Neural correlates of the Pythagorean ratio rules

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Millennia ago Pythagoras noted a simple but remarkably powerful rule for the aesthetics of tone combinations: pairs of tones – intervals – with simple ratios such as an octave (ratio 2 : 1) or a fifth (ratio 3 : 2) were pleasant sounding (consonant), whereas intervals with complex ratios such as the major seventh (ratio 243 : 128) were harsh (dissonant). These Pythagorean ratio rules are the building blocks of Western classical music; however, their neurophysiologic basis is not known. Using functional MRI we have found the neurophysiologic correlates of the ratio rules. In musicians, the inferior frontal gyrus, superior temporal gyrus, medial frontal gyrus, inferior parietal lobule and anterior cingulate respond with progressively more activation to perfect consonances, imperfect consonances and dissonances. In nonmusicians only the right inferior frontal gyrus follows this pattern. *NeuroReport* 18:1521–1525 © 2007 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Introduction

More than two and a half millennia ago, Pythagoras proposed a simple but remarkably powerful rule for the aesthetics of tone combinations [1]: pairs of tones – intervals – with simple ratios, such as an octave (ratio 2 : 1) or a fifth (ratio 3 : 2) were pleasant sounding or consonant to the ear, whereas intervals with a complex ratio such as a major seventh (ratio 243 : 128) were harsh or dissonant sounding. As all Western classical music harmonies and melodies are based, at their root, on progressions of consonant intervals and resolutions of dissonant ones, the Pythagorean ratio rule is central. The positive correlation between physical complexity and level of perceived dissonance is likely not a coincidence: some underlying neurophysiologic mechanism must be responsible for translating the frequency ratios into subjective qualia in an orderly and consistent manner. Much recent work (e.g. Ref. [2] and References therein) has found that cortical activation patterns measured by functional MRI (fMRI) can reveal much about pitch and interval perception. We have studied, using fMRI, the cortical activation patterns of musicians and nonmusicians to consonant and dissonant intervals. We find that neural activation is much more engaged in all participants when they listen to dissonant intervals compared with listening to consonant intervals. We also find that in musicians all the cortical areas that are activated during the intervals task show the Pythagorean response ratio: sevenths showing greater responses than sixths, which show greater responses than fifths. In nonmusicians, we find a single area that responds according to this rule: the right inferior frontal gyrus (IFG). The basis for the Pythagorean ratio rules might lie in cortical activation patterns.

Interestingly, although much exploration of the neural basis of the Pythagorean ratio rules has not taken place, a number of recent papers have dealt with the different, but potentially related, question of the neural correlates of listening to emotionally evocative music [3–8]. These papers have found that emotionally evocative music activates a network of brain areas that have been associated with emotion processing. Blood and colleagues [3] studied, using positron emission tomography (PET), the neural correlates not only of sad and happy segments of music, but also of pleasant (consonant)/harsh (dissonant) segments. They used more complex stimuli than those in our study, incorporating consonance/dissonance into chords, not intervals, and using a melodic structure and not isolated presentations of intervals. They found a preferential increase in blood flow in response to dissonance in the right parahippocampal gyrus and a preferential decrease in the right orbital frontal cortex and medial subcallosal cingulate.

Consonant intervals are traditionally divided into the so-called 'perfect' consonances – unisons, octaves and fifths – that vibrate with simpler frequency ratios, and the 'imperfect' consonant intervals – major and minor thirds and sixths – that vibrate with more complex ratios. Major and minor seconds and sevenths and the tritone or the diminished fifth/augmented fourth constitute the dissonant intervals with the most complex ratios.

For centuries after Pythagoras, his tuning system based on exact perfect consonances predominated. As Western music increased in complexity and range, however, slight modifications to the Pythagorean scale became necessary to preserve consistently tuned intervals across extremely large intervals (greater than one or two octaves) and small ones (half steps and intervals that are difficult to standardize using Pythagorean tuning). The difficulty arising from the increased range is apparent when one goes through 12 perfect fifths, for example, from the note C to a C seven octaves higher: the ratio of the harmonic to the fundamental starting tone is $(3/2)^{12}$=129.746. Going from a C to one seven octaves higher via the octave route, however, produces a tone with a frequency that has a ratio $(2/1)^7$=128 times higher than the starting tone. This small difference ultimately requires some temperament or modification of pure harmonic intervals to construct and tune instruments that can play pieces written with tones that span multiple octaves. Numerous fixes or temperaments for this problem have been devised over the centuries [1]. The one used almost universally today is known as equal temperament, in which the discrepancy of 1.746 is divided by narrowing each of the 12 previously perfect fifths in the seven-octave span, resulting in the 12 notes of the chromatic scale. Thus in equal temperament the fifths are no longer perfect, only close.

With this caveat of equal tempering – the temperament in which Western listeners are accustomed to hearing music – informing our search for neural correlates to the Pythagorean rules, we chose to study the neural activation pattern associated with hearing the perfect fifth (1.498 : 1), major sixth (1.682 : 1) and major seventh (1.888 : 1). Our a-priori hypothesis was that there would be a significant difference between the activation patterns for the perfect fifth and the major seventh with, perhaps, the activation pattern associated with the major sixth being somehow intermediate to the other two. Such a pattern would be a cortical 'reflection' of the Pythagorean ratio rule.

Methods

Participants

Thirteen paid participants without perfect pitch by self-report (six musicians and seven nonmusicians) were scanned in a 3-T whole-body Siemens Trio scanner (Siemens Medical Solutions, Erlangen, Germany). Of the musicians, all were pianists and four were men with an average age of 20.3 years. Music lessons were started before they were 5.5 years old. The musicians reported that they had played for an average of 3 h/day for the previous 5 years. All musicians were undergraduate students in the music program at Indiana University majoring in piano performance. Of the nonmusicians, three were men, their average age was 22.5 years and they all had fewer than 2 years of any musical experience and no private lessons. The nonmusicians were also undergraduate or graduate students at Indiana University. Informed consent was obtained and the study protocol was approved by the Indiana University Human Subjects Review Board.

Stimulus presentation

All participants completed two runs of the consonant/dissonant intervals task, each of which consisted of three different types of intervals: major sevenths, major sixths and fifths. Each interval was presented in a pseudorandom order as a single event for 4 s with a 12-s interevent interval. Six of each type of interval were presented per run for a total of 18 intervals per run. To avoid brain activation pattern associated with given tones, the fundamental note for each participant was randomized across the octave between the A below and above the middle C. Participants were asked to simply listen to the intervals. We had a passive listening task to avoid requiring performance in a task that the musicians could do, and which the nonmusicians could not. In other words, we did not want to confound activation to the stimulus with activation to the level of performance in a task. The intervals were presented as an extra listening task after another study on music perception that involved syntax decisions to be made on hearing sentences and chord progressions. The participants were, therefore, naive to the purpose of this study. In addition, presenting the intervals within the context of another study was performed to isolate the activation patterns associated with the sounds of the intervals themselves from other musical context effects.

Data collection

Anatomical images were acquired using conventional parameters. All scanning was performed with a Siemens Trio 3-T MRI housed in the Psychological and Brain Sciences department at Indiana University. T2* scan parameters were as follows: repetition time (TR), 2 s; echo time (TE), 30 ms; flip angle (FA), 90°; 219 images/slice, with 25 coronal slices (4-mm thick and 0-mm gap) acquired parallel to the anterior commissure–posterior commissure (AC–PC) plane. Stimuli were presented through Siemens headphones. Functional data underwent slice time correction, three-dimensional motion correction, linear trend removal and Gaussian spatial blurring (full-width at half-maximum, 4 mm) using the analysis tools in Brain Voyager (Brain Innovation, Maastricht, The Netherlands). Individual functional volumes were coregistered to anatomical volumes with an intensity-matching, rigid-body transformation algorithm.

Data analysis

Analyses were conducted with the Brain Voyager software package and customized Matlab scripts. Statistical parametric maps (SPMs) of blood oxygenation level-dependent (BOLD) activation were created for the average activation for all participants using a statistical threshold of $P<0.0001$ (uncorrected). From this analysis, we then created SPMs for each group separately (musicians and nonmusicians) and then for each individual participant, using a threshold of $P<0.01$. The SPMs were corrected using the false discovery rate method, which controls for the expected proportion of false-positive voxels among those that are suprathreshold [9]. We then contrasted the dissonant intervals with consonant ones, which resulted in several regions of interest (ROIs). We only considered the regions that (a) were apparent in the group maps, (b) were also apparent in a majority of the individual maps, (c) had 10 contiguous voxels of significant activation and (d) passed our statistical thresholds. We then looked at the hemodynamic response curves within these ROIs to investigate whether the responses to the three intervals followed a Pythagorean response pattern. The peaks of these response curves are presented in Fig. 1.

Results

We first performed a simple contrast in all participants between the dissonant and consonant intervals. We were interested in this contrast for two reasons: first, as an initial analysis of how the brain responds to these types of intervals, and second, to determine the ROIs for further in-depth analyses. When BOLD activation to dissonant intervals was directly compared with activation to consonant intervals (fifths in this case), several brain regions were engaged more during the dissonant than the consonant intervals. All participants had significantly greater activation to the dissonant intervals in their IFGs: bilaterally (location of peak activation in Talairach [10] coordinates: x,y,z) (i) at (−10, 18, 9) and (43,19,1) (Fig. 1a); in the left superior temporal gyrus (STG) (−58, −30, 14), in the left middle temporal gyrus (MTG) (53, 32, 9) (Fig. 1b), in the left middle frontal gyrus (MFG) (−39, 43, 14) (Fig. 1c), in the inferior parietal lobule (IPL) (−47, −49, 41) (Fig. 1d), in the left precentral gyrus (−38, −23, 55) in the anterior cingulate (−5, 8, 44) (Fig. 1e), sub-cortically in the thalamus (+/−13, 10, 10), and in the right cerebellum (13, −74, −19). This group pattern, however, varied depending on whether or not the participants were musicians.

Specifically, the musicians did not have a dissonance–consonance difference in the right IFG, left precentral gyrus, left MTG, or in the thalamus. No regions were activated in the musicians that were not significantly active in the average maps.

We then performed further analyses to determine the response patterns of the BOLD activation within the ROIs determined by our first contrast. Here, we were interested in seeing whether or not we would see a neural pattern that reflected the Pythagorean response ratio: that is, sevenths greater than sixths greater than fifths. As shown in Fig. 1, this analysis provided us with interesting results. In musicians, neural activation in five ROIs evoked a pattern that conformed to the Pythagorean ratio: left IFG (Fig. 1a), left STG (Fig. 1b), left MFG (Fig. 1c), left inferior parietal lobule (Fig. 1d) and the anterior cingulate (Fig. 1e). In novices, one ROI evoked this pattern: the right IFG (Fig. 1a). Overall, whenever the musicians showed significant activation to dissonant over consonant intervals, the BOLD response pattern reflected the Pythagorean ratio rule.

Discussion

Several results from this experiment are worth noting. First, the neural activation to dissonant intervals is significantly greater overall than consonant intervals when we examine activation of all participants. In fact, no brain region displayed the reverse pattern of activation. Why would the dissonant intervals recruit neural regions more than consonant intervals? One hypothesis is that dissonance in general might activate neural systems more than consonance. Another hypothesis involves the baseline used: we used all possible comparisons among the three interval types. Perhaps the fifths and sixths are not different enough to produce significantly different activation patterns. This explanation, however, does not address why the fifths are never higher than sevenths (see Fig. 1, no activation of fifths > sevenths). Our results therefore suggest that when it comes to auditory perception of intervals, 'harsh' sounding, dissonant intervals will always recruit a music-processing system more than a pleasant sounding, consonant interval.

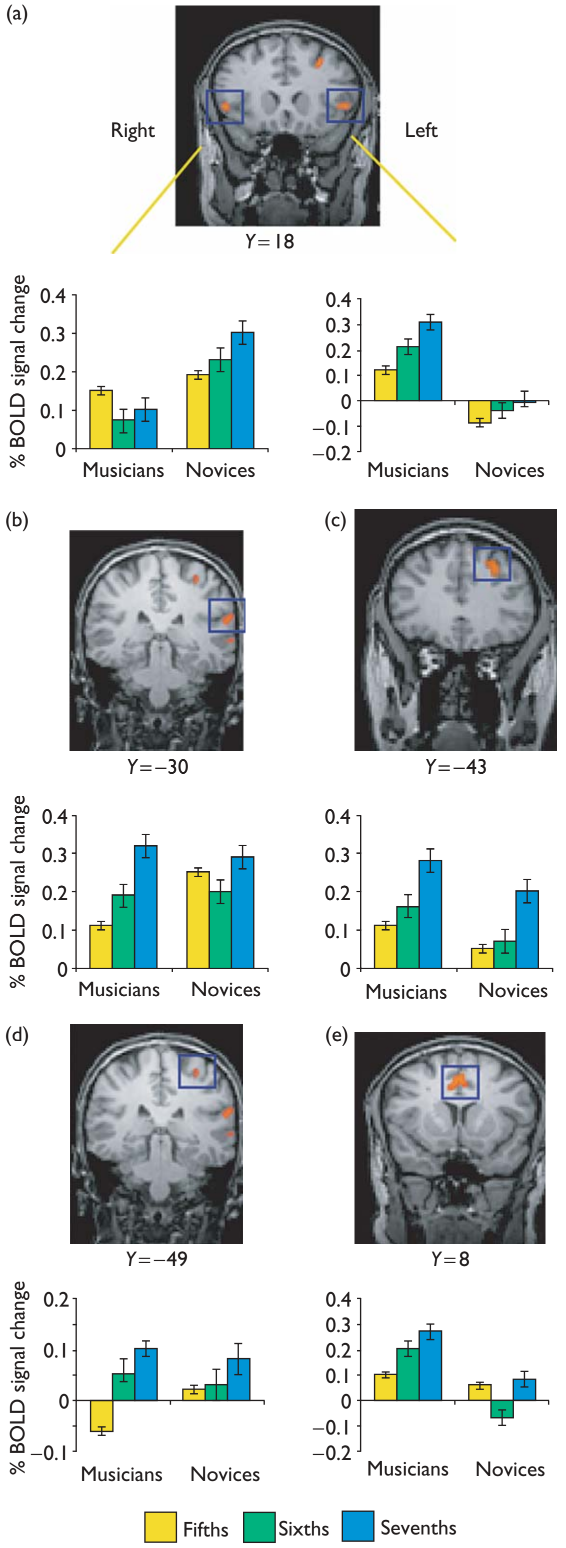

Fig. 1 Regions of interest (ROIs) following the Pythagorean response rule. (a) Inferior frontal gyrus (IFG): right follows rule for nonmusicians, left for musicians. (b) The left superior temporal gyrus (STG) follows the Pythagorean rules for the musicians, as do the left middle frontal gyrus (MFG) (c), the left inferior parietal lobule (d) and the anterior cingulate (e). Activation is shown that is at $P < 0.001$ for a group analysis. Histograms depict blood oxygenation level-dependent (BOLD) responses to all interval conditions in the ROIs.

As we noted, there has been considerable work on neural activity associated with pleasant and unpleasant stimuli [3–8,11,12]. It would have thus been helpful if, after scanning, we had asked the participants about their opinions of the emotional nature of the stimuli we presented. In future studies either by us or by others, it will be helpful to do so.

The second result of interest is that the pattern of activation to dissonant intervals reveals the involvement of several interesting brain regions including the IFG, the MFG, the STG and the anterior cingulate (Fig. 1). Several of these regions have been shown to be involved in music perception in previous work (for review, see Ref. [2]). Zatorre *et al.* [13], for example, in a tone-listening task, found increased activation in the auditory cortices (STG) and the left posterior dorsolateral frontal cortex in musicians with and without perfect pitch, and in the right IFG in participants without perfect pitch, but not with perfect pitch. In addition, Maess *et al.* [14] found that nonmusicians presented with syntactically inappropriate sequences of chords showed increased neural activity in bilateral IFG compared with neural activity in response to syntactically appropriate sequences. In general, music processing is thought to follow a similar neural path as language processing, but is often more lateralized to the right, at least in nonmusicians [15]. Our results demonstrate that nonmusicians show significant activation in the right IFG to dissonant intervals, whereas musicians show more activation in the left IFG. This finding supports the hypothesis that musicians might use the language network more for processing music than do nonmusicians [12]. Activation in the anterior cingulate might be related to the 'error detection' [16,17] occurring, whereas the musicians attend to dissonant intervals. The nonmusicians, however, reported that the dissonant intervals sounded more harsh than the consonant intervals, but showed less anterior cingulate activation. Blood and colleagues [3] found a decreased blood flow response to dissonance (and an increased blood flow response to consonance) in the right orbitofrontal cortex. A number of reasons may explain why we did not find this as well. The orbitofronal cortex is more difficult to image with fMRI than with PET scanning; hence this might be why we did not obtain this response. Alternatively, it could be that Blood and colleagues used consonant and dissonant stimuli but in the more complex context of more than two note chords in a progression, whereas we were looking at activation due to responses to isolated pairs of notes (intervals).

The third, and perhaps most significant, finding from this study is that the Pythagorean pattern of response emerges in the left IFG, the left STG, the left MFG, left inferior parietal lobule and the anterior cingulate in musicians (see Fig. 1), and that this pattern only emerges in nonmusicians in the right IFG. In an fMRI study investigating neural activation to both syntactically irregular and syntactically simple chord progressions, Koelsch *et al.* [18] found that the pattern of activation that correlated with irregular chord progressions was stronger in musicians than in nonmusicians in the bilateral IFG and in the right anterior STG. This effect was significant for both adults and children, and the results suggest that the difference between musicians and nonmusicians is observable before the age of 10 years. This overlap of function is notable because both syntactic processing and dissonance judgments are abilities that are honed with music training. When considered along with Koelsch's results, data from this study suggest that the left IFG and STG are central neural regions involved in music training. Our results, however, differ from theirs in that there was no significant right STG activation to dissonant over consonant intervals. Perhaps the left STG might be involved in judgments of musical tension as indicated by the relative levels of consonance and dissonance between simultaneous pitches, whereas the right STG might be involved in making syntactic judgments based on sequential ordering of successive pitches or chords.

We thus find that the basis of the Pythagorean rules might lie in cortical activation patterns, specifically in the IFG, the left STG, MFG, IPL and anterior cingulate. The hypothesis would predict, for example, that activation patterns upon hearing the interval of a second (third) should be similar to that from a seventh (sixth), and different from that induced by a sixth or third (second or seventh) or perfect fifth. It is somewhat curious, perhaps, that this response pattern manifests predominantly in musicians. It would be interesting to see if, within the imperfect consonances or dissonances, there are subtle differences in activation patterns that perhaps correlate with the simplicity of Pythagorean ratios. Finally, Bach on a number of occasions, as for example in the third trumpet part in measure 24 of his Cantata 130, actually used the fact that some of the partials of the harmonics sound so far out of tune, or just wrong, in any temperament as to sound wrong – the seventh partial, a B-flat above a C fundamental is very flat – to emphasize crucial words in the text such as 'devil'. Such intervals then sound not only very dissonant, but also wrong at least to musicians, and thus lead to predictions of the neural correlates of hearing such intervals. One might predict that in all groups these intervals show neural activation as being more dissonant than the response to a major seventh. Also, perhaps only in musicians, either in isolation or in context, areas of the brain that react to musical syntax [14] respond equally well to such strategically placed wrong notes. Further study of the cortical activation pattern as a part or whole of the explanation for the Pythagorean ratio rules is warranted.

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