P300 amplification. One common interpretation of P300 amplification is that it reflects context-updating associated within attention and working memory (Patal, and Azzam 2007; Polich, 2007). In its original form, this account refers to the active comparison of incoming stimuli with those that have preceded it leading, in cases where there is change, to an amendment of the current schema to reflect the new stimulus context (Donchin, 1981). Allied accounts suggest that the P300 indexes the appearance of an infrequent stimulus or marks the closure of perceptual epochs when stimulus regularity is breached (Verleger, 1988). Other researchers highlight the role of arousal based on the finding that amplitude changes can be induced by manipulating arousal level which, it is assumed, constrains the availability of attentional resources (Polich and Kok, 1995). That said, the sensory-motor accounts of beat induction and rhythm perception described above highlight processes involved in temporal prediction, sensory-motor integration, motor timing, and action planning that are not so clearly attentional in nature (Schwartz and Kotz, 2013; Todd and Lee, 2015) and which, accordingly, raise further ambiguity about the psychological origin of the observed P300 response. Although this ambiguity needs to be addressed before the implications of the current data for sensory-motor processing can be fully realised, we should perhaps emphasise that such ambiguity does not overshadow our key finding that the P300 amplification observed during synchronous movement is partly vestibular in origin.

One question that arises is whether GVS affected audition prior to those processes indexed by the P300 change. The retro-insular activation observed with fMRI during GVS

(Lopez et al., 2012) alludes to an early sensory interaction, as does the modulation of short- and long-latency (N1 and N2) auditory evoked potentials by acoustic (albeit not transmastoidal) activation of the vestibular end-organs (Todd et al., 2014a, 2014b). The closer association of the N1 and N2 to cognitive than reflexive functioning perhaps makes them most likely modifiable by oddball rather than standard stimuli within the current paradigm. However there is no published evidence to indicate that the perceptual characteristics of the auditory stimuli were sufficient to elicit vestibular potentials and, perhaps more important, our statistical analysis did not find any evidence to suggest that the N1 and N2 ERP components elicited by our auditory stimuli were influenced by the presence/absence of vestibular stimulation. We must be mindful that absence of evidence is not evidence of absence, however, this result is consistent with the idea that the vestibular effect is focused around the P300 generators.

A further question that arises is whether it is simply the predictive nature of the vestibular signal that explains its effect on the P300, or whether the signal exerts a more unique, modality-specific influence. In other words, might synchronous visual or tactile stimuli achieve the same effect? The design of our study does not allow us to discount this possibility. However the design does allow us to propose that, regardless of other sensory inputs that might moderate the P300 response to auditory oddballs, vestibular stimuli exert an independent effect. The significant influence of vestibular inputs in decoding auditory structure is underlined in a recent rat study conducted by Shin (2011) which linked changes in the auditory P300 to bodily movement. Shin recorded the P300 and hippocampal theta rhythm (a marker of self-motion during locomotion) while the rats performed an auditory oddball experiment, and found that the onset of the P300 was closely tied to increases in the frequency and power of the theta rhythm. The broader implication - that stimulus updating incorporates information about concurrent motor activity - resonates with our finding that the P300 was only enhanced when the vestibular cue overlapped with the target stimulus. It is possible that

this enhancement simply reflected the increased resource needed to update processes involved in temporal tracking and rhythm perception when allied changes occurred in both auditory and vestibular input, as opposed to when a change only occurred in the auditory input. But a more intriguing possibility is that coincident vestibular inputs summoned greater processing resources because, by providing egocentric (e.g., head-centered) information about the relative location of auditory targets, they were of particular relevance to action planning and other embodied processes. Such a possibility is consistent with the idea that movement and cognition are interdependent (O'Keefe and Nadal, 1978) and leads to the prediction that vestibular cues will likely modulate the P300 and other 'late' ERPs in other sensory domains and embodiment paradigms.

In sum, we believe that our data further clarify how the vestibular system contributes to auditory-motor synchronisation. We do not wish to imply that vestibular signals are the only possible source of predictive timing within the auditory domain. For example, Iordanescu et al. (2013) reported that temporal bisection is more sensitive when initiated by a voluntary action (key press) than by a passive cue. Likewise, Morillon and colleagues (2013) showed that participants are better able to classify a target beat as higher or lower pitch when tracking an underlying reference beat via key press. Although movements as seemingly subtle as a key press may in fact displace the head and thereby initiate a vestibular response, these data are consistent with other aspects of the motor response facilitating auditory perception. While synchronised vestibular signals seem sufficient to magnify P300-related processes linked to beat perception, further study is needed to determine their necessity.

4. Method and Materials

4.1. Participants

Twenty three right-handed volunteers with self-reported, unimpaired hearing and no documented neurological or psychiatric history participated in the study. Prior to analysis, 5

datasets were excluded due to participants feeling the sub-sensory GVS stimulation (N=3), poor performance on the deviant tone counting task (<50% accuracy, N=1), and technical problems with the EEG acquisition (N=1). The remaining 18 participants (8 females, 10 males) had a mean age of 23 years (SD=4). The study was approved by the University of Kent School of Psychology ethics committee and complied with the Code of Ethics of the World Medical Association (Declaration of Helsinki). All participants gave informed written consent prior to participation, and were paid £10 for their participation.

4.2. Experimental Stimuli and Procedure

After GVS and EEG electrode application, participants were seated in a comfortable chair in a windowless, air-conditioned room. The experiment was controlled using E-Prime software. Three blocks of a classic auditory oddball paradigm with two sinusoidal tones of 50ms duration were administered. Standard tones had a frequency of 600Hz and were presented with a probability of 0.75, while deviant tones had a frequency of 700Hz and were presented with a probability of 0.25. There were approximately 200 trials in each block, although the precise number differed each time to compel participants to count rather than simply recall the number of deviants from an earlier block. Tones were presented with a stimulus onset asynchrony of 1000ms (i.e., 1Hz) at 75dB(A). These stimulus parameters were chosen partly because they fall outside the range typically associated with the induction of vestibular evoked myogenic potentials and modulation of both short- and long- (i.e., N1 and P2) latency auditory cortical potentials (see Todd et al., 2014a, 2014b). Each block lasted approximately five minutes during which time participants were asked to silently count deviant tones, presented via a desktop computer's inbuilt loudspeakers. Pseudo-randomization was applied to ensure that two deviant tones could not appear in a row. To minimise distraction and eye movements, throughout the task participants faced a black computer screen displaying a white fixation cross. In two of the experimental blocks, sub-sensory GVS was applied below

participants' pre-determined sub-sensory threshold (see below). In one block, GVS was applied at the same frequency as tone presentation (1Hz, stim1 block), while in another block, it was applied at a different frequency (0.8 Hz, stim08 block). In a third block, no GVS was applied (sham block). The order of the blocks was counterbalanced across participants.

4.3. GVS protocol

In the active stimulation blocks, participants received sub-sensory, binaural alternating current to the left and right mastoids. Current was delivered through a pair of 3cm² carbon-rubber, self-adhesive, disposable stimulating electrodes (ComfortEase, Empi) placed over the mastoid processes and connected to a Magstim Eldith Transcranial DC Stimulator Plus™ device. To ensure complete electrical contact with the electrodes, surrounding skin was cleansed with an alcohol swab and conductive Tac-gel™ coated on the undersides of the electrodes. To establish participants' individual sensory thresholds, we followed a stepwise protocol in which a mild, super-sensory signal of 1mA was first applied; at this amplitude a feeling of painless tingling occurs underneath one or both electrodes. We then systematically decreased the amplitude by 0.1 mA until the participant said that he/she could no longer feel any unusual sensation. This judgement was reaffirmed by twice reapplying the same current – if at this point a participant reported any unusual sensation then the stepwise reduction was resumed. The mean current at which participants could not feel any sensation was 0.3 mA (SD=0.08; minimum=0.2 mA, maximum=0.4mA). Consistent with the elicitation of a central vestibular response, currents of this magnitude have been shown to reliably evoke a short-latency, torsional slow-phase eye movement in which, to counteract the perceived tilt/roll towards the cathodal electrode, the top of the eyes rotate towards the anodal electrode (Cauquil et al., 2003). Participants were informed that although they would receive periods of active stimulation during the experiment, there would be periods when no stimulation was

discharged. To maintain participant blinding, the device was operated from an adjacent control room. During sham stimulation, no current was discharged to the electrodes.

Although supersensory stimulation was not applied in the actual experiment, it was applied beforehand (after sensory thresholding) to confirm that the stimulation set-up was eliciting vestibular responses at the desired frequencies. Participants were administered 1mA after which the amplitude was steadily increased by 0.1mA until a stable illusion of sideways rocking was reported. The mean level at which this occurred was 1.7mA (SD=0.34; minimum=1.2 mA, maximum=2.2 mA). Participants then received the super-sensory signal for two minutes during which time the signal was discharged at a frequency of 1Hz for 1 minute and 0.8Hz for the other minute (the order of which was counterbalanced). During this period they were also asked to tap their index finger on the space key of a computer keyboard in time with their perceived side-to-side head movements. Median tapping frequency was 0.83 Hz (SD=0.2) in the 0.8 Hz GVS block and 1.0 Hz (SD=0.2) in the 1 Hz GVS block. These tapping frequencies confirmed that the two stimulation frequencies were eliciting vestibular responses that would be, as planned, either out- or in-phase with the auditory stimuli.

4.4. Electrophysiological Measures

A Brain Vision ActiCap cap was used for continuous recording of electroencephalographic (EEG) activity from 16 Ag/AgCl electrodes over central scalp sites (F3, F4, Fz, FC3, FC4, FT9, FT10, C3, C4, Cz, CP3, CP4, CPz, P3, P4, Pz). These electrodes matched the P300-related region of interest described in our previous studies (Schmidt-Kassow et al., 2013; Schwartze et al., 2011). During EEG acquisition, AFz served as ground. Electrodes were referenced on-line to electrode FCz and recordings were re-referenced to averaged FT9 and FT10 off-line. Impedances were kept below 10 k Ω . Eye movements and blinks were recorded with two additional sets of bipolar electrodes placed above and below participants' left eye and on the outer canthus of each eye. EEG was digitized using a QuickAmp amplifier (Brain

Products, Munich, Germany) with a sampling frequency of 500 Hz and an anti-aliasing filter of 140Hz.

EEG data analysis was carried out with Brain Vision Analyzer 2. Prior to segmentation, EEG and EOG activity was band-pass filtered (0.1-30 Hz, 12 dB/oct), and a bandstop filter with a frequency of .9 Hz and a bandwidth of .6 Hz (filter order=4) was applied to remove the GVS artifact from the EEG data. This same band-stop procedure was applied to data in all three stimulation blocks (including sham) to ensure identical processing procedures. EEG activity containing blinks or horizontal eye movements was corrected using a semi-automatic ocular ICA correction approach. The continuous EEG record was then segmented into epochs of 1500ms, starting 500ms before the onset of the critical auditory stimulus. Semi-automatic artifact detection was run to identify and discard trials with non-ocular artifacts (drifts, channel blockings, EEG activity exceeding $\pm 100\mu\text{V}$). This procedure resulted in an average trial-loss of 5.1% per condition. Finally, epochs were averaged for each participant, condition and electrode site, with a 100ms pre-stimulus baseline correction. Only those standard trials that directly preceded a deviant trial entered the statistical analysis to provide equal number of standard and deviant trials.

4.5. Statistical analysis

Statistical analyses were carried out with the software IBM SPSS Statistics 22 (IBM Corporation 1989, 2011, USA). ERPs were computed separately for standard and deviant tones, and are plotted for each stimulation block in Figure 1. Three prominent peaks were identified from these waveforms as N1 (between 100 and 200ms), N2 (200-300ms) and P3 (250-500ms). Peak amplitudes (i.e., the most negative points in the N1 and N2 intervals, and the most positive point in the P3 interval) were identified for standard and deviant trials in each stimulation block separately using an automatic procedure, and data was analysed in the area $\pm 25\text{ms}$ around each peak. ERP amplitudes were computed for electrodes F3, F4, Fz, C3, C4, Cz, P3, P4, and Pz. ERP amplitudes for each component were analysed using a repeated-measures ANOVA that crossed region (anterior, central, posterior), laterality (left, midline, right), stimulation (sham, stim08,

stim1), and tone (standard, deviant). Bonferroni-Holm corrected follow-up tests were conducted where appropriate (Holm, 1979).

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Figure Legends

Figure 1. Grand average ERPs elicited by tones (standard or deviant) in each stimulation block (sham, GVS stimulation at 0.8Hz (stim08), and GVS stimulation at 1Hz (stim1)) at three representative midline electrodes (Fz, Cz and Pz). Note that negativity is plotted upwards.

Figure 2. Difference waveforms (deviant minus standard), showing time course and amplitude differences for each stimulation block (sham, GVS stimulation at 0.8Hz (stim08), and GVS stimulation at 1Hz (stim1)) at three representative midline electrodes (Fz, Cz and Pz). Scalp maps show the topography of this difference for each stimulation block, for the time intervals 250-300ms, 300-350ms, 350-400ms and 400-450ms (P3) relative to tone onset.

Highlights

- We tested if vestibular signals change the P300 response to auditory pitch deviants
- A change was only seen when vestibular and auditory signals were synchronised

- The result helps clarify how vestibular signals influence auditory perception

