Acquired Amusia and the Search for Notes in the Brain

A Review of

Uetsuki, S., Kinoshita, H., Takahashi, R., Obata, S., Kakigi, T., Wada, Y., & Yokoyama, K. (2016). A case of expressive-vocal amusia in a right-handed patient with left hemispheric cerebral infarction. *Brain and Cognition, 103*, 23-29.

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I. Amusia, an Overview

Introduction

For the vast majority of humans, there are few experiences that rival that of listening to a beloved song from childhood or hearing for the first time a melody destined to stay ingrained in the mind. We collectively pay billions of dollars annually to hear music, to consume performances, yet still we are not satisfied: we play music, we sing it to ourselves, it exists with many of us through every high and low of our lives. Whether you believe Steven Pinker's characterization of music as mere "auditory cheesecake"[1] or agree that it must hold some deep, evolutionary relevance for our species, it is clear that humans have developed a unique capability to process, respond to, and create auditory signals which are appreciated as having melody, rhythm, contour, dynamics – in short, as being music. Music, like language, sight, and every other domain of cognition central to most human experience, certainly resides in the brain. If there are neural underpinnings to our musical abilities, though, where and what exactly are they?

Modern cognitive neuropsychology has worked in recent years to answer these questions and more about the psychological and biological systems which enable our vast range of musical experiences. One of the most effective tools available to researchers in this pursuit is to study individuals who, either by congenital defect, neurodegenerative disease, or traumatic brain injury, have either failed to acquire or lost musical abilities. This syndrome, known as *amusia*, can involve one or more deficits in any of the abilities associated with musical appreciation and production including pitch production, rhythm comprehension, note differentiation, and emotional responsiveness, among others. While amusia has not been studied nearly as much as other brain-

[1] Pinker, S. (1997). *How the mind works*. New York: Norton.

related syndromes, such as aphasia, there still exists a wealth of theoretical and experimental literature to explore and draw conclusions from about the neural representations of music and musical abilities. This paper in particular will focus on the recent publication “A case of expressive-vocal amusia in a right-handed patient with left hemispheric cerebral infarction” from Shizuka Uetsuki and her colleagues (Uetsuki, Kinoshita, Takahashi, Obata, Kakigi, Wada, & Yokoyama, 2016). In conjunction with other work from the field, I will analyze the content and conclusions of this case-study and propose future directions for research. We begin here, though, with a more detailed introduction to the study of music, and lack thereof, in the brain.

What exactly is amusia?

As stated above, amusia is a loss or impairment of musical capacity, but beyond that it is tricky to pin down an exact definition for the syndrome because of the many forms it may take. Most commonly, amusia is a congenital deficit marked by an inability to differentiate between pitches within one semitone (100 cents) of one another – in everyday life this may be known as tone deafness (Mandell, Schulze, & Schlaug, 2007). As noted by the present case study though, amusia can also be acquired with the onset of a lesion, and a wide swath of clinical studies have documented forms of amusia resulting from lesions to either or both hemispheres. This basic uncertainty leads us to this next key question in the Uetsuki et al. paper and the science of amusia generally.

What brain regions might be in play in amusia?

Previous case studies are indeed diverse in their findings: some suggest that expressive amusia (difficulty producing pitches) may be right lateralized while reception deficits are due to damage to the left hemisphere, others that the right hemisphere is more active while subjects sing familiar songs, and many others that amusia is more common from right hemisphere patients and that linguistic deficits stem from lesions in the left hemisphere (Uetsuki et al., 2016). Perhaps the only area of concordance found from my analysis of many papers on the topic is that the frontal lobe is consistently implicated in musical processing, and at times regions in the superior temporal lobe are as well.

One recent study using Voxel Based Morphometry identified fifty-one patients with amusia using the Montreal Battery for Evaluation of Amusia (MBEA, discussed below) and correlated their impairment with a lack of grey matter in regions of the left inferior frontal gyrus (BA 47) and the left superior temporal sulcus (BA 22), thereby proposing a general left fronto-temporal network responsible for melodic and rhythmic discrimination (Mandell et al. 2007). The novel suggestion of the Mandell et al. paper, though, was that this network might also regulate motor mechanisms. In short, humans may map motor actions to sounds (pitch production) via a feedback loop that allows for the real-time correction of motor actions based on perceptual feedback (whether sung notes sound in tune), and an impairment in this auditory-motor feedback loop or mapping system may be responsible for some common amusic deficits such as tone deafness (Mandell et al., 2007). This theorized connection between specific neural networks and the overarching cognitive abilities impaired in the case of amusia brings us to this next question.

What cognitive functions are in play?

As seen above, motor processing has been implicated with the key cognitive function in play here, musical processing, and this interaction especially will be expounded upon throughout the rest of this review. However, it bears noting here some of the breadth in opinion among scholars and researchers. I particularly take note of the work of those who believe that linguistic processing also (or instead) holds a special relationship with musical abilities.

In 2003, Anirrudh Patel published a compelling review in *Nature* of his argument for the existence of neurobiological convergences between linguistic and musical processing. Both domains of cognition, music and language, involve a hierarchical structure of discrete elements (notes and words) that constitute complex syntaxes of interlocking dependencies, tension, and relaxation (Patel, 2003). The upshot of these similarities in seemingly distinct cognitive domains is that shared underlying architectures may be responsible for the syntactic integration necessitated by both abilities (the shared syntactic integration resource hypothesis from Patel, 2003). If that is so, could it be that damage to left frontal lobes resulting in Broca's aphasia simultaneously leads to comorbid amusia?

The simple answer from the literature to this elegant idea is 'no', at least not consistently. Two studies can highlight the difficulty, however, of ascertaining exactly how linguistic and musical deficits overlap, or do not. There is indeed long-standing literature that establishes the existence of comorbid aphasia and amusia in cases of right frontal lesions (Botez & Wertheim, 1959). On the other hand, an analysis of 24 Broca's aphasia patients found that 21 could produce good melody – the authors of that study also proposed that in these cases the right hemisphere is dominant over the left for singing capacity (Yamadori, Masuhara, & Okubu, 1977).

Where does this case-study come in?

With so much unresolved theory and so many seemingly conflicting studies, it would seem difficult for any single case study to make great strides in the study of amusia. That has not stopped Uetsuki and her colleagues from Japan from trying, however. It is important to note that this case study, for reasons that will become clear, does not consider in any meaningful way the proposed interaction between the patient's linguistic and musical systems, and this lack of consideration I believe can be considered as an implicit revocation of the shared syntactic integration resource hypothesis developed by Patel. Instead, as we will see, the authors place more importance on an attempt to lend evidence to the existence of a motor-feedback system described several years ago by Mandell et al., although it is still up to any responsible reader or reviewer to determine how well-bolstered this theory is. Thus, we turn now to the details of Uetsuki et al. from 2016.

II. Case Study: Summary and Analysis

Experimental questions

"A case of expressive-vocal amusia in a right-handed patient with left hemispheric cerebral infarction" tackles jointly the questions of *where* and *how* music is processed in the brain. The first issue, of location, is handled jointly by structural and functional magnetic resonance imaging (MRI) techniques, however this review will focus on the anatomical rather than neural activation-based claims, so as to stay more firmly in the realm of cognitive neuropsychology. The second issue, of the cognitive systems underlying musical abilities, is largely dealt with via a series of neuropsychological batteries and experiments, discussed in detail below, the results of which are used to consider especially how important motor processing is to amusia-caused pitch production deficits.

Hypotheses

In this case study, the authors proposed no specific hypotheses prior to their experimental evaluation of the patient. However, as discussed previously, there are some important hypotheses inherent to the study of amusia and the brain, including the findings that singing abilities are right lateralized whereas language abilities are left lateralized – this is a result that is especially challenged in the present paper. The alternative theory explored here is that there may be variation in the lateralization of these abilities, and even that in the realm of music that certain musical abilities can be dependent on entirely different brain systems and/or hemispheres (i.e. there should be no particular reason why rhythm comprehension and pitch discrimination should rely on the same neural structures). Further, based on their theoretical conclusions, it appears that Uetsuki and her team were seeking to support and develop the motor-auditory feedback system hypothesized by Mandell et al. (even though this study was not specifically cited in their publication).

Patient information

The single patient in Uetsuki et al.'s case study, who is never given a name or initials, is a 53 year-old, right-handed, Japanese woman who was hospitalized after suffering subarachnoid bleeding stemming from a ruptured aneurysm in her left middle cerebral artery. The necessary emergency surgery led to the creation of a large lesion in her left hemisphere, including the left inferior frontal gyrus, parts of the precentral gyrus, anterior insula, and posterior superior temporal gyrus, as well as to regions of subcortical white matter in the left frontal and inferior parietal lobule. The vast damage to the left frontal regions of the patient was documented by a post-operative MRI. Despite this large lesion, hospital staff reported that during her hospitalization, the patient was alert, attentive, and appeared to understand and communicate fluently.

The patient self-reported (it is not clear exactly when) that her singing ability had declined. This deficit was noticeable because, although the patient never played instruments, she received formal music education in school and claimed to have enjoyed hearing and singing music throughout her life. Her family members subsequently reported she was indeed a good singer with a good ear for memorizing and reproducing melodies, a skill that came in handy during karaoke sessions. It was further found by her doctors that the patient had no significant family history or any previous personal history of brain damage. The healthy controls chosen throughout the experiments for comparison purposes were chosen to match the patient on as many of the attributes listed above as possible (age, sex, educational level, and premorbid musical ability).

Initial neuropsychological tests

The authors reported that the patient's initial issues with a line bisection task (a test of visuospatial acuity) soon went away after her operation, as did some problems with her gait and walking ability. She scored a 27/30 on a mini-mental examination and passed with proficiency the Japanese Standard Language Test for Aphasia – this result is presumably why the authors forewent pursuing any connection between linguistic and musical abilities, although neither tests is discussed in any detail. She also quickly recovered her writing and reading abilities. Although the patient's frontal lobes, which are responsible largely for executive and control functions, were largely affected by her lesion, she scored a 15/18 on a frontal assessment battery, which included the Wisconsin card sorting task (other tasks were not specified). This placed her within a normal range of executive function as compared to typical adults.

First battery of tests for amusia

After self-reporting issues with singing, the patient was referred to a therapy center where an initial battery of tests for amusia was administered. These three main tests were a tone pitch discrimination task, the Montreal Battery for Evaluation of Amusia (MBEA), and a familiar song recognition test. The first task involved playing a 440 hertz (Hz) tone for two seconds and another tone that varied between 400 and 490 Hz immediately afterwards (in 10 Hz intervals). Each comparison interval was randomly sampled through twice and the patient was asked if this second tone was higher, lower, or equal to the initial 440 Hz tone. Her responses were compared with those of 11 healthy controls. The MBEA is a common assessment tool that, although it is not described in detail in any of the studies that utilize it, involves scoring a subject on six sub-tests of musical ability and comprehension: scale, contour, interval, rhythm, meter, and memory. The last task involved presenting the patient with the melodies (played on piano) to 20 pieces of music, ranging from nursery rhymes to well-known Japanese songs, and asking her for the title of the song. The results of each of these initial amusia tests are described at the bottom of this page.

Methods of original experiments

After receiving initial testing in therapy, the experimenters involved with the current paper stepped in and designed two further tests for the patient. The first tested her ability to reproduce rhythms: 10 short, random patterns were tested twice each, after each of which the patient was asked to tap the table with the pattern she had just heard in response. 9 healthy female controls also completed this task for statistical comparison. Each tapping response was rated by two of the papers authors who had formal musical training – if both raters were in agreement, the response was marked as correct. The second original experiment tested the patient's ability to sing a familiar song from memory (it is important to remember here that the initial self-report of musical deficit was an inability to sing well). The patient, and 3 matched controls, were given a starting note and then recorded singing the national anthem of Japan. The researchers used software to analyze the notes sung by these participants in comparison with the actual pitches in the song.

Results

On the tone pitch discrimination task, it was reported that the patient's erroneous judgments were essentially on par with those of the matched controls, indicating a relatively typical ability to discriminate pitch. Mistakes by all participants were all made within a semitone range (+/- 25 Hz) from the 440 Hz initial tone. On the MBEA, the patient scored at or above the cutoff for diagnosis for amusia in all of the categories: she received a 22/30 on scale (at the cutoff), 26/30 on contour, 22/30 on interval, 25/30 on rhythm, 26/30 on meter, and 25/30 on memory. However, the authors noted that these scores were on the borderline of diagnosis and decidedly below average (81%

across tests as opposed to 88% for non-musician adults). Lastly for the initial battery of tests, the patient recognized and named all 20 of the familiar songs played to her on piano with no issues.

The results of the experiments designed and carried about by Uetsuki et al. are reported in somewhat greater detail. In line with the results from the MBEA, the patient performed well on the test of reproducing rhythms. In fact, her scores in comparison with controls were a full point above the average (8/10 on each of 10 test patterns with a standard deviation of 1.05), indicating normal rhythmic comprehension and processing. The key task of singing ability, though, revealed quite a different story. Based on software analysis of the pitch frequencies of the patient's recording of the Japanese national anthem, it was found 35/40 of the notes she sang were incorrect (not within +/- 100 cents, or one semitone, of the target note). A linear regression analysis revealed her correlation of sung note measured frequency to correct note target frequency was .76 while the controls were consistently around 1.00 (indicating they were singing close to the correct fundamental frequencies consistently). It was also noted that her errors especially came with an increase in pitch (higher frequencies) – although wrong notes were sung throughout, higher notes were especially prone to being off the mark. The patient only had a contour error rate of 10% (i.e. 4/40 notes were not sung higher or lower relative to the previous note as they should have been), further showing that her understanding of the melody was relatively intact but off-pitch.

Interpretation

The authors confidently reported that their patient suffers from expressive-vocal amusia without any comorbid linguistic, motor, memory, or executive function deficits. Her problems in singing (namely, missing 87.5% of the notes to a well-known song she previously could sing well) were attributed to an issue in pitch interval production rather than rhythmic or other musical deficiencies. They further suggest that the patient's scores on the MBEA might be too low for someone who enjoyed singing, which could indicate actual perceptual musical deficits.

As mentioned in the first section of this paper, left hemisphere damaged patients with amusia tend to have problems perceiving and reproducing rhythms, while right hemisphere damage commonly results in more difficulties with pitch production and perception. The findings of this current case are nearly the exact opposite. A lesion to this patient's left hemisphere, which would typically lead to aphasia and possibly rhythmic amusia, instead led to no apparent damage of the linguistic network and definite pitch issues. A reasonable conclusion drawn by the authors is that this patient's neural system enabling pitch-interval control is left lateralized while her language capabilities are dependent on the right hemisphere. This finding necessarily complicates the textbook-ready neuropsychological view of lateralization in the brain, which often implies uniformity in the distribution of processes in all of our brains.

While the authors could only find one other documented patient like this one before in the literature (having amusia without aphasia following wide damage to the left hemisphere), they were able to generalize some of their findings to a wider theoretical context. Most importantly, and this issue will be taken up below, they suggest that the patient's issues with tuning may be fundamentally a fine motor issue. Her surgery potentially disrupted an internal auditory-motor feedback system necessary to perceive and correct sung notes in real-time (see the description Mandell et al., 2007) – the resulting inability to regulate her own pitch with her laryngeal muscles led to the documented singing problems.

Further analysis

Without knowing why this is the case, my main issue with this paper is its short length and the corresponding lack of information and exploration into a lot of interesting points. For instance, it is reported that the patient does not have aphasia or any other evident linguistic problem, but the implications of this finding for the field and on the results of previous studies are not grappled with. There is material here by which to more explicitly combat previous research teams who have claimed to have definitively localized certain elements of musical processing or to have experimentally established a link between the resources sustaining language and music. However, that work is left to a conscientious reviewer to do.

I also find there to be a lack of careful consideration of the patient's initial motor problems. Recall that although there were no findings of gross motor issues, post-surgery the patient had issues with her gait. Could it be that although more evident motor issues cleared up quickly, it was/is still possible to isolate the fine motor problems potentially responsible for her pitch production deficits? The next section will focus on this concern. With more presentation of some supplementary research into the science of sound production, the motor representations of music in the brain, and further explication of the methods and tests used in therapy, the present paper could have more successfully imparted what are altogether convincing, interesting, and relevant results to the future study of amusia.

III. Future Directions

What do we know now?

It should be well-established by now that the present case study delegitimizes any belief in a standard lateralization or localization of musical abilities in the brain. By combining post-operative MRI documenting extensive damage to the patient's left frontal regions with an extensive range of tests for musical impairment, it is clear that her (and by extension others) pitch production abilities are dependent largely on the left hemisphere while other abilities in the cognitive domain of music such as rhythmic comprehension are located elsewhere (presumably the right hemisphere along with language faculties). I believe further experimentation with the patient documented in Uetsuki et al. could yield no further interesting answers to the question of *where* tackled by the authors. However, given the same patient I will propose here some further research into the question of *how* her particular deficit arose – what neural networks were affected, which cognitive domains are implicated, and how should we think about deficits of this kind?

What is there left to discover?

I will note first that I am still interested in the potential functional connections between elements of language and music processing described by Patel in 2003. I do not believe this patient to be a good candidate to explore his theories, though, because her amusia-related deficits do not encompass some of the hierarchy-based musical abilities hypothetically linked to language networks, such as melodic/chord comprehension and enjoyment, or the parsing of complex rhythms (Patel 2003). Instead, there is plenty of room by which to further investigate the proposed motor-music feedback loop proposed by Mandell et al. and touched upon in Uetsuki et al. as well.

As reported, the patient has preserved a relatively normal ability to discriminate between pitches when played individual tones. Then why should she display such a poor ability to regulate her own voice, especially considering she was previously known to be a good singer? Recall that there were two main proposals raised in the paper to explain her main deficit, neither of which was definitively relied upon or proven. The first was drawn from the patient's below average scores on the MBEA tests which could show a borderline musical perceptual deficit. The other was a fault in a motor-pitch production feedback loop mentioned several times already.

I hypothesize that the second possibility is far more likely given the relative weakness of the evidence for the first and the existence of previous research proposing the same motor feedback loop. An alternative hypothesis is that the patient's perceptual musical abilities were indeed damaged without any corresponding motor problem which resulted consequently in an inability to sing a simple song like the Japanese national anthem in tune. This would mean that the initial battery of tests, which included the MBEA and the pitch discrimination task (telling whether a note is higher, equal, or lower relative to another), were too simplistic or not sensitive enough to statistically recognize this inability. I propose here an original experiment in order to differentiate between these two hypotheses and further answer the experimental questions taken up by Uetsuki et al. This experiment would investigate how well aware the patient is of her own failings in pitch production. Although she initially self-reported having a singing deficit, it is important to experimentally address this issue in order to determine quantitatively whether the deficit can be attributed more to a motor or perceptual problem.

A new experimental design

Examining the same patient as Uetsuki's team did, I would design another pitch discrimination task, with one important difference. While the first tone in each trial would still be a precise, computer-generated tone, the second would be a response tone given by the patient herself and recorded and analyzed for its frequency in a manner similar to the anthem recording and analysis done previously. Each trial would consist of the participant hearing a pitch for two seconds, waiting for two seconds, and then attempting to sing back the pitch she just heard into a microphone. She would then be asked whether she thought the note that she sang in response was higher, lower, or equal to the tone she just heard. The trials would vary by giving a range of starting pitches from the lower end to the higher end of the patient's natural vocal range (probably from around 220 to 600 Hz in increments of 40 Hz), and each of these 10 trials would be repeated twice. Both the comparison between target and produced note and the patient's corresponding answers would be recorded (naturally for a within-subject analysis). A note would be marked as sung correctly if it lands within +/- 100 cents (1 semitone) of the target pitch.

Variable analysis

Unlike in the previous original experiment examining the patient's singing abilities, the dependent variable in this experiment is not whether she sings the note correctly with regards to the target pitch. Instead, the correctness measurement of her singing – higher, lower, or equal as determined by software comparison of the frequencies of the target and response tones – is the independent variable. The dependent variable is whether the patient's own given response is in agreement with this correctness measurement or not. Each time the patient's assessment of her own pitch matching ability is in line with the actual analysis of the two notes would be recorded as a correct trial, and each time it was not (e.g. she said her note was too low when it was equal etc.) would be recorded as an incorrect trial. Anyone conducting this experiment could be well-assured that there would be variability in the data because we already know that the patient gets some notes right, but she also misses quite a few notes, especially as they go up in frequency.

Potential results and interpretations

The analysis should initially reveal a concordance with previous testing, chiefly that higher notes are missed more consistently by the patient. If this is not found, the methods, data collection, and analysis of both experiments should be rigorously examined to determine the cause of the discrepancy.

Out of 20 trials, if *t*-tests reveal that the patient is performing at or below chance level on this task, this would constitute evidence that there is a serious perceptual problem underlying the patient's amusia that was not previously noticed by the MBEA or pitch discrimination task.

Otherwise, this task would reveal that the patient has good intuitive comprehension of the nature and manifestations of her singing deficit. This would leave as the only reasonable conclusion that, despite having a perceptual grasp of the problems with her singing, the patient has an inability to take turn this perception into a non-conscious regulation of her laryngeal fine muscle movements. Given that there was no gross motor damage or other motor deficits related to speech reported in the Uetsuki et al. case study, it is likely that this motor problem is not muscular but based instead in the neural mechanisms of pitch production. Therefore, the theory of a neural feedback loop between the motor regions (which were not encompassed by the patient's lesion) and the pitch producing region of her left frontal lobe would seem increasingly likely. If this were shown to be the case, it would be clear that, at least with regard to singing ability, there exists a physical and systematic connection between motor and musical abilities, but that potential finding raises one last important question: should we necessarily consider these separate abilities to begin with?

Final thoughts

I will assume here that the more likely and interesting experimental result occurs to and bolsters the claims of Uetsuki et al. and Mandell et al. – the patient has a fine motor disability which impairs a feedback loop which typically would allow her (and all singers) to effectively monitor and regulate their pitch. This is documented by Uetsuki et al. as a case of expressive-vocal amusia, but does this classification inherently mean that it is a *musical* ability that has been impaired? What even constitutes a musical ability? As we have seen in this review, there are many brands of amusia that are tested for, tests that investigate abilities as wide ranging as rhythm production and pitch discrimination. I believe it is possible that findings like those from my hypothetical experiment might force neuropsychologists to reconsider whether music can even be considered a singular, isolable cognitive domain like language is. If different aspects of the deficits that make up the global syndrome of amusia can be shown to be more dependent on other cognitive systems than each other, it will seem arbitrary and potentially hindering to continue grouping them together. Perhaps a fuller vision of our rich mental life will one day show that our appreciation of melody does indeed require the same resources which enable the parsing of linguistic syntax, our pitch discrimination abilities necessitate above all good auditory functioning, or that singing is fundamentally a regulatory motor ability.

Study of the patient in the Uetsuki et al. case study has already proven to have the potential to help scientists re-envision much of what we currently consider music processing, and if I were running a lab in this field, thanks to papers like this, I would immediately begin investigating some of the questions posed in the paragraph preceding. On a more basic level, a study like this also has the ability to inform the public and experts alike how the brain works generally, both in terms of the non-universality of the localization of functions and the complex interdependencies between seemingly disparate cognitive domains.

When we listen to a song we love, perhaps it is mere “auditory cheesecake” as Steven Pinker has suggested. However, future scientific research can still do much to explain why the disparate ingredients of this particular cheesecake are so delicious when mixed together: the crumbly bread base of rhythm, the the creamy, complex filling of chords and harmony, and the sweet, evocative melody drizzled on top. All of these rely on different processes to make them, and different taste buds to appreciate them, but together they can swirl together into something magnificent.

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