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What makes medical students better listeners?

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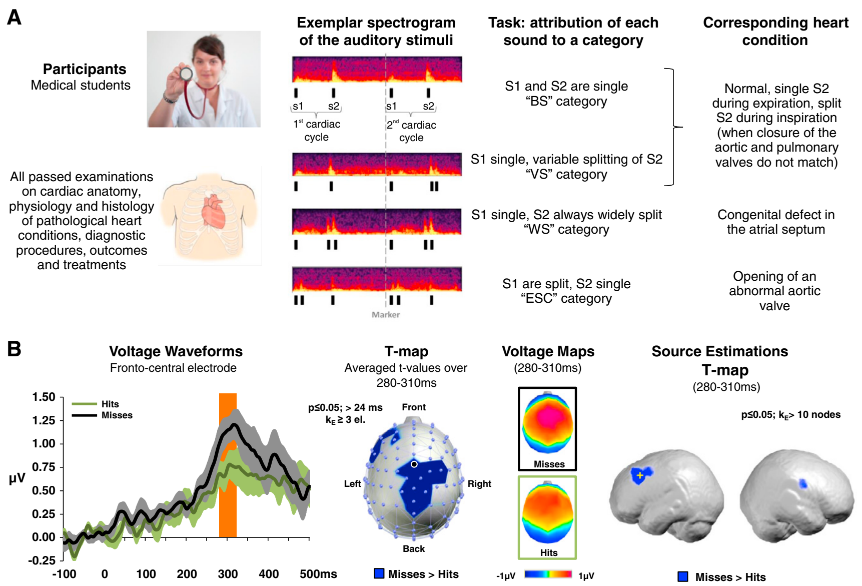

Figure 1. Paradigm and main results.
(A) General procedure. One cardiac cycle comprises two consecutive sounds attributed to the closing of the mitral and tricuspid (S1) followed by aortic and pulmonary (S2) valves. Medical students categorized heartbeat sounds. Auditory evoked potentials (AEPs) elicited by correctly (Hits) and incorrectly (Misses) diagnosed trials were compared at the onset of the second cardiac cycle. See also Supplemental Information. (B) Main results. AEPs elicited by Hits (in green) and Misses (in black) are shown from an exemplar electrode (Cz; mean ± s.e.m.). Activity between Hits and Misses was statistically compared across the electrode montage using a millisecond-by-millisecond paired t-test (criteria indicated in inset). Statistical t-maps on the electrode montage show the spatial distribution of the electrodes with a significant difference over the 280–310 ms post-marker onset (indicated by the orange rectangle), with higher activity for Misses than Hits. Significant differences in distributed source estimations within the previously defined time period were observed within the left middle frontal gyrus (MFG) and right pre-/postcentral gyrus (PoG/PrG). Statistical t-maps are displayed on the average MNI brain ($p \le 0.05$, $k_E \ge 10$ nodes). Both clusters showed a higher activity for incorrect (Misses) as compared to correct (Hits) recognition. The maximal t-value (yellow +) was located in the left MFG cluster.

Diagnosing heart conditions by auscultation is an important clinical skill commonly learnt by medical students. Clinical proficiency for this skill is in decline [1], and new teaching methods are needed. Successful discrimination of heartbeat sounds is believed to benefit mainly from acoustical training [2]. From recent studies of auditory training [3,4] we hypothesized that semantic representations outside the auditory cortex contribute to diagnostic accuracy in cardiac auscultation. To test this hypothesis, we analysed auditory evoked potentials (AEPs) which were recorded from medical students while they diagnosed quadruplets of heartbeat cycles. The comparison of trials with correct (Hits) *versus* incorrect diagnosis (Misses) revealed a significant difference in brain activity at 280–310 ms after the onset of the second cycle within the left middle frontal gyrus (MFG) and the right prefrontal cortex. This timing and locus suggest that semantic rather than acoustic representations contribute critically to auscultation skills. Thus, teaching auscultation should emphasize the link between the heartbeat sound and its meaning. Beyond cardiac auscultation, this issue is of interest for all fields where subtle but complex perceptual differences identify items in a well-known semantic context.

Medical students, who had acquired solid knowledge of cardiology at the time of testing, underwent AEP recordings while listening to quadruplets of heartbeat cycles and diagnosing them. One cardiac cycle comprises two consecutive sounds attributed to the closing of the mitral and aortic valves, respectively. Four conditions were used in our study and differed in the nature of the first or second sound, which could be single or 'split' (Figure 1A; details in Supplemental Information). For each of the four conditions, auditory recordings from several patients were used, representing the natural variation present in clinical practice. The task was to identify the condition portrayed by each sound based on recordings of four heart cycles. Prior to EEG recording, subjects practiced recognizing the four types of heartbeats until reaching 70% accuracy. During the AEP recording subjects listened to a new set of stimuli (involving different exemplars of the four conditions) and assigned them to the corresponding category (Figure 1A and Figure S1). Mean accuracy in the categorization task was below 70% but statistically well above the chance level and remained so for the whole recording session; response times were faster for correct than incorrect responses (Supplemental Information).

Brain activity elicited by the second heart cycle was compared between trials with correct (Hits) *versus* incorrect identification (Misses), regardless of the specific condition (Figure 1B). Analysis of AEPs across the electrode montage revealed a significant difference over the time period of 280–310 ms after the onset of the second heart cycle. Estimations of brain sources of differences observed during this period revealed greater activity for Misses than Hits in MFG ($t_{(10)} = -4.36$; $p < 0.001$) and in the right prefrontal cortex ($t_{(10)} = -2.72$; $p = 0.02$). Of note, no such differences were present when the same analysis was performed on AEPs yielded by the first heart cycle of the excerpt — before the subjects heard sufficient acoustic information to label

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each heartbeat sound (Figure S2A, Supplemental Information).

Our results indicate that successful fine-grained discrimination, as those of heartbeat sounds, relies critically on labelling, which is provided by semantic rather than acoustic representations. Several lines of evidence support this interpretation. First, successful heartbeat discrimination modulated the same MFG region as previous studies on semantic categorization in humans [5,6] and non-human primates [7]. Similarly, intracranial recordings have revealed differential activity during correct *versus* incorrect auditory categorization within frontal, but not supratemporal, sites; correct responses being associated with lower high-gamma activity [8]. The same frontal region was associated with expertise in birdsong recognition, again lesser activity being associated with correct recognition [3]. Taken together, these studies highlight the critical contribution of higher-order processing and, particularly, of the sharpening of neural representations within the semantic 'expert' network as a necessary step for correct recognition. When a percept activates a sharply tuned semantic representation, it is likely to be correctly recognized whereas a broader activation tends to be associated with incorrect recognition.

Second, differences in neural activity between correct and incorrect heartbeat categorization occurred during the same period that has characterized semantic processing in previous studies. Semantic processing starts as early as 70 ms post-stimulus onset with segregation of broad semantic categories, whereas more narrow categories are discriminated at subsequent stages [9]. Within-category discriminations [3] are known to occur at later time periods, which partially overlap with the critical time period revealed here. As highlighted by the temporal hierarchy model of auditory object recognition [9], this critical period is well embedded in the semantic processing sequence.

Third, perceptual processing within early-stage auditory areas was shown to play a role in auditory spatial discrimination [4] and in learning to categorize novel sounds [10], in two instances without a semantic link. Our study investigated fine-grained auditory discrimination within a semantic context; differences in neural processing at the level of early-stage auditory areas were not critical to successful discrimination. Control analyses confirmed that our methods were sufficiently sensitive to detect acoustic differences across heartbeat types (Figure S2B, Supplemental Information), since AEPs to acoustically different heartbeat sounds (simple vs. split), analyzed independently of whether they were correctly recognized or not, yielded differential activity at early latencies (45–55 ms) within left auditory cortices.

In conclusion, successful discrimination of heartbeat sounds depends critically on the access to the neural representations of their meaning. To our knowledge, this is the first demonstration that fine-grained discrimination of sound objects, with only minor differences in auditory features, can be enhanced by labelling provided by the semantic link. Beyond the conceptual importance, our findings are of practical relevance to auscultation training, where emphasis should be put on linking the sound and its meaning. Thus, in addition to the discrimination of acoustic features of heartbeat sounds (for example, single *versus* split), the whole semantic context of the corresponding heart condition should be called upon during auscultation teaching. The same approach is likely to be beneficial in other instances, such as visual recognition in radiological analysis or in relearning to recognize environmental sounds after cochlear implants.

SUPPLEMENTAL INFORMATION

Supplemental information includes experimental procedure, additional behavioural and EEG analysis, as well as two figures, and can be found with this article online at http://dx.doi.org/10.1016/j.cub.2016.05.024.

AUTHOR CONTRIBUTIONS

Conceptualization, S.C. and R.D.M; methodology and formal analysis, R.D.M., M.M.M., J.F.K., and P.J.M; resources (heartbeat stimuli), W.R.T.; investigation, R.D.M; writing – original draft, R.D.M and S.C.; writing – review and editing, R.D.M., S.C., M.M.M., W.R.T., P.M., and J.F.K; funding acquisition: S.C.

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