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Faculty of Biology and Medicine Publication

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Published in final edited form as:

Title: Location-independent and location-linked representations of sound objects.

Authors: Bourquin NM, Murray MM, Clarke S

Journal: NeuroImage

Year: 2013 Jun

Volume: 73

Pages: 40-9

DOI: [10.1016/j.neuroimage.2013.01.026](https://doi.org/10.1016/j.neuroimage.2013.01.026)

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Location-independent and location-linked representations of sound objects

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32 pages

4 Figures

Conflict of interest: none

ABSTRACT

For the recognition of sounds to benefit perception and action, their neural representations should also encode their current spatial position and their changes in position over time. The dual-stream model of auditory processing postulates separate (albeit interacting) processing streams for sound meaning and for sound location. Using a repetition priming paradigm in conjunction with distributed source modeling of auditory evoked potentials, we determined how individual sound objects are represented within these streams. Changes in perceived location were induced by interaural intensity differences, and sound location was either held constant or shifted across initial and repeated presentations (from one hemispace to the other in the main experiment or between locations within the right hemispace in a follow-up experiment). Location-linked representations were characterized by differences in priming effects between pairs presented to the same vs. different simulated lateralizations. These effects were significant at 20-39 ms post-stimulus onset within a cluster on the posterior part of the left superior and middle temporal gyri; and at 143-162 ms within a cluster on the left inferior and middle frontal gyri. Location-independent representations were characterized by a difference between initial and repeated presentations, independently of whether or not their simulated lateralization was held constant across repetitions. This effect was significant at 42-63 ms within three clusters on the right temporo-frontal region; and at 165-215 ms in a large cluster on the left temporo-parietal convexity. Our results reveal two varieties of representations of sound objects within the ventral/What stream: one location-independent, as initially postulated in the dual-stream model, and the other location-linked.

Keywords

Sound recognition; auditory processing streams; auditory cortex; auditory evoked potentials; repetition priming

1. Introduction

Today's view of auditory processing is very much influenced by the dual-stream model (Rauschecker and Scott, 2009), which is derived from electrophysiological studies in non-human primates (Rauschecker and Tian, 2000; Kaas and Hackett, 2000) as well as from activation (Alain et al., 2001; Maeder et al., 2001; De Santis, Clarke, and Murray, 2007) and lesion studies in humans (Clarke et al., 2000; 2002). Its basic tenet, segregation of auditory processing between the ventral/What stream, leading ultimately to the identification of a sound object, and the dorsal/Where stream, leading to its localization, is well supported by several lines of evidence. The dorsal/Where stream has been shown to be involved in different aspects of auditory spatial processing (Arnott et al., 2004), including the refinement of auditory spatial representations associated with training-induced improvement in discrimination (Spierer et al., 2007a, 2011) and the explicit judgment of sound positions (as demonstrated by transcranial magnetic stimulation: Lewald, Wienemann, and Boroojerdi, 2004; At, Spierer, and Clarke, 2010). Neural activity within the ventral/What stream codes for environmental sound objects (Murray et al., 2006; De Lucia, Clarke, and Murray, 2010a) and exhibits repetition-induced priming effects, which have been reported with two types of paradigms. First, a series of studies described a decrease in neural responses to repeated vs. initial stimulus presentations that were themselves separated by intervening stimuli or by separate study and test sessions (Bergerbest et al., 2004; Murray et al., 2008; De Lucia et al., 2010b; Bourquin et al., 2012a). Repetition priming effects usually manifest as suppression but sometimes as enhancement (Henson et al., 2000); depending on parameters that are currently unclear. Second, other studies used an adaptation paradigm, with initial and repeated presentations paired together in (nearly) immediate succession (e.g. Altmann et al., 2008 a ,b; 2010; Doehrmann et al., 2008). The underlying rationale is that the recovery from an adapted level of responsiveness reveals sensitivity to a given stimulus or cognitive dimension (Grill-

Spector and Malach, 2001). One advantage conferred by the first type of paradigm, where initial and repeated presentations are separated by intervening stimuli, is that repetition-related effects can be dissociated more readily from habituation to low-level stimulus features. Furthermore, several previous auditory evoked potential studies used this approach successfully to investigate repetition priming effects within sound object representations (Murray et al., 2008; Bourquin et al., 2012a) and their further use will allow more readily for a synthesis of findings.

It is likewise worth noting that the overwhelming majority of these previous studies examining repetition-induced plasticity in sound representations concentrated on semantic (and not spatial) features of sound object representations and used centrally presented stimuli for primes and repeats. One exception is found in Altmann et al. (2008a) who investigated pattern vs. location changes with an fMRI adaptation paradigm. They found modulations for pattern changes within the ventral/What stream and modulations for location changes within the dorsal/Where stream.

Using the repetition priming paradigm the present study examined how the combined information of sound object identity and its location is represented within the auditory processing streams. The study was driven by the hypothesis that the human auditory cortex carries both location-independent and location-linked representations of sound objects. The former was expected to be characterized by repetition effects independent of the respective lateralizations of the prime and the repeat, and the latter to yield different repetition effects in pairs with the same vs. different lateralizations. Previous work, which did not vary the spatial location of stimuli across initial and repeated presentations, revealed priming effects at 156-216 ms post-stimulus onset within cortical regions known to be part of the ventral auditory

stream, on the middle temporal gyrus and within the superior temporal sulcus on the left side (Murray et al., 2008); these effects were in terms of the global field power and not in terms of modulations in the topography of the auditory evoked potentials. These effects are believed to characterize a semantic, non-spatial representation of sound objects, but this hypothesis has never been actually tested. The existence of position-linked representations of sound objects is suspected on the basis of a recent 7T fMRI study; out of two early stage auditory areas known to be selective for sound recognition (as opposed to sound localization; Viceic et al., 2006), one was shown to be modulated by the position of environmental sounds, while the other was not (van der Zwaag et al., 2011). Results presented in this paper suggest that the auditory ventral/What pathway carries a dual representation of sound objects, one position-independent and the other position-linked.

2. Materials and Methods

2.1 Main Experiment

2.1.1 Subjects

Twelve right-handed male subjects (mean \pm SD lateralization index = 84.08 ± 6.30 ; Oldfield, 1971) aged between 20-38 years (mean \pm SD = 26.3 ± 5.5 years) participated in the study. None had a history of neurological or psychiatric illness, and all reported normal hearing. They provided written informed consent and were paid modestly for their participation in the experiment. This study was approved by the Ethics Committee of the Faculty of Biology and Medicine of the University of Lausanne.

2.1.2 Experimental procedures

Subjects listened to environmental sounds and classified them, as rapidly as possible, as produced by a living or manufactured source by pressing one of two buttons of a serial

response box while continuous 160-channel EEG was recorded (detailed below). They performed a sound categorization task, which minimized the necessity to process spatial information for task completion. In this way, we could determine orthogonal influences of spatial information on object processing as well as repetition effects. Each of the 40 sound objects (20 from living: baby crying, bird, cat, coughing, chicken, clearing throat, cow, crow, dog, donkey, frog, gargling, laughter, owl, pig, rooster, scream, sheep, sneezing, and whistling; and 20 from manufactured sound sources: accordion, bicycle bell, car horn, cash register, church bell, cuckoo clock, doorbell, door closing, flute, glass shattering, guitar, harmonica, harp, organ, piano, police siren, saxophone, telephone, trumpet and violin; as already used by Murray et al., 2006) were presented twice (initial and repeated presentation) within a block after 0 to 5 other intervening sounds. The sounds were delivered through insert earphones (ER-4P; www.etymotic.com) at a sound pressure level of 88dB to the ear receiving the more intense sound and 35dB to the opposite ear 88dB. This generated an intensity ratio of 72:28 and an IID of 8.2dB, using the formula $IID = 20\log(72/28)$. As described in the follow-up study (see below), they were perceived at ca 65°. Similar IIDs were used in previous studies yielding lateralizations of similar angular values (e.g. Tardif et al., 2006; Spierer et al., 2009). Within each of the 16 blocks, sounds were presented with a pseudo-random inter-stimulus interval of 1600 ms to 2400 ms (in 100 ms steps). The lateralization of the initial and the repeated presentations of a given object within a block were either the same or different (same = S: R-R, L-L; different = D: R-L, L-R; the 4 possibilities each accounted for 25% of the pairs within a block and were mixed pseudo-randomly). The initial and the repeated presentations of a given sound object were either acoustically different exemplars of the same sound object (e.g. of the same dog barking) or identical exemplars. This was done to minimize cross-over effects across blocks (along with the use of a break between blocks; see also Murray et al., 2008 for a similar approach). The four possibilities accounted each for

25% of the pairs within a block and were pseudo-randomly distributed across the 16 blocks of the whole experiment. The relationship between the acoustic nature of the repeated exemplar (identical or not) and its position with respect to the initial presentation (same or different) was pseudo-randomized and balanced across sound objects and subjects. Because prior research has demonstrated equivalent priming and repetition suppression effects with both acoustically identical and different exemplars (De Lucia et al., 2010b), we reasoned that any effects linked to using identical vs. distinct exemplars would be counter-balanced across our factors of interest (i.e. same/different sound lateralization and initial/repeated presentation). Moreover, the repeats at the same lateralization and those at different lateralizations were equally often preceded by stimuli in the same or different position (Fig. 1) to avoid bias arising from spatial attentional priming induced by the preceding stimulus (Posner, 1980).

The time lag and the number of intervening items between the initial and repeated presentations of a given sound object ranged from 2 to 12 sec. (0 to 5 distinct intervening items, none of which were exemplars of the same auditory object) and they were kept constant across participants. In order to avoid systematic bias arising from order presentation across subjects, the presentation order of the blocks was determined by a Latin square design. The blocks were separated by six minute breaks, during which the participants were exposed to another kind of auditory stimuli (series of four pure tones) which were irrelevant to the experimental paradigm. This was in part done to allow sufficient time for an effective “resetting” of priming effects from one block to the next and therefore to minimize any carry-over effects from one block to the next (Murray et al., 2008). The whole experiment lasted approximately 2.2 hours.

2.1.3 EEG recording and pre-processing

Continuous EEG was recorded at 1024Hz through a 160-channel Biosemi ActiveTwo system (Biosemi, Amsterdam, Netherlands). EEG pre-processing and analyses were performed using Cartool (Brunet, Murray, and Michel, 2011; <http://sites.google.com/site/fbmlab/cartool>). EEG epochs including 100 ms pre- to 500 ms post-stimulus onset were averaged, and auditory evoked potentials (AEPs) were calculated for the four experimental conditions: congruent and incongruent pairs; initial and repeated presentations. Trials with eye blinks or transient noise were rejected offline using a semi-automated $\pm 60\mu\text{V}$ criterion at every channel as well as visual inspection of the raw EEG signals. The average number of accepted epochs was 269 ± 2 (mean \pm standard deviation) for each of the four AEPs calculated per subject. For the analysis involving the collapsing of data across all initial presentations vs. all repeated presentations (irrespective of whether or not the perceived location remained constant), this figure increased to 537 ± 4 epochs. There was no significant difference in the number of accepted trials across the experimental conditions for the main analysis ($F_{(3,9)} < 0.21$, $p = 0.89$) or for the analysis involving collapsed data ($t_{(11)} < 0.81$, $p = 0.43$). Prior to group averaging, data at artefact channels from each subject were interpolated using 3-dimensional splines (Perrin et al., 1987). Data were then recalculated against the average reference and band-pass filtered between 0.68 and 40Hz. Data were baseline corrected over the 100 ms pre-stimulus period during group-averaging.

2.1.4 Source estimations and analyses

Our analyses here are based solely on distributed source estimations. This approach is akin to what is routinely performed in magnetoencephalographic studies of brain function (Ahlfors et al., 2010; Michel and Murray, 2012). We estimated the intracranial sources of the AEPs as a function of time using a distributed linear inverse solution (ELECTRA) and applying the local autoregressive average (LAURA) regularization approach to address the non-uniqueness of

the inverse problem (Grave de Peralta Menendez et al., 2001, 2004; Michel et al., 2004). The inverse solution algorithm is based on biophysical principles derived from the quasi-static Maxwell's equations; most notably the fact that independent of the volume conductor model used to describe the head, only irrotational and not solenoidal currents contribute to the EEG (Grave de Peralta Menendez et al., 2001, 2004). As part of the regularization strategy, homogenous regression coefficients in all directions and within the whole solution space were used. The version of LAURA used here employs a realistic head model with 3005 nodes arranged within the gray matter of the Montreal Neurological Institute's (MNI) average brain. This implementation of LAURA was generated with the Spherical Model with Anatomical Constraints (SMAC; Spinelli et al., 2000). As an output, LAURA provides current density value (in $\mu\text{A}/\text{mm}^3$) at each node. Prior fundamental and clinical research have documented and discussed in detail the spatial accuracy of this inverse solution, which is on the order of the grid size of the solution points (here $\sim 6 \times 6 \times 6 \text{mm}$; Grave de Peralta Menendez et al., 2004; Michel et al., 2004; Gonzalez Andino et al., 2005a,b; Martuzzi et al., 2009). Statistics on the source estimations was performed on a millisecond-by-millisecond level over the 500 ms post-stimulus interval (graphical user interface programmed and provided by Dr. Jean-Francois Knebel of the Functional Electrical Neuroimaging Laboratory; www.unil.ch/fenl). Only effects meeting the following triad of criteria were considered significant: 1) nodes meeting or exceeding the $p \leq 0.05$ significance threshold, 2) a cluster extent threshold of $k_E \geq 15$ contiguous nodes, and 3) a temporal contiguity of at least 18 ms (20 data points at 1024Hz). The spatial extent criterion was determined using the AlphaSim program (available from the Analysis of Functional NeuroImages website: <http://afni.nimh.nih.gov>) and as described in former reports from our and others' groups (e.g. Toepel et al., 2009; Britz and Michel, 2010; De Lucia et al., 2010a; Knebel et al., 2011; Knebel and Murray, 2012; Bernasconi et al., 2011; Toepel et al., 2012; Thelen et al., 2012). This program performs 10,000 Monte Carlo

permutations on the 3005 nodes of our lead field matrix to determine the false discover rate for clusters of different sizes and a given level of presumed spatial smoothness (here 6mm FWHM). This simulation yielded an equivalent node-level p-value of $p \leq 0.0005$ for a given moment in time. The temporal criterion was selected based on works that examined the impact of varying levels of temporal autocorrelation on the probability of observing a significant difference at a given point within a time series and is an extrapolation of criteria proposed assuming 90% temporal autocorrelation (cf Table 1 in Guthrie and Buchwald, 1991).

To identify effects of same vs. different lateralizations, source estimations of the initial presentation was subtracted from the repeated one and means were calculated for each subject for pairs with the same (ΔS) and for pairs with different lateralizations (ΔD). In this way the influence of specific lateralization of the initial presentation, which could be to the right or to the left, was cancelled out. The source estimation differences for pairs with the same vs different lateralizations were then statistically contrasted with a paired t-test. To ascertain if a given effect of sound source repetition followed from enhancement or suppression in a given region, we separately compared the ΔS and ΔD source estimations against zero. To identify nodes exhibiting a general effect of sound repetition, we contrasted source estimations to initial and repeated presentations of sounds collapsed across their position of presentation. We would emphasize that all of these analyses were performed dynamically (i.e. for each time-sample spanning both pre-stimulus and post-stimulus intervals).

2.2 Follow-up Experiment

A follow-up experiment was conducted to address the potential criticisms that i) location-linked effects were observed because perceived lateralizations were far apart, within different hemispaces and ii) the use of IIDs of +8.2dB and -8.2dB could be assimilated to right vs. left monoaural conditions. In this experiment, location-independent and location-linked repetition

priming effects were investigated in a second group of subjects using lateralizations of 15dB difference in sound pressure level (which generated an intensity ratio of 55:45 and an IID of 1.7dB) and 53dB difference in sound pressure level (yielding an IID of 8.2dB with the formula $\text{IID} = 20\log(55/45)$) within the right hemispace. As assessed behaviourally after the AEP recordings, the lateralizations were perceived as significantly different ($t_{(10)} = 7.62; p < 0.0001$), at 14.6° (S.D. = 14.4°) and 65.0° (S.D. = 21.8°), respectively. The latter value is in agreement with previous studies which used similarly large IIDs for complex sound lateralizations (Clarke et al., 1999; Spierer et al., 2009; Duffour-Sokolov et al., 2012) and precludes an assimilation with mono-aural conditions.

2.2.1 Subjects

Eleven right-handed subjects (mean \pm SD lateralization index = 85.6 ± 18.5 ; Oldfield, 1971) aged between 23-28 years (mean \pm SD = 25.1 ± 1.8 years) participated in the follow-up experiment. None had a history of neurological or psychiatric illness, and all reported normal hearing. They provided written informed consent. This study was approved by the Ethics Committee of the Faculty of Biology and Medicine of the University of Lausanne.

2.2.2 Experimental Procedures

Subjects listened to environmental sounds and classified them, as rapidly and accurately as possible, as produced by a living or manufactured source by pressing one of two buttons on a serial response box while continuous 160-channel EEG was recorded (same procedures as in the main experiment). The stimuli were the same sounds as in the main experiment, except that they were lateralized to the right hemispace with an IID of **1.7** or **8.2** dB. The sounds were presented twice (initial and repeated presentation, respectively) within a block and the lateralization of the initial and the repeated presentations of a given object were either the

same or different (same = S: **8.2-8.2dB, 1.7-1.7dB**; different = D: **8.2-1.7dB, 1.7-8.2dB**; the four possibilities accounted each for 25% of the pairs within a block and were pseudo-randomly distributed across the 8 blocks of the follow-up experiment. After they had completed the AEP recordings, subjects were asked to listen to the stimuli again and to indicate their perceived position; the angular responses were averaged and compared with a paired t-test (a response at the mediosagittal plane corresponded to 0°, that at the level of the right ear to 90°). The follow-up experiment lasted approximately 1.1 hours.

2.2.3 EEG recording and pre-processing

Data were acquired with the same hardware and pre-processed in the same way as in the main experiment above. EEG epochs including 100 ms pre-stimulus to 500 ms post-stimulus onset were averaged, and AEPs were calculated for the four experimental conditions: congruent and incongruent pairs; initial and repeated presentations. The average number of accepted epochs was 135 ± 1 (mean \pm standard deviation) for each of these four AEPs calculated per subject. For the analysis involving the collapsing of data across all initial presentations vs. all repeated presentations (irrespective of whether or not the perceived location remained constant), this figure increased to 270 ± 1 epochs. There was no significant difference in the number of accepted trials across the experimental conditions for the main analysis ($F_{(3,8)} < 0.15$, $p = 0.92$) or for the analysis involving collapsed data ($t_{(10)} < 0.20$, $p = 0.85$).

2.2.4 Source estimations and analyses

Source estimations were performed as in the main experiment, with the exception that analyses were *a priori* restricted to the clusters and time periods identified in the main experiment. For each cluster and time period exhibiting position-linked effects, the average source estimation in response to the initial presentation was subtracted from that to the

repeated presentation for each subject for pairs with the same (ΔS) and for pairs with different lateralizations (ΔD). These source estimation differences were then statistically contrasted with a paired t-test. For the cluster exhibiting a position-independent effect, we contrasted source estimations to initial and repeated presentations of sounds collapsed across their position of presentation.

3. Results

Behavioral results

In the main experiment all subjects readily categorized stimuli as living vs. manufactured (mean accuracy \pm s.e.m: 95% \pm 0.02% correct responses); a 2 x 2 repeated measure ANOVA with factors of i) Presentation (initial vs repeated) and ii) Lateralization within prime repeat pairs (same vs different) revealed a significant main effect of Presentation ($F_{(1,11)}=5.56$; $p=0.04$), but not of Lateralization ($F_{(1,11)}=0.47$; $p=0.51$) or interaction between the two factors ($F_{(1,11)}=0.15$; $p=0.70$). The response times were also analyzed with a 2 x 2 repeated measure ANOVA, which did not reveal any significant main effect or interaction (main effect of Presentation: $F_{(1,11)}=2.37$; $p=0.15$, main effect of Lateralization within prime repeat pairs: $F_{(1,11)}=3.92$; $p=0.07$, and interaction between the two factors: $F_{(1,11)}=3.31$; $p=0.10$). The use of pairs where the initial and the repeated presentations of a given sound object were acoustically different or identical did not significantly influence response times (Table 1); a 2 x 2 x 2 repeated measure ANOVA with factors of Acoustical-nature, Presentation and Lateralization within prime repeat pairs did not reveal any significant main effect or interactions (main effect of Acoustical-nature: $F_{(1,11)}=0.19$; $p=0.68$, main effect of Presentation: $F_{(1,11)}=2.37$; $p=0.15$, main effect of Lateralization within prime repeat pairs: $F_{(1,11)}=3.92$; $p=0.07$, Acoustical-nature and Presentation interaction: $F_{(1,11)}=0.98$; $p=0.35$, Acoustical-nature and Lateralization within prime repeat pairs interaction: $F_{(1,11)}=0.20$;

$p=0.67$, Presentation and Lateralization within prime repeat pairs interaction: $F_{(1,11)}=3.31$; $p=0.10$, and Acoustical-nature, Presentation and Lateralization within prime repeat pairs interaction: $F_{(1,11)}=0.04$; $p=0.84$).

Behavioral data from the follow-up experiment showed a very similar pattern of accuracy and reaction times to the main experiment. Participants were highly accurate (i.e. >95%). The 2x2 ANOVA using the accuracy data did not reveal either a main effect or an interaction (all p 's > 0.35). The repeated measure ANOVA with response times did not reveal any significant main effect or interaction (main effect of Presentation: $F_{(1,10)}=2.32$; $p=0.16$, main effect of Lateralization-within-prime-repeat-pairs: $F_{(1,10)}=3.76$; $p=0.08$, and interaction between the two factors: $F_{(1,10)}=0.076$; $p=0.79$).

Evoked potentials to primes and repeats

AEPs showed a significant effect of presentation at different time frames at individual electrodes (example of electrode Fz in Fig. 2). Time frame-wise paired t-tests performed on the whole electrode montage revealed significant modulations at frontal, occipital and left temporo-parietal sites over the 130-220 ms (revealing a modulation of the auditory N1-P2 complex).

Repetition priming effects for same vs. different lateralizations

Differences in priming effects for pairs presented at the same vs. different lateralizations (ΔS vs. ΔD), were analyzed with millisecond-wise paired t-tests on all solution points of distributed source estimations, including over the pre-stimulus period. Over the 20-39 ms post-stimulus onset period, a significant difference was observed in a left temporal cluster comprising the posterior parts of the superior and middle temporal gyri (but not the planum

temporale) (Fig. 3). Additional analyses compared responses to zero-levels and revealed that during this time window, congruent pairs resulted in significant repetition suppression over the 22-40 ms post-stimulus onset interval and incongruent pairs resulted in repetition enhancement over the 24-39 ms post-stimulus onset interval (no effects were observed at earlier latencies, including during the pre-stimulus period). Over the 143-162 ms post-stimulus onset period a significant difference was found in a left frontal cluster comprising the inferior and partially the middle frontal gyri. During this time period there was significant repetition suppression for pairs at the same lateralizations and significant repetition enhancement for pairs at different lateralizations; the mean activity of the cluster was statistically different from zero over the 144-167 ms and over the 144-160 ms post-stimulus onset period for the ΔS vs. ΔD conditions, respectively.

The follow-up experiment specifically tested for these repetition priming effects over the 20-39 ms post-stimulus period within the above left temporal cluster as well as over the 143-162 ms post-stimulus period within the left frontal cluster. The follow-up experiment failed to replicate the finding over the 20-39 ms post-stimulus period ($t_{(10)}=0.13$; $p=0.45$). By contrast, effects over 143-162 ms within the left frontal cluster were indeed replicated ($t_{(10)}=1.91$; $p<0.05$). Pairs presented at the same lateralization resulted in repetition suppression, and pairs presented at different lateralizations resulted in repetition enhancement.

Position-independent repetition priming effects

Spatio-temporal patterns of neural activity associated with position-independent representations were identified by comparing initial presentations vs. repeats independently of whether sounds were presented at the same vs. different lateralizations across initial and repeated trials. The time frame-wise paired t-tests (IP vs. RP) performed on source

estimations were applied to all solution points, including the pre-stimulus period (Fig. 4). Over the 42-63 ms post-stimulus onset period, three individual clusters within the right fronto-temporal region yielded statistically significant repetition enhancement: i) the posterior part of the inferior frontal gyrus and anterior part of the insula; ii) the anterior parts of the middle and superior temporal gyri; and iii) the fusiform and parahippocampal gyri, the hippocampal formation and the amygdala. Over the 165-215 ms post-stimulus onset period, a large cluster within the left hemisphere yielded statistically significant repetition suppression. It comprised the posterior parts of the supratemporal plane (including Heschl's gyrus and planum temporale) and of the superior, middle and inferior temporal gyri; the fusiform, lingual and middle occipital gyri; the inferior parietal lobule and the inferior part of the superior parietal lobule.

Analyses of data from the follow-up experiment did not meet our significance criterion either over the 42-63 ms post-stimulus onset period ($t_{(10)}=0.69$; $p=0.51$) or over the 165-215 ms post-stimulus onset period ($t_{(10)}=1.20$; $p=0.13$). However, statistically significant repetition suppression was observed over a slightly earlier and overlapping time period (150-170 ms post-stimulus onset period, $t_{(10)}=2.82$; $p<0.05$).

Discussion

Our results suggest that the auditory ventral/What pathway carries a dual representation of sound objects. They demonstrate a truly position-independent representation of individual sound objects, as initially postulated in the dual-stream model (Arnott et al., 2004; Scott, 2005; Rauschecker and Tian, 2000; Rauschecker and Scott, 2009; Leaver and Rauschecker, 2010; van der Zwaag et al., 2011). But they also reveal, for the first time, a position-linked representation of sound objects within the ventral/What stream.

Position-independent sound object representations

The dual-stream model of auditory processing postulated that the identity of sound objects is coded within the ventral/What and auditory spatial information within the dorsal/Where stream (Kaas and Hackett, 2000; Rauschecker and Tian, 2000). A series of priming studies confirmed that semantic coding involves the ventral/What stream, but did not address the issue of position-independent representations since they used non-lateralized stimuli; repetition suppression occurred within the left temporal convexity at 150-200 ms post-stimulus onset (Bergerbest et al., 2004; Altmann et al., 2008b; Murray et al., 2008; De Lucia et al., 2010b). Using lateralized environmental sounds we have been able to show, for the first time, that the semantic representation on the left temporal convexity is indeed position-independent, providing thus strong support for the dual-stream model. The repetition suppression which we observed on the left hemispheric convexity at 165-215 ms post-stimulus onset period was significant for pairs presented at the same as well as at different lateralizations and reflects thus solely the semantic identity of primes and repeats. Although the time period over which it occurred was very similar to that described in previous studies with non-lateralized environmental sounds (Altmann et al., 2008b; Murray et al., 2008), the present priming effect involved larger parts of the left convexity. In particular we observed not only the involvement of the ventral/What stream as in previous EEG and fMRI studies (Bergerbest et al., 2004; Altmann et al., 2008b; Murray et al., 2008; De Lucia et al., 2010b), but also a contribution of the dorsal/Where stream. The latter may have been involved in our study because of the use of lateralized stimuli which, even in passive listening paradigms, tend to activate the inferior parietal lobule (Maeder et al., 2001). This effect may have been enhanced by the previously described participation of the dorsal stream in the semantic coding of action related sounds. Listening to a mixture of environmental sounds, without

lateralization, was shown to activate the left supramarginal and angular gyri (Lewis et al., 2004); among these sounds those produced by actions involved the posterior parietal and beyond it prefrontal, premotor and motor cortices (Lewis et al., 2005; Pizzamiglio et al., 2005; Gazzola et al., 2006; Hauk et al., 2006; Lahav et al., 2007; De Lucia et al., 2009; Giusti et al., 2010; Bourquin et al., 2012b). The left inferior parietal regions were also activated by consonant and syllable discrimination in sublexical tasks (Dehaene-Lambertz et al., 2005; Zaehle et al., 2008), illustrating further the interactions between networks involved in sound recognition and sound production (Hickok and Poeppel, 2007).

The use of lateralized stimuli revealed an additional, very early semantic and position-independent coding, characterized by a repetition enhancement on the left anterior and inferior temporal and ventral prefrontal cortices at 42-63 ms post-stimulus onset. The enhancement occurred independently from lateralization cues, both for pairs presented at the same and different lateralizations. As above, this effect therefore likely reflects solely the semantic identity between primes and repeats. No priming effect was reported in this time window in previous studies, which used non-lateralized environmental sounds (Altmann et al., 2008b; Murray et al., 2008). Thus, it may reflect activity in a neural population that encodes for semantic and spatial aspects of sound objects, but is selectively modulated by semantic content. Such an interpretation is supported by electrophysiological studies in non-human primates. Neuronal responses within the ventral prefrontal region were found to be affected by both the location and the type of the auditory stimulus (Cohen et al., 2004), although their characteristics during specific tasks suggested that they are primarily part of the non-spatial, ventral auditory pathway (Cohen et al., 2009). More generally, it is important to consider the timing of these effects with respect to current knowledge concerning signal propagation and analysis within the auditory system; a point to which we return below.

Position-linked representations of sound objects

Position-linked coding of sound objects, i.e. the combination of the information pertaining to a specific object and its particular position, is ethologically relevant in at least three situations. First, it allows to keep track of a given sound source over (short periods of) time. This is also the type of position-linked coding which we have observed within our paradigm; different priming effects were observed as a function of the stimulus repetitions being at the same vs. different lateralization. Repetition suppression was observed for the repeat of the same object at the same lateralization and repetition enhancement for the same object at a different lateralization. These priming effects were found during two time periods. A very early priming effect occurred at 20-39 ms post stimulus onset on the posterior part of the left superior temporal gyrus. A previous study showed that this same region was more sharply tuned to spatial than phonetic information (albeit this effect occurred, however, later, at 70-150ms; Ahveninen et al., 2006). The second priming effect occurred at 143-162 ms post stimulus onset on the left inferior frontal gyrus. By virtue of its connections, the homologous region in non-human primates is thought to be part of the ventral/What stream (Romanski and Averbek, 2009). Its neurons were found to be modulated by both the location and the type of auditory stimuli (Cohen et al., 2004). Second, the combination of semantic and spatial information may help to identify a specific object. An everyday example is the ringing of a smartphone, which if located in one's pocket will be identified as one's own and not that of a colleague. Third, combined encoding of sound object identity and location is essential for segregating sound objects in noisy surroundings (Yost, 1991; Bregman, 1990). If this depends on the position-linked representations demonstrated in this study, it sheds light on the dissociation found in patients with focal hemispheric lesions. Sound localization deficits, including the complete inability to perceive the spatial aspects of sounds (referred as spatial

deafness) were found to be associated with the preserved capacity to use (auditory) spatial cues for the segregation of sound objects (Bellmann and Clarke, 2003; Spierer et al., 2007b).

Our results suggest that the ventral/What stream supports a dual representation of sound objects, of which one combines the identity of a sound object and its location. This raises the question of how and at what level the two interact. Current evidence suggests that the position-linked representation of sound objects originates in early-stage auditory areas. The seminal non-human primate study which demonstrated an early separation between the What and Where streams within early-stage auditory areas, also clearly documented the existence of a subpopulation of neurons with a combined selectivity for semantic and spatial information (Tian et al., 2001). A recent study indicates that a similar specialization within early stage auditory areas exists in man. Among the histologically identified early-stage auditory areas in man (River and Clarke, 1997; Wallace, Johnston, and Palmer, 2002), two were found to be selective for sound recognition as opposed to sound lateralization: AA and ALA (Viceic et al., 2006). Neural activity elicited by environmental sounds within ALA, but not AA, was found to be modulated by the position of the stimuli (van der Zwaag et al., 2011).

The existence of position-linked representations of specific objects raises several questions that need to be addressed in future studies. Are large spatial changes (such as left vs right hemispace) and small ones (small displacements within one hemispace) coded in the same way? How is prior knowledge integrated into these representations (e. g. my mobile phone is in my right pocket)? Do position-linked representations have access to working memory or even episodic memory? How do position-linked representations interact with actions? Are there instances in which position-linked representations require interactions between the ventral and dorsal streams?

Ultra rapid discrimination of sound objects

Using lateralized environmental sounds we have observed repetition effects in the AEPs as early as 20-39 ms and 42-63 ms post-stimulus onset. This is well before the later effects at 143-162 and 165-215 ms, which occurred at roughly the same time window as in previous studies with non-lateralized environmental sounds (Altmann et al., 2008b; Murray et al., 2008) and precedes even living vs. non-living categorization effects observed at 70-100 ms (Murray et al., 2006; De Lucia, Clarke, and Murray, 2010a; De Lucia et al., 2012). Very short latencies for stimuli with spatial cues have been reported previously in magnetoencephalographic studies. Lateralization of tone bursts modulated N20m in the superior temporal gyrus and the middle frontal region on the right side and at N50m in prefrontal and parietal regions (Itoh et al., 2000). Different azimuthal positions of a tapping knife modulated neural activity at 40-60 ms bilaterally in medial and at 100 ms in lateral Heschl's gyrus (and at 180 ms in the right posterior superior temporal gyrus; Brunetti et al., 2008). Furthermore, neural computation which occurs at very short latencies after stimulus onset is behaviorally relevant; transcranial magnetic stimulation applied over the right parietal cortex was shown to impair spatial discrimination of nearby sound sources within the contralateral hemispace at 20 ms (but not at 80 or 90 ms) and within the ipsilateral hemispace at 80 ms (but not at 20 or 90 ms; At et al. 2011).

In light of the timing of the present effects, it is important to recall the rapid propagation of auditory responses across cortical regions, which has been demonstrated in human studies. Response onsets within primary auditory cortices have been observed reliably at ~8-10 ms post-stimulus onset with propagation to belt and parabelt regions within 2-3 ms thereafter (e.g. Howard et al., 2000; Brugge et al., 2003; see also Steinschneider et al., 1982; Schroeder

et al., 2001). Beyond the auditory cortex, N1 responses to auditory stimuli were recorded by subdural electrodes at ~80 ms post stimulus onset over the right prefrontal cortex (Liasis et al., 2001). Very early events could also reflect processing within cortico-subcortical loops; auditory brainstem responses to complex sounds, recorded at 6-10 ms post stimulus onset, were shown to interact with higher level cognitive processing (Skoe and Kraus, 2010 a; Chandrasekaran et al., 2009) and to be subject to repetition effects (Skoe and Kraus, 2010b). Thus, effects observed here before ~60 ms post stimulus onset could already reflect the consequence of recursive volleys of activity within auditory cortices. Data from non-human primates likewise show differential responses to complex sounds at these latencies within either belt/parabelt regions (e.g. Perrodin et al., 2011; Ghazanfaar et al., 2005; Lakatos et al., 2005) or frontal regions (e.g. Russet al., 2008; Romanski et al., 2002) as well as within regions implicated in the mirror-neuron system (e.g. Kohler et al., 2002).

Repetition enhancement

Three different mechanisms may account for the repetition enhancement observed in this study. First, repetition enhancement could reflect changes in one of the object characteristics that were monitored by the network, here lateralization changes of a given object. Second, repetition enhancement could be characteristic of an episodic memory trace, as described in previous fMRI studies of visual or auditory-verbal priming (Blondin and Lepage, 2005; Buchsbaum and D'Esposito, 2009). This interpretation could be relevant for repetition enhancement occurring at 42-63 ms post stimulus onset in regions including the parahippocampal gyrus and hippocampal formation. Third, repetition enhancement could reflect the difficulty of comparing stimuli with varying spatial characteristics. The difficulty of a task was shown to influence priming effects in the visual domain. Whereas repetition priming with familiar faces or familiar symbols yielded repetition suppression, the use of

unfamiliar stimuli or of physically impossible objects resulted in repetition enhancement (Soldan et al., 2008a; 200b; George et al., 1999; Henson et al., 2000).

In conclusion, the current study revealed repetition-induced modulations of spatio-temporal patterns of neural activity that are compatible with a dual representation of sound objects within the ventral/What stream, one position-independent and the other position-linked. This suggests that the ventral/What stream is able to process some spatial information. By virtue of their carrying both features, position-linked representations likely play a role in the binding process of object identity and position “What I hear is located here”, including over time “What I hear here is What I heard there”.

Acknowledgments

Cartool software (<http://sites.google.com/site/cartoolcommunity>) was programmed by Dr. Denis Brunet, from the Functional Brain Mapping Laboratory, Geneva, Switzerland, and is supported by the EEG Brain Mapping Core of the Centre for Biomedical Imaging (www.cibm.ch) of Geneva and Lausanne. We thank Dr. Jean-François Knebel for programming additional analysis tools, Dr. Lucas Spierer for assistance during data acquisition, and Prof. Peter G. H. Clarke for comments on the manuscript. This work was supported by Swiss National Science Foundation grants 3200030-124897 to S.C. and 310030B-133136 to M.M.M.

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Initial and repeated presentations of a sound object: same lateralization

Initial and repeated presentations of a sound object: different lateralization

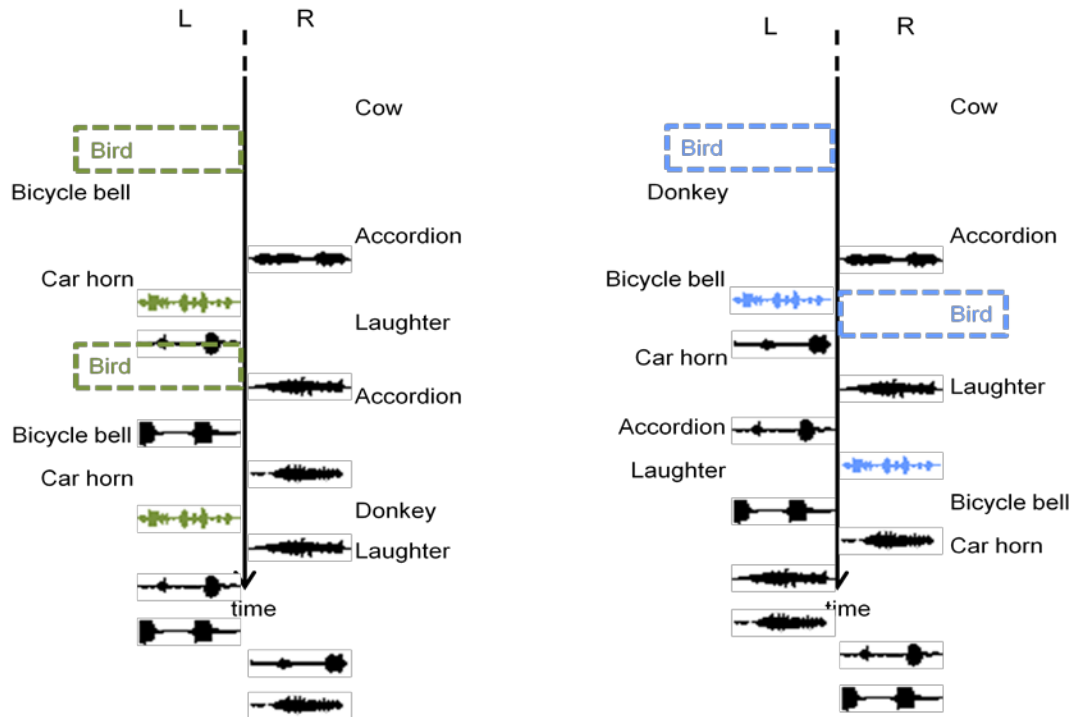


Figure 1. Sound sequences with initial and repeated presentations of sound objects. Within a block the initial and repeated presentations of a given object had either the same (as highlighted in green; left panel) or different lateralizations (in blue; right panel). Furthermore within each block i) 50% of the stimuli were lateralized to the left (L) and 50% to the right (R); ii) the initial and the repeated presentations of the same object were separated by 0-5 intervening items; and iii) the repeated presentations and their immediately preceding stimuli had equally often the same or the opposite lateralization.

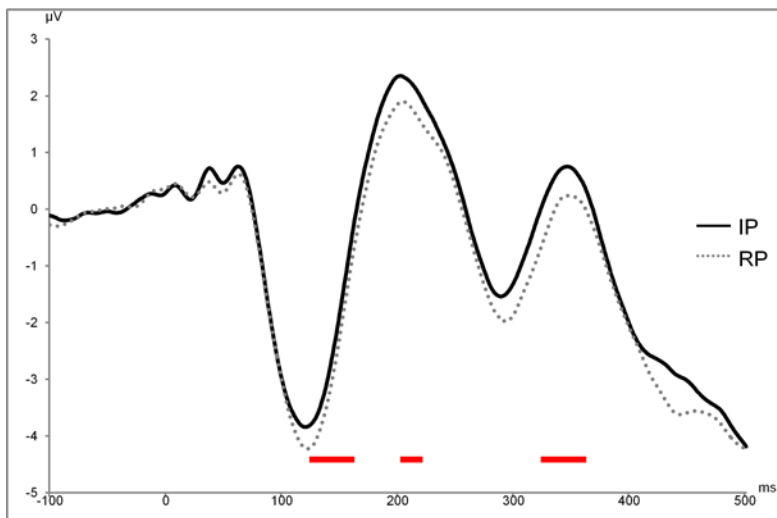


Figure 2. Evoked potential modulations at a frontal midline site (electrode Fz) for initial (black line) and repeated presentations (grey-dotted line within incongruent pairs; the red bars highlight periods of significant difference ($p < 0.05$)).

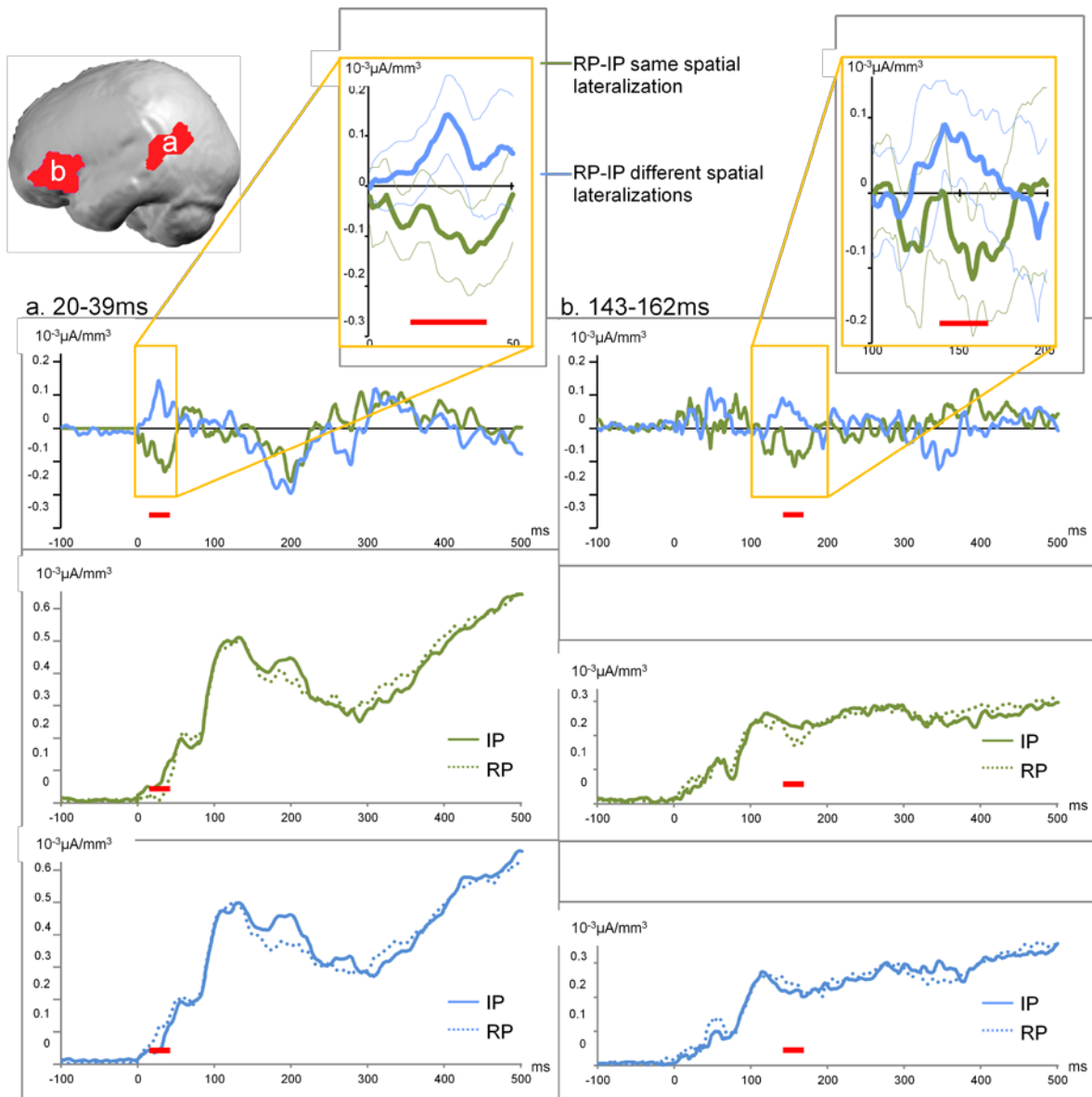


Figure 3. Repetition priming effects in pairs with the same and different lateralization expressed as difference in strength of repeated minus initial presentations (RP-IP). The inverse solution modulations presented a significant effect of congruency at 20-39 ms in the posterior parts of the superior and middle temporal gyri (cluster a) and at 143-162 ms in the inferior and middle temporal gyri (cluster b). Neural activity in either cluster is shown as RP-IP (top), including a zoom-in centered on the period of significant difference, where the confidence interval is indicated (thin line), and as IP and RP for pairs with the same (middle) or different lateralization (bottom). During both periods of significant difference repetition yielded suppression in pairs with the same lateralization and enhancement in pairs with different lateralization. Red bars indicate periods of significant difference, where the following three criteria applied: i) $p \leq 0.05$ at node level; ii) a cluster extent threshold of $k_E \geq 15$ contiguous nodes; and iii) a temporal contiguity of at least 18ms.

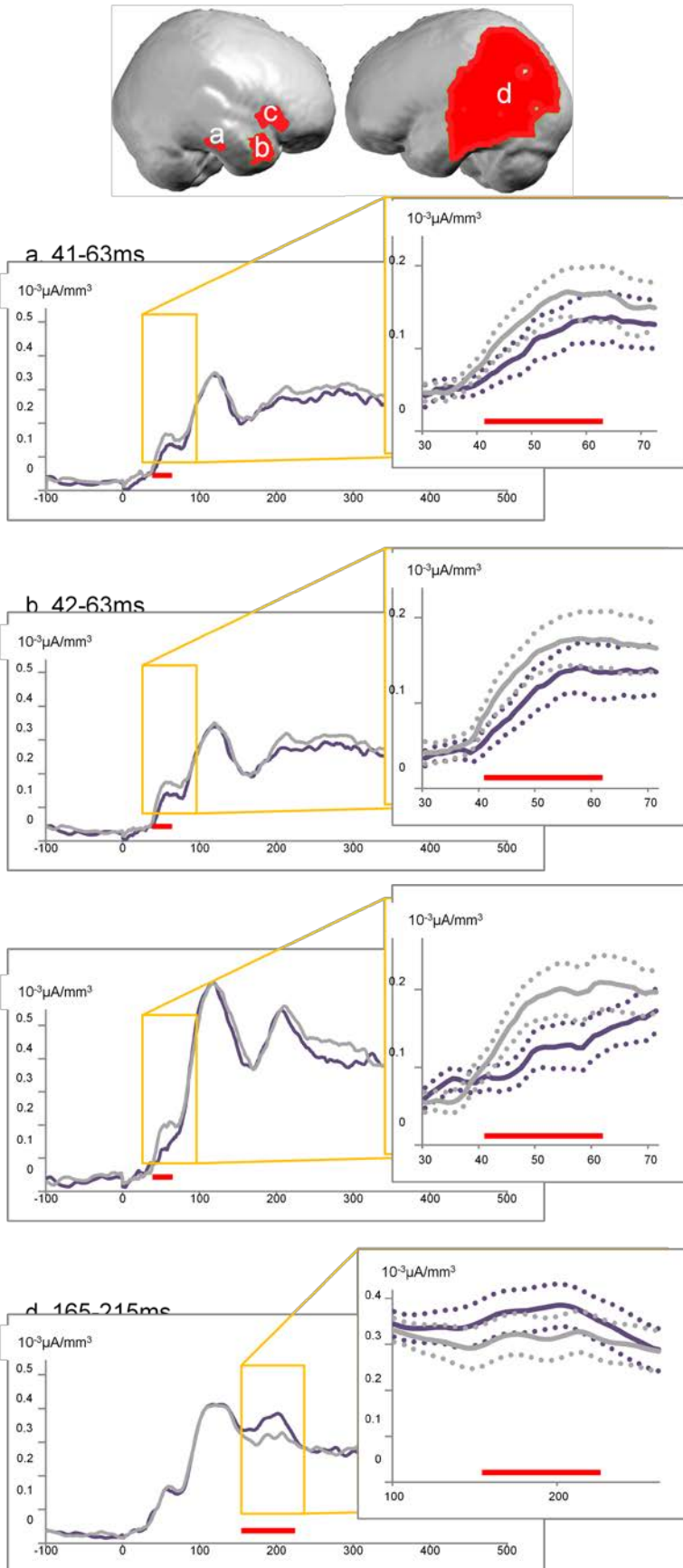


Figure 4. The inverse solution modulations of initial vs. repeated presentations showed significant differences at two time periods, distributed over four clusters. Over the 42-63 ms

period repetition enhancement was present on the right middle temporal (cluster a), anterior temporal (b) and inferior frontal (c) regions. Over the 165-215 ms period repetition suppression was present in the left temporo-parietal brain region (d). In comparison to the initial presentation (dark line), neural activity was higher for the repeated presentation (light line) during the 42-63 ms period and lower during the 165-215 ms period in the corresponding clusters. The significant periods are highlighted in the zoom-ins, where the interval of confidence is indicated (dotted line); red bars indicate periods of significant difference.