

Neuroscientific Investigations of Musical Rhythm: Recent Advances and Future Challenges

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Neuroscientific research into music has increased noticeably over the last two decades, but how (or if) the findings have improved our understanding of music is debatable. This question is considered in this article, which first describes advances in neuroimaging techniques, and then reviews findings from research in the neuroscience of music (with a focus on rhythm and meter). Some of the difficulties encountered by researchers are highlighted, from lack of consensus about timing mechanisms to difficulties in comparison of neuroscientific findings across different studies. The article ends with a description of several new methodological developments that are likely to feature prominently in future investigations of music and neuroscience.

Keywords: Rhythm; Neuroscience; fMRI; MEG; Timing; Music

Introduction

Research in cognitive neuroscience has increased dramatically over the last two decades, and research into the neuroscience of music is no exception. The 1990s were christened ‘the decade of the brain’ in America, and the field has received plenty of attention ever since. Large investments have been made to acquire MRI scanners and to train researchers in the methods necessary for analyzing the resulting data. Twenty years ago, scientists and the public alike were excited about the potential for making truly groundbreaking findings. Today, if media coverage is anything to go by, our interest in neuroscience research shows little signs of flagging, and music research in particular continues to capture the public interest. It is important to evaluate what advances have come from the large investment of monetary and intellectual resources. Has this investment produced findings that have influenced how we think about music?

In this article, I will introduce the various neuroimaging methods used in the neuroscientific study of music, and the relative advantages and disadvantages of each.

The focus will be on rhythm research, as this is my own area of expertise, and it is an area of music cognition that is attracting increasing interest, from a variety of perspectives. After a review of research in the neuroscience of rhythm comes a consideration of how these findings have (or have not) enlightened our understanding of musical rhythm. I will then consider why more advances have not been made, and how the current situation may be improved. Finally, I will briefly highlight some new methodological developments that are likely to feature prominently in future investigations of music and neuroscience.

Main Neuroimaging Methods

Cognitive neuroscience combines the experimental strategies and paradigms of cognitive psychology with neuroscientific techniques to examine how brain function supports mental processes. In the field of human cognitive neuroscience, non-invasive recording methods are most commonly used. Although recording neural activity directly with penetrating electrodes has excellent temporal and spatial resolution, it is too invasive to investigate human brain function except when clinical opportunities arise (e.g., Liegeois-Chauvel et al., 1999). However, major developments in non-invasive techniques now mean that excellent spatial and temporal resolution can be achieved in healthy volunteers.

Non-invasive brain imaging techniques can be divided into those measuring the electric or magnetic fields generated by neuronal activity (electroencephalography [EEG] or magnetoencephalography [MEG]) and those measuring the hemodynamic or metabolic consequences of neuronal activity (positron emission tomography [PET] or functional magnetic resonance imaging [fMRI]). These two classes of techniques provide complementary data: EEG and MEG have superior temporal resolution and are useful for exploring the time course of neural activity, whereas fMRI and PET provide superior spatial localization, indicating where in the brain such activity is occurring.

Electrophysiological Methods

EEG/MEG signals are directly coupled to neuronal electrical activity, and these methods can measure activity with millisecond temporal resolution (Nunez, 1981; Hämäläinen et al., 1993). Neurons send and receive signals through the entry of either positive or negative ions (depending on whether the signal is excitatory or inhibitory), and the movement of these charged ions causes a current flow. The current flow results in an unequal distribution of electrical charges, or an electrical potential. EEG is sensitive to electrical potentials (Humphrey, 1968). The potentials from individual neurons are too small to be measured in EEG, so a typical surface EEG reading arises from the summation of the potentials created by synchronous activity of thousands or millions of neurons, with the greatest signal contribution made from neurons in the outer layers of the cortex. Neurons that are deeper in

the cortex, or in midline or deep brain structures, make less contribution to the EEG signal.

Determining the neural source of the signal is somewhat tricky in EEG, in part because the signal is 'blurred' by the membranes covering the brain, cerebrospinal fluid and skull. This blurring obscures the signal's true intracranial source. Determining the source(s) of an EEG signal is also difficult because of the 'inverse problem' of estimating which sources might have given rise to the signal recorded on the scalp (Pascual-Marqui, 1999). That is, for any distribution of signals outside the head, there are an infinite number of configurations of sources within the brain that are consistent with that distribution. This 'inverse problem' is comparable to reconstructing an object from its shadow: only some features (the shape) are uniquely determined, others have to be deduced using additional information (Hauk, 2008). However, by imposing reasonable modelling constraints, useful inferences about the activity of interest can be made. The simplest possible model is that only one source (called a 'dipole') is generating the signal. The goal is then to determine for every sample of time where in the head the dipole is, what its orientation is and how strong it is (the dipole moment). We also want to know the anatomical location. In this case, the activation centers derived from PET or fMRI can sometimes be used as initial guesses (or 'seeds') for dipole locations (Dale & Halgren, 2001; Dale & Sereno, 1993).

The best-known EEG data are derived from event-related potentials (ERPs), or the variations in electrical potential strength over time. Essentially, signals from each electrode are averaged over many presentations of the same stimulus. The signal is called an 'evoked response' because it is a time-locked average of the neural response evoked by a stimulus. The evoked response will show certain positive or negative 'peaks', called 'components'. Components with certain latencies and amplitudes are argued to be associated with specific mental operations. For example, an evoked response called the 'mismatch negativity', or MMN, is a component that occurs approximately 100–200 milliseconds after a repeated auditory stimulus is changed, and is thought to indicate pre-attentive responses to changes in auditory stimuli (Näätänen, 1992). Components frequently found in studies of music include the P600 (a positive peak ~ 600 ms after the stimulus) and early right anterior negativity (ERAN), both elicited by syntactic incongruities (Koelsch et al., 2000, 2001, 2005; Patel et al., 1998); the P300, a positive peak about 300 ms after a stimulus, which reflects violations of expectancy (Jongsma et al., 2004); and the N400, a negative component, about 400 ms after a stimulus, which reflects semantic integration but can also be elicited by words that are incongruent with musical contexts (Koelsch et al., 2004). For rhythmic violations, for example, an N150 (a negative component ~ 150 ms after the violation) has been observed (Geiser et al., 2009; Vuust et al., 2005). ERPs can tell us about processing difficulty (a larger N400 component will be observed for more difficult semantic integrations), or about the effects of attention (if a component only occurs when participants are attending to a violation, that suggests the brain cannot process that aspect of the stimuli automatically, and that some other attentionally demanding process is required).

A second type of EEG-based phenomenon is the rhythmic, or oscillatory, responses present in electrophysiological signals (Basar et al., 1999; Llinas, 1988). Oscillatory activity differs from the traditional ERP in that it reflects higher frequencies of brain activity. One advantage of measuring oscillatory responses is that they are temporally more focal, and thus responses to events close in time (such as successive tones in a rhythm) do not overlap as they do for the lower frequency evoked responses (Snyder & Large, 2004). Oscillatory activity is often divided into multiple frequency ranges, such as Alpha (~ 8 to 12 Hz), Beta (~ 12 to 30 Hz) and Gamma (~ 30 to 100 Hz), though the exact boundaries between bands vary between research groups.

Oscillations in particular frequency bands (e.g., the Gamma band) have been argued to provide the infrastructure for binding information together, and are potentially involved in object representation, attention, memory and consciousness (Joliot et al., 1994; Llinas & Ribary, 1993; Tiitinen et al., 1993). Thus, oscillatory neuronal behavior might provide a framework to coordinate information within and across brain areas into unified percepts. Increased synchrony at Gamma band frequencies is found in musicians when listening to music, and the authors suggested that the Gamma band activity may coordinate memory for musical patterns with anticipation about how the music will unfold (although this is speculative) (Bhattacharya & Petsche, 2001; Bhattacharya et al., 2001). In studies of rhythm, Beta and Gamma band activity has also been implicated in anticipation of tones (Iversen et al., 2009; Snyder & Large, 2005).

Magnetoencephalography (MEG)

The basis of MEG recording lies in the fact that the current flow induced by neural activity also generates a magnetic field. MEG can measure these induced magnetic fields (Cohen, 1968). Thus, MEG and EEG measure signals from the same neurophysiological processes, but in different ways, which leads to some important differences. For example, magnetic fields decay more quickly as a function of distance than electric fields. This means that MEG signals have even less contribution from deeper sources than EEG signals (Hämäläinen et al., 1993).

Because the magnetic fields generated by even thousands of neurons with overlapping activity are very small, extremely sensitive magnetic field detectors are required. These detectors are known as ‘superconducting quantum interference devices’, or SQUIDS. The MEG output is a measurement of magnetic field strength at each point in time, and at each sensor location around the head. Averages of stimulus-locked waveforms can be generated, called ‘event-related fields’ (ERFs) instead of event-related potentials as in EEG. The analysis and interpretation of ERFs and ERPs is similar. Peaks that have names in EEG are given an ‘m’ suffix in MEG to indicate that they are magnetic field peak equivalents in MEG (e.g., the ERP component called the ‘MMN’ is called the ‘MMNm’ when it is recorded in MEG).

Like EEG, MEG data is analyzed to model the origin of the current source at each point in time. However, because magnetic fields are less distorted by the resistive

properties of the skull and scalp, the signal blurring is less than that found with EEG. This leads to MEG's greater spatial resolution. As a result, it is customary to co-register the source information with MR structural images so that the origins can be determined in an anatomical context. An interesting application of this is present in work by Schneider et al. (2002). They used MEG to measure the evoked response to sine wave tones in professional, amateur and non-musicians, and localized these responses in each participant's structural MRI scan. Musical training led to a stronger response to the tones (even greater in professionals than amateurs), which was localized to a particular area of auditory cortex (specifically, anteromedial Heschl's gyrus). The amount of gray matter in this area was correlated with the evoked response strength, and both the MRI and MEG measures correlated with performance on a test of musical aptitude. Together, the measures suggested that the structural and functional brain differences in auditory cortex reflected musical aptitude.

Given the high temporal resolution of MEG and its ability to localize fields in a useful anatomical context, the technique offers a link between the high spatial-resolution data available with fMRI, on the one hand, and invasive electrophysiology, on the other. The signal to which MEG is sensitive is likely to be the same activity that fMRI measures (indirectly), meaning that comparability between these two methods should be high.

One promising approach to MEG data analysis combines ERF peak analysis with spatial localization (Salmelin et al., 1994; Vihla et al., 2006). The various peak responses are identified and localized to reveal the location and timing of signals associated with a particular cognitive operation. Each peak is presumed to be associated with the distinct processes involved in completing the task. This approach enables one to track the spatial and temporal course of processing through the brain, matching responses to stages and modules of cognitive theories (Poeppel & Marantz, 2000).

Hemodynamic Methods

Hemodynamic methods offer excellent spatial resolution (on the order of millimetres), but they are based on signals whose time course ranges from seconds (fMRI) to tens of seconds (PET). These techniques rely on the principle of neurovascular coupling: put simply, when neurons are active, they deplete their supplies of oxygen and glucose. To replenish them, blood flow increases, bringing glucose and releasing oxygen to these neurons at a greater rate. In PET imaging, one can measure either the change in blood flow or metabolism to index neural activity (Raichle, 1987). To do this, particular molecules are tagged with radioactive tracers. Oxygen is tagged to measure blood flow, and glucose is tagged to measure metabolism. The tracers gradually accumulate in brain areas that have greater neural activity, and after a 60–90 second delay, a measurement is made to determine the areas with the most accumulation. The areas of accumulation during a control task

can be compared to the areas of accumulation in an experimental task, and any differences anatomically localized. The temporal resolution of this technique is quite coarse, as the cumulative average of neural activity over the entire block is measured. Not all cognitive processes of interest can be investigated using block designs, and this remains a significant limitation of PET methodology.

Like PET, fMRI also indexes neural activity by measuring vascular changes, but unlike PET, it takes advantage of the different magnetic properties of oxyhemoglobin and deoxyhemoglobin, present in oxygenated or deoxygenated blood, respectively. After neural activity, the subsequent increase in oxygenated blood (and therefore oxyhemoglobin) leads to magnetic signal variation that can be detected using an MRI scanner. This is known as the 'blood-oxygen-level-dependent' (BOLD) response (Kwong et al., 1992; Ogawa et al., 1990; Turner et al., 1991). It takes time for the oxygenated blood to reach the neurons, so the BOLD response only begins to rise above baseline after enough oxyhemoglobin has arrived to change the magnetic signal. The change is detectable around two to three seconds after the start of neuronal activity, and reaches its peak at about four to six seconds. A set of images covering the whole brain (a brain volume) is typically acquired every two to three seconds. Multiple positions within the brain are sampled in every volume—typically around 100,000 such positions, or 'voxels', which gives rise to a series of three-dimensional images of brain activity. Typically, hundreds of brain volumes are accumulated, then averaged together to increase sensitivity. The need for averaging is due to the small magnetic signal changes being detected (on the order of 0.5–5% in a scanner with a magnetic field of 1.5 Tesla).

In summary, the tools to characterize both the temporal and spatial aspects of brain activity have undergone major methodological developments. Each technique has its pros and cons, and is sensitive to different characteristics of the brain response (spatial versus temporal aspects, surface versus deep structures). Some techniques are much more widely used than others. One influential consideration has been availability—PET requires a nearby cyclotron (an accelerator of subatomic particles) to generate radioactive isotopes, and fMRI has only recently become widely available as more MR scanners are installed in hospitals and research institutions. MEG is still only of limited availability, whereas EEG is widely available. Another consideration is cost. PET and fMRI are both expensive, and MEG is orders of magnitude more expensive than EEG (and also more expensive than fMRI). Finally, all these techniques require substantial processing of the signal and complex statistical procedures to produce meaningful results. Expertise in fMRI and EEG in particular are now widespread, whereas MEG expertise remains more limited (but is increasing).

The Aim of Functional Localization

Much of cognitive neuroscience research into music and rhythm processing has focused on functional localization. A variety of studies, typically using brain lesion

and neuroimaging approaches, have attempted to delineate the anatomical organization of the music processing system.

What is the use of localization? The now-discredited practice of phrenology was based on the reasonable concept of localizing traits to particular brain areas, ‘measured’ by examining the size of bumps on the overlying skull. However, phrenology was based on rather naïve conceptualizations of mental processes, and the skull is not systematically related to the function of the brain area underneath. Years of cognitive psychology research have yielded more sophisticated models of the processes that underlie mental function. In addition, unlike bumps on the head, the signals measured by PET and fMRI do directly relate to neural processing. The goal of functional localization is to identify regions of the brain and their temporal relationships associated with the performance of a task. The unique strength of functional brain imaging is that it can tell us about these processes in the brain that is of most interest to us—the human brain. This is a particular strength for investigations of rhythm and music, as these behaviors are not observed in the same way in other species (particularly not in our nearest evolutionary relatives; Bispham, 2006; Merker, 2000; Merker et al., 2009). fMRI is also unique in allowing us to investigate healthy, intact brains, without the confounds of pathology and the plastic reorganization in response to disease or developmental abnormalities (Dolan, 2008).

It is important to realize that most investigators who use fMRI methods seek not just to localize brain function, but to map the parts of the system that act in different combinations for different tasks. Although much fMRI work to date appears to have a localization objective, this may simply be a reflection of the relative youth of the field. Earlier studies may act as a first pass survey of candidate areas, with more complex mapping about the inter-relationships between areas to come. Even in the last few years, identification and discussion of relations between active brain regions features more prominently in the literature (Ramnani et al., 2004; Rykhlevskaia et al., 2008). The newer approaches being used to investigate how and when neural areas interact are summarized at the end of this article.

Neural Investigations into Timing and Rhythm

Definitions

Because many of the words associated with rhythm and timing have been defined in different ways, it is important to clarify how they are used in the next sections. ‘Rhythm’ is defined here as the pattern of temporal intervals in a stimulus sequence. The pattern is generally indicated by the onsets of a stimulus (a tone, click or other sound), and inter-onset-intervals generally define the lengths of the temporal intervals in the sequence. Often, listening to a musical rhythm gives rise to a sense of ‘pulse’, sometimes termed the ‘beat’. The pulse or beat is a series of regularly recurring, precisely equivalent psychological events that arise in response to a musical

rhythm (Cooper & Meyer, 1960; Large, 2008). Although pulse arises in response to a rhythmic stimulus, it is not defined as a stimulus property (Benjamin, 1984; Lerdahl & Jackendoff, 1983; London, 2004; Palmer & Krumhansl, 1990). Often, the individual pulses or beats are perceived to possess differing degrees of accent, or stress, which gives rise to meter. 'Meter', 'metrical structure' or 'metrical hierarchy' refer to patterns of regularly recurring stronger and weaker pulses (Epstein, 1995; Lerdahl & Jackendoff, 1983). Thus, rhythms can induce an internal pulse (we 'feel the beat'), and internal organization of these pulses can lead to the perception of a recurring pattern of relative pulse strengths, called 'meter'. The process of synchronizing the endogenous pulse with an external rhythm is called 'entrainment' (although this term also has broader uses).

Investigating Timing

From a bottom-up perspective, timing is one logical place to begin investigating the neural instantiation of rhythm processing. For one, it can be broken down into rather simple components. Timing processes have also been widely investigated using a variety of techniques, and from a variety of perspectives (not the least of which include movement, language, perception and memory (Eagleman et al., 2005; Ivry & Spencer, 2004; Mauk & Buonomano, 2004)). In addition, a number of timing models exist, which may have components that can be tested for their presence in the brain. However, despite this potential, there is little consensus in the timing field about the best way to model timing, or how timing is accomplished neurally. Timing has been modelled with neural clock or counter mechanisms, represented as either pulses (firing) or neural oscillations (Buhusi & Meck, 2005; Ivry & Richardson, 2002; Ivry & Spencer, 2004), but timing can also be implicit, or an emergent property of movement (Ivry & Spencer, 2004; Spencer et al., 2003). Neural oscillator approaches have arguably had more success in capturing ways that higher-level features of temporal patterns, such as pulse and meter, can arise from the responses of neural nonlinear oscillators to rhythmic stimuli (Large, 2000, 2008; Large & Kolen, 1994).

Functional neuroimaging studies, as well as studies of brain-damaged patients, have linked components of timing processes to several cortical and sub-cortical regions, including the cerebellum, basal ganglia, parietal cortex, premotor cortex and supplementary motor area (SMA) (Ferrandez et al., 2003; Macar et al., 2004; Nenadic et al., 2003; Rao et al., 1997, 2001). These areas are traditionally thought to be involved in various aspects of movement. The basal ganglia are a group of structures deep in the brain that have a role in motor control, action selection and learning (Graybiel, 2005; Graybiel et al., 1994; Mink, 1996; Redgrave et al., 1999). The cerebellum allows coordination and fine-tuning of movement by integrating sensory and motor information (Diedrichsen et al., 2007; Gao et al., 1996; Thach, 1998). Premotor and supplementary motor areas are strongly interconnected with the basal ganglia and cerebellum, and have roles in planning, voluntary control and execution

of movement (Boecker et al., 1998; Catalan et al., 1998; Gerloff et al., 1998; Grafton et al., 1998; Picard & Strick, 1996).

Several theories have been proposed to dissociate the different roles of these commonly activated motor areas in timing processes. One replicated neuroimaging result is that directing attention to the timing of a stimulus activates the SMA, and orienting attention to a particular point in time activates parietal cortex (Coull & Nobre, 1998; Coull et al., 2004). This distinction is relevant to studies showing that greater attention is allocated to times of pulse expectancy (Jones & Boltz, 1989; Jones et al., 2002); this may be mediated by the parietal cortex. Another proposal distinguishes between systems required for the timing of suprasecond and subsecond durations (Ivry & Spencer, 2004; Lewis & Miall, 2003). In this framework, 'cognitively controlled' timing, reliant in part on the basal ganglia, is the 'measurement of supra-second intervals not defined by movement and occurring as discrete epochs'. This is contrasted with 'automatic' timing, which relies on the cerebellum and involves 'the continuous measurement of predictable sub-second intervals defined by movement' (Lewis & Miall, 2003). This distinction is supported by reviews of the neuroimaging literature, but has yet to be conclusively confirmed.

Much timing research has focused on the role of subcortical areas, particularly the cerebellum and basal ganglia. Patients with cerebellar lesions are impaired on perceptual and motor timing tasks (Ivry et al., 1988, 2002; Spencer et al., 2003), and neuroimaging studies of timing often find cerebellar activity (Bengtsson et al., 2009; Kawashima et al., 2000; Lutz et al., 2000). The basal ganglia are also directly involved in timing. Patients with Parkinson's disease have impaired basal ganglia function, and show impaired timing abilities (Artieda et al., 1992; Elsinger et al., 2003; Harrington et al., 1998; Malapani et al., 1998). Furthermore, neuroimaging studies have shown that the basal ganglia are active in timing tasks, particularly those that require people to carry on tapping intervals from memory (Lewis et al., 2004; Rao et al., 1997). The abundance of studies has led to reasonable consensus about which areas are frequently observed in timing tasks, but assigning functions to different areas has proved more difficult. Some timing models (Large, 2008; Meck et al., 2008) indicate that the communication between these different areas gives rise to particular timing behaviors (rather than the behaviors being localizable to a single area), and therefore more sophisticated or comprehensive models of how brain regions interact will be important in future.

Investigating Rhythm

Although research into timing is crucial for revealing its basic properties, many neural models of timing do not appear adequate to explain complex rhythm processing. For example, the distinctions between cognitively controlled and automatic timing do not neatly map onto rhythm perception. Rhythm perception appears to have characteristics of both systems, as the length of the intervals in

musical rhythm spans from approximately 100 milliseconds to two seconds (Parncutt, 1994; Warren, 1993). Moving up from individual intervals, rhythms contain metrical hierarchies that also span the subsecond and suprasedond domain. Therefore, perception of musical rhythm and meter may require integration of automatic and cognitively controlled processes.

fMRI Studies. To move on from automatic versus cognitively controlled or supra versus subsecond distinctions, several recent neuroimaging experiments have investigated perception and reproduction of more complex musical rhythms. These studies generally show substantial overlap with the timing literature in activated areas: premotor cortex, supplementary motor area, cerebellum and the basal ganglia (Bengtsson et al., 2009; Chen et al., 2008a; Grahn & Brett, 2007; Lewis et al., 2004; Mayville et al., 2002; Schubotz & Cramon, 2001; Ullén et al., 2003). The overlap suggests that rhythm processing does share some neural substrates with timing, and that the two processes are not completely independently mediated in the brain. The activated brain areas also respond similarly to both perception and production of rhythms (Schubotz et al., 2000). However, so far it has been difficult to tease apart the involvement of areas in basic timing and more complex rhythm processing.

One proposal that has been made is the potential role of the basal ganglia in generating endogenous pulse, or 'feeling the beat'. Two fMRI studies examining beat perception reported basal ganglia responses when regular rhythms that induced perception of a beat were compared to similar rhythms that did not induce a beat (Grahn & Brett, 2007; Grahn & Rowe, 2009). Using converging methodology, a follow-up study in Parkinson's disease patients (for whom basal ganglia function is impaired) found a specific impairment in discriminating changes in rhythm with a beat (Grahn & Brett, 2009). Whether the role of the basal ganglia is in the initial encoding/extraction of the beat or some later process (such as internal generation of the beat) remains to be determined. Another concept that is emerging from the neuroimaging literature is that rhythm perception may require interactions between the auditory and motor systems. At least two studies have found increased coupling of neural activity between auditory and premotor cortex during rhythm processing (Chen et al., 2006; Grahn & Rowe, 2009).

EEG/MEG Studies. EEG studies have had success in distinguishing specific neural components for different aspects of rhythm processing. Geiser et al. (2009) measured ERP responses to changes in metric organization (removal or addition of one eighth note to a repeating rhythm which shifts the induced metric pulse structure from regular 3/4 time to a more unusual 5/8 or 7/8 time) or changes in a rhythmic pattern (e.g., substituting two faster notes in the place of one slower note without shifting metric structure). The experimenters also manipulated participants' attention. In one condition, participants were doing an unrelated pitch change detection task, in which the rhythm and meter changes occurred, but were not important to the task. In the

other condition, they attended to the temporal changes and responded each time they heard either a meter or a rhythm change. Thus, rhythmic and metric perturbations could be examined when the perturbations were not attended (pitch task) or attended (rhythm/meter task). In agreement with previous work (Jongsma et al., 2005; Vuust et al., 2005) they found a negative ERP component about 100–150 ms after the perturbation. Most interestingly, this deflection was elicited in the rhythm condition regardless of whether the participants were attending to the pitch changes or the temporal changes. Metric changes, however, only elicited the negative deflection in the attended condition. These findings suggest that encoding of metrical hierarchies is a more complex and attention-demanding process than encoding of surface rhythmic patterns.

A recent MEG study investigated rhythm sequences that contained increasingly salient violations of rhythmic expectancy (Vuust et al., 2009). The researchers expected to observe event-related components reflecting an error term (induced by the violation of expectancy) and also a component indicative of subsequent evaluation of the internal model of the rhythmic sequence. The error term was predicted to be encoded by the mismatch negativity component (MMNm). As evaluation should occur after the error, the authors predicted that after the MMNm, they would observe a P3am component, usually associated with the evaluation of a change for subsequent behavioral action. Their predictions were confirmed: mismatch negativity (MMNm) and a subsequent P3am component were both observed, and were strongest for the condition with the biggest expectancy violation. Musicians showed greater sensitivity than non-musicians to milder violations, with larger MMNm peaks which occurred slightly earlier. The authors suggest this reflects a better internal representation of the metrical structure in the musicians that enables them to make more precise predictions about incoming stimuli. The musicians' brains therefore respond more strongly and more quickly than non-musicians to any deviation from their predictions.

As mentioned earlier, one interesting approach to the modelling of rhythm has been to use nonlinear neural oscillators. Neural oscillation arises from interactions of excitatory and inhibitory neural populations. Through mathematical modelling of these interactions, the universal properties of neural oscillation can be deduced, and these properties examined for features that may correspond to properties of rhythmic behavior. This 'neural resonance' (neural oscillators resonating with rhythmic stimuli) approach naturally gives rise to properties such as pulse and meter, which are aspects of rhythms that have not been easily accounted for by other types of models (Large & Snyder, 2009). The plausibility of this approach is supported by recent work with zebrafish larvae (Sumbre et al., 2008), which shows that a rhythmic stimulus can entrain neuronal ensembles, and that the ensembles carry on responding at the entrained interval after the stimulus has stopped, exhibiting a 'memory' of the interval. This neural response is also related to behavior: researchers found strong correlations between the neural ensemble activity and the zebrafish larvae flipping its tail. Thus, even for primitive animals, neural entrainment to a stimulus can give rise

to rhythmic behavior. Work in humans, described below, also shows neural correlates consistent with the predictions of neural resonance theory.

Investigations of neural oscillatory processes in the rhythm domain have revealed interesting findings in the higher frequency Beta and Gamma ranges. The neural oscillations are thought to reflect communication between different brain regions, and are modulated by various sensory and cognitive processes. For example, the Beta-band oscillation has been strongly associated with motor tasks, and has been observed in sensory and motor cortices (Salmelin et al., 1995), as well as basal ganglia and cerebellum (Baker, 2007; Salmelin & Hari, 1994). The Gamma band has been associated with attention and memory (Jensen et al., 2007), anticipation and binding processes (Bhattacharya et al., 2001) in the brain.

Oscillatory brain responses were measured recently in a study of rhythmic expectancy and metric encoding that used an isochronous sequence of tones (Snyder & Large, 2005). Every other tone was physically accented, which gave rise to a strong perception of a beat on the accented tone. They measured neural responses to occasionally omitted tones, and found that neural responses were much greater for tones 'on the beat' than not. They also found increases in induced oscillatory activity at the time of the omitted accented tone. The increased oscillatory activity in absence of the stimuli was interpreted as reflecting a temporal expectancy in line with the metrical interpretation, and provides a potential neural marker of pulse, or beat expectancy. These findings are in line with predictions of neural resonance theories of timing.

Iversen et al. (2009) extended the findings of Snyder and Large (2005) using MEG. They measured brain responses evoked by a repeating rhythmic pattern of two tones followed by a rest. Listeners were instructed to impose different metrical interpretations on the rhythm by mentally placing emphasis (feeling a beat) on either the first tone or the second tone. As the stimulus was the same in both conditions, differences in brain activity reflected the endogenous metrical interpretation. The metrical interpretation influenced early evoked oscillatory neural responses to the tones, specifically in the upper Beta range (20–30 Hz). The Beta response was stronger (by 64%, on average) when a tone was imagined to be the beat, compared to when it was not. A second experiment established that the beta increase was very similar to that observed when the tones were physically (rather than mentally) accented. As Beta responses are closely linked to motor processing, these findings parallel those found in fMRI studies: the motor system influences metrical interpretation of rhythms, even in the absence of overt movement. Fujioka et al. (2009) have also found increased Beta and Gamma oscillations during processing of the beat. They reported that Gamma-band synchrony increased immediately after each tone in a sequence of regularly presented tones, but also after an unexpected omission, suggesting an association with an endogenous anticipatory process. Taken together, the findings of these different groups provide converging evidence that increases in the induced Beta- and Gamma-band synchrony could be neural markers of endogenously generated pulse and meter.

The Benefits of Using Neuroscience Methods to Study Rhythm

Brain imaging techniques have been criticized for being unnecessarily expensive and not contributing to discrimination between psychological models (Coltheart, 2006; Page, 2006). However, these techniques do have some undisputable advantages over behavioral techniques. One advantage is that when overt behavior cannot be measured, the brain's response may still provide information that can be measured: it gives us another dependent variable to test. A recent preliminary study of newborns illustrates this advantage (Winkler et al., 2009). Infants (two or three days old) listened to simple rhythms while their brain responses were measured with EEG. Every so often, an omission of part of the rhythm occurred. In some cases, this omission did not disrupt the feel of the beat in the rhythm, but other times it did. The researchers wanted to know if the newborns could 'feel the beat', and therefore also tell when the beat was disrupted. It is not possible to ask a newborn to press a button, but their brains answered for them. A clear difference was observed in their EEG measurements when listening to an omission that disrupted the beat as compared to an omission that did not disrupt the beat. The authors suggested that beat perception may be innate. This may or may not prove to be true; infants can hear in the womb from about six months, and this pre-natal learning may play a role. In addition, infants' rhythm perception is influenced by being 'bounced' in time with music (Phillips-Silver & Trainor, 2005), so any prenatal dancing on the part of the mother may need to be taken into account. The fact that rhythm perception can be influenced by culture suggests any innate predispositions are also shaped by subsequent experience (Cross, 2001; Iversen et al., 2008), but the Winkler (2009) study does nicely illustrate how neuroscience can provide data in situations where behavioral measures are more difficult to obtain.

An additional important use of neuroscientific methods is when behavioral results do not allow two competing models to be distinguished. One example of this is the debate over interval-based (timing of discrete events) versus beat-based or entrainment (timing in relation to a steady pulse) models of timing (Keele et al., 1989; McAuley & Jones, 2003; Pashler, 2001; Schulze, 1978). Interval-based timing has the advantage of parsimony: many things that we time have no regular beat, so if a beat-based timing system were to exist, it would be in addition to some type of interval timing mechanism. One justification for a beat-based timing system is if it provides more accurate timing. To test whether accuracy was better for beat-based timing (thereby justifying the non-parsimonious existence of an additional timing system), Pashler (2001) conducted two experiments. In one study, participants heard a sequence of standard tones (all demarcating the same length interval) followed by two test tones. Participants compared the interval between test tones to the interval between the standards. If optimal precision required beat-based timing, performance should have been best in blocks in which the interval between standard and test reliably matched the standard interval (i.e., the test interval occurred 'on the beat' set up by the standards). No such effect was observed. In another experiment,

participants heard two test tones and reproduced the intertone interval by producing two keypresses. Entrainment to the beat was apparent: first-response latency clustered around the standard interval and was positively correlated with the produced interval. However, responses occurring on or near the beat showed no better temporal accuracy than off-beat responses. This was taken as evidence that beat-based timing is unlikely to exist, as better temporal accuracy was not observed when beat-based timing could have been used. However, the conclusion may only hold in this particular experimental set-up. Other studies have shown an advantage for beat-based timing in different tasks (McAuley & Kidd, 1998; Schulze, 1978). One way of resolving these conflicting findings could be to show that a beat-based system exists, but also can be active without *necessarily* improving performance. This could explain why, in some cases, the behavioral results do not distinguish between the predictions of beat-based and interval-based timing.

This is exactly what was attempted in a behavioral and fMRI study briefly mentioned earlier (Grahn & Brett, 2007). The results of the behavioral study indicated that when rhythms composed of multiple different interval lengths (similar to those that occur in musical rhythm) were reproduced, the rhythms designed to induce a beat were reproduced much more accurately than those that did not induce a beat. The behavioral benefit suggested that a beat-based mechanism does exist, and improves timing performance when more difficult temporal tasks are tested (as opposed to tasks using single intervals). An fMRI study was conducted using the same stimuli. A specific network of areas (including the basal ganglia) was more active during perception of beat-inducing rhythms compared to other rhythms, even when the task was manipulated so that no significant behavioral performance differences occurred. This indicates that the beat-based system can be active without an observable behavioral benefit. Thus, the fact that some previous work does not find a behavioral beat-based timing benefit does not necessarily mean that such a mechanism was not active or used at the time.

The Impact of Neuroscience on Our Understanding of Rhythm

Rhythm has remained less tractable than pitch, harmony and timbre when it comes to localizing its specific neural substrates. Rhythm is likely to be supported by at least some of the same processes that are involved in timing, and timing is a crucial component of many perceptual and motor functions. It may therefore be a less localized process than timbre perception or other aspects of pitch processing. There may also be redundancy in timing networks across the brain, obscuring dissociations that exist between different timing systems. Redundancy would particularly affect neuropsychological studies that are conducted to determine how damage to an area affects a particular function. If another brain area can compensate for the functions of the damaged area, then the function of the damaged area may be obscured.

Another complication in the study of rhythm is the level of automaticity in the processing of temporal features of sound. Many studies ask participants to direct

their attention to certain aspects of stimuli in order to examine processing related to each aspect, such as monitoring musical sequences for a pitch deviant (attention to pitch) compared to a temporal deviant (attention to time). However, temporal aspects of a stimulus may be implicitly processed, regardless of whether a participant is specifically attending to the temporal dimension. In fact, because predicting the timing of a stimulus can facilitate better processing of other aspects of the stimulus, such as pitch (Jones et al., 2002), participants have an incentive to attend to time even when directed not to or when timing is not explicitly relevant to the task. The automaticity of attending to temporal features is supported by two recent neuroimaging studies that had two overlapping rhythm types, but used very different tasks (Grahn & Brett, 2007; Grahn & Rowe, 2009). In the first study, participants had to indicate when a rhythmic change occurred. In the second, participants passively listened to the rhythms, monitoring for a pitch deviant. Nearly identical activation differences between different rhythm conditions were observed in both studies, despite the fact that temporal aspects of the stimuli were relevant for the first study, but irrelevant for the second study.

An additional issue that is not necessarily specific to rhythm, but pertains to much of the fMRI literature, is what the important axes are that determine involvement of, or interaction between, commonly activated neural areas. One proposed axis is the degree to which rhythmic structure is present in a sequence (e.g., does it induce a beat or metrical representation). Context may also be an important axis (such as linguistic versus musical, or perception versus production). A different axis that has been used in more than one study is degree of 'temporal complexity'. However, no unified definition for this exists. Each researcher formulates a new measure of complexity, which may be clearly and sensibly defined but not related to another researcher's definition. We actually have little idea of exactly what factors make a rhythm seem 'complex'. The presence of integer-ratios versus noninteger-ratios has been suggested (Lewis et al., 2004; Sakai et al., 1999), and its simplicity is attractive. However, the tendency toward categorical perception may render the mathematically complex 1:2.2:3.8 to be perceived the same as the mathematically simple 1:2:4. Beyond very simple sequences, it is unclear if the integer/noninteger-ratio distinction is useful. One study claimed to show activation differences between integer-ratio and noninteger-ratio sequences, but never statistically compared the two conditions (Sakai et al., 1999), meaning there may have been no reliable difference at all. Indeed, another study addressing this question showed that integer-ratio and noninteger-ratio sequences could be rendered statistically indistinguishable in the brain, but significant differences between different types of integer-ratio sequences existed, based on their metric structure (Grahn & Brett, 2007).

A further complication arises when one considers how other aspects of musical structure may impact perception of rhythm and metre. Many researchers in the field have examined the influences of various aspects of musical structure (Dawe et al., 1993, 1995; Ellis & Jones, 2009; Hannon et al., 2004; Huron & Royal, 1996; Povel & Okkerman, 1981; Temperley, 1963), but integration of all these findings into a single

model has been difficult. Additional basic research (along the lines of that done by the researchers cited above) that tests the mutual influences and boundaries of different grouping principles will need to be done to improve the information upon which models can be based.

A final issue that is particularly pertinent to fMRI studies is that of subtraction logic. FMRI is a subtractive technique—that is, an increase in activity can only be measured as an increase *relative* to another condition, and changes in activity are generally assessed by subtracting activity measured in a control condition from activity measured in the condition of interest. Subtraction logic (in either behavior or in neuroimaging) rests on the crucial ‘assumption of pure insertion’ (Sternberg, 1969), or that changing one process will not change the way other processes are performed. Although violations of subtraction logic have been demonstrated experimentally (Zarahn et al., 1997), the logic is still widely used because it greatly simplifies the inference-making process. If this assumption is violated, a difference in the observed neuroimaging signal between conditions may be due to one of those other altered processes, rather than the process of interest. The choice of a baseline condition is crucial, as well as consideration of uninteresting factors that may differ between conditions. Studies often differ in their choice of baselines (rest is common, but many choose a simple version of the task and stimuli as a closer control condition). Exacerbating this is the fact that thresholded maps are used to convey activation results, which highlight the differences between patterns of results without indicating how different they really are. For example, if an area is significantly active, it is represented as color on a brain. If an area *almost* reaches the threshold, but not quite, it is not represented. Thus, what may appear to be big differences across two conditions or two studies (color versus no color) may not turn out to be significantly different at all when directly compared. This means that one study could show activation in the supplementary motor area and premotor cortex, and another study could show activation in auditory cortex and cerebellum; yet if those two studies were statistically compared, there may be no significant differences between their respective activation patterns. One rarely has the chance, however, to directly compare activations across different published studies (and occasionally some authors fail to do it even within the same study), so the potentially nonsignificant differences are all that are seen.

Three recent studies illustrate the complexities surrounding the choice of baseline and difficulties with thresholded maps: all three examined the neural correlates of perception or production of metric and nonmetric rhythms. Two of the studies used a single rhythm per condition that subjects were familiarized with before the task, whereas the other study used new rhythms on each trial. Given the similar rhythm conditions, it seems that reasonable overlap should exist, and that where it does, one may more confidently conclude that the overlapping areas play specific roles in metric processing, regardless of task. However, a summary of the findings make it clear that consensus is not easily reached. The first study, by Chen et al. (2008b), had participants listen to a pre-learned rhythms then tap in synchrony to each.

The authors analyzed which areas were increasingly active as complexity of the rhythm increased, and found a correlation in dorsal premotor cortex. They also compared neural activity in musicians and non-musicians, and found that an area of prefrontal cortex was more active for musicians than non-musicians. The second study, by Bengtsson et al. (2009), included the same rhythm conditions, but also contained an isochronous condition, and a random condition, in which the intervals of the metric condition were presented in random order (and therefore not learned by the participants ahead of time). The participants listened to the stimuli, and at the end of each stimulus indicated whether it was a random or a learned sequence. They analyzed which areas showed activity that overlapped for each condition minus the random condition, and found activation in the SMA, premotor cortex, cerebellum and right frontal areas. For metric compared to nonmetric, an area of anterior medial prefrontal cortex was found, whereas nonmetric compared to metric activated medial cerebellum. The last study (Grahn & Brett, 2007), used a rhythm discrimination task (same/different task) and analyzed activity elicited during the listening phase of the task. Although the style of the different conditions likely became familiar to the participants over the course of the study, the specific rhythms were not learned ahead of time. Listening to rhythms compared to rest produced activity in auditory cortex, SMA, premotor cortex, cerebellum and basal ganglia. The metric simple rhythms elicited increased basal ganglia, SMA and posterior inferior frontal activity compared to the nonmetric conditions. Musicians showed greater activity in the cerebellum, right premotor cortex and SMA compared to non-musicians, but this increase was independent of rhythm type.

Clearly, there were factors that differed between the studies. One of the most obvious was whether the rhythms were learned by the participants ahead of time, or were novel to them during the scanning session. Another was whether the rhythms were heard and then reproduced, discriminated or classified. Finally, the choice of comparisons, baselines and analyses strongly influences the pattern of activity found. Therefore, the findings are probably not in conflict, but rather motivated by different questions and analyzed in different ways. However, the nature of fMRI data presentation prevents overarching conclusions from being easily drawn, and little consensus is gained from three independent studies investigating very similar rhythms.

A separate, but interesting, problem was highlighted by Peoppel and Embick (2005) about research into language and the brain and may be applicable to music. They refer to a 'conceptual granularity mismatch' between cognitive and neurobiological mechanisms we use. In other words, the theories we invoke to account for musical computation are not necessarily related to the computations of the biological systems in question. Musical theories have been conceived along the lines of syntax, meter, rhythm and harmony. Neurobiological computations are achieved by synapses, neurons, oscillations and circuits. How do we directly map one onto the other? According to Peoppel and Embick, with this mapping, a worst-case-scenario that could result from granularity mismatch is 'long-term interdisciplinary

cross-sterilization rather than cross-fertilization between linguistics and neurobiology, or, for that matter, linguistics and other empirical disciplines'. Could one easily substitute music theory for linguistics? In some ways perhaps, in others perhaps not. Conceptualization of pulse and meter and terms of neural oscillators clearly shows a direct mapping to neural mechanisms, and neural correlates are being seen in EEG and MEG (Fujioka et al., 2009; Iversen et al., 2009; Snyder & Large, 2005). Pitch perception is thought to rely crucially on phase-locked responses of neurons, again showing a clear musical to neural mapping (Grothe & Klump, 2000; Langner, 1992). Tonality has been related to statistical learning (Krumhansl, 1990; Saffran et al., 1999), which is certainly a property of neuronal ensembles. We should heed the concept granularity mismatch message: we must maintain communication between neuroscientific, computational and music theoretical research fields to maximize the returns and relevance of each field individually.

Advances in Neuroimaging Methods

This final section highlights some of the advances being made in neuroimaging techniques that will be relevant for future neuroscientific investigations into music. As we have seen, neural overlap features strongly in neuroimaging studies of timing and rhythm, and interactions between activated areas will be crucial to working out the neural mechanisms. We are coming closer to being able to address these questions. For example, multivoxel pattern analysis (MVPA) techniques can make more effective use of information in the fMRI signal, potentially distinguishing representations that contain neural overlap. In addition, examinations of connectivity between different neural areas can tell us more about the dynamic temporal interactions occurring in the brain. What follows is a review of a selection of the techniques in development for functional neuroimaging data.

fMRI and Pattern Analysis

One main disadvantage of fMRI is that it measures a signal that inherently reflects neuronal mass activity. Interdigitated networks below the resolution of the voxel cannot be distinguished. This problem has been highlighted above: many areas appear to respond to simple timing tasks as well as complex rhythm tasks (e.g., cerebellum, premotor cortex, basal ganglia). Observations of overlapping activity across stimuli or tasks are frequently used as evidence of overlapping function when comparing fMRI studies. However, there is an alternative interpretation: two overlapping but functionally independent neural populations are present and active within the common region. Here common activation does not mean a common function. Conventional fMRI analyses cannot discriminate between these two interpretations. MVPA is a technique that can potentially discriminate overlapping functional activations (Peelen & Downing, 2007; Peelen et al., 2006) by taking advantage of the fact that voxels will have differing proportions of neurons that may

be involved in the different processes of interest. The MVPA approach uses pattern-classification techniques to extract the signal that is present in the *pattern* of responses across multiple voxels, even if (considered individually) the voxels might not be significantly responsive. The results of MVPA experiments can support or reject claims about neural mechanisms that are shared across rhythm perception and production, rhythm and timing, or meter and rhythmic processing.

Connectivity

Despite the low temporal resolution of fMRI, measurements of neural interaction between brain regions can still be made. To answer questions about the interaction between areas we require analyses of connectivity. Many people are familiar with the concept of ‘anatomical connectivity’: that of a direct neuronal connection between two brain areas; a connection comprised of neuronal axons. In the past, the majority of our knowledge of these anatomical connections came from histological studies of animals, with relatively little direct information in humans. Now, diffusion tensor imaging (DTI) has become more widely available, providing visualizations of white matter tracts *in vivo* (Basser, 1994). DTI studies have already provided information about how musical experience may change anatomical connectivity between brain areas (Bengtsson et al., 2005; Schmithorst & Wilke, 2002), or how differences in anatomical connectivity correlate with language processing ability (Gold et al., 2007; Niogi & McCandliss, 2006).

However, as much of the brain is interconnected anatomically (either directly or indirectly), studies of anatomical connectivity cannot indicate which connections are actually being used at any given time. Answering these questions requires analyses of functional or effective connectivity (Aertsens & Preissl, 1991). Functional connectivity measures the correlations between the concurrent activities of different brain regions. Functional connectivity is a correlation, and may not mean that one area is directly influencing another. A common input to both areas may cause their activity to be correlated.

To determine if the activity in a particular area is *causally* influencing the activity in another area, one performs effective connectivity analyses. Methods of effective connectivity analysis include structural equation modelling and dynamic causal modelling (Friston & Harrison, 2003). To take a rhythm processing example, these analyses could indicate whether basal ganglia activity during beat perception results from bottom-up (information flow from basal ganglia to cortical motor areas) or top-down processing (beat calculations are done outside the basal ganglia, but the basal ganglia use the information to make predictions or synchronize movement accurately).

Additional Techniques and Advances

Other neuroscientific methods (or novel combinations of methods) are likely to play a larger role in future. Transcranial magnetic stimulation (TMS) is a non-invasive

method of exciting cortical neurons, using a weak electric current that is induced in the tissue by a rapidly changing magnetic field (which is generated by a coil at the surface of the scalp). The method is ideal for stimulating the cortical surface, although deeper structures such as the basal ganglia are generally beyond reach. Because TMS can disrupt neuronal processing, it can be used to conclude whether an area is *necessary* for a particular task to be successfully carried out. As most neuroimaging techniques can only examine correlations between stimuli or tasks and neural activity, TMS will be a useful tool to follow up neuroimaging results. TMS work in domain of music has begun (Bueti et al., 2008; Malcolm et al., 2008; Ridding et al., 2000; Wilson & Davey, 2002), but will likely grow in the future.

Conclusions

Research into the neuroscience of rhythm perception and production has already yielded interesting insights. Neural markers of anticipation of the beat and representations of metric structure have been found in EEG and MEG, especially in Beta- and Gamma-band synchrony. Comparisons of rhythm and meter perception suggest that rhythm perception may rely on automatic, pre-attentive processing, whereas meter perception requires attention. There is evidence for a specific network of neural areas that support beat perception, a process that arguably is crucial for musical rhythm perception. The distributed and overlapping nature of the activations observed for both timing and rhythm tasks lends support to theories that propose distributed processing, and also strengthens the idea that perception and production rely on similar mechanisms.

A wide variety of computational approaches have been created for models of timing and rhythm perception. There is still no consensus on the best approach, but recent studies have yielded neuroscientific support for the predictions of neural resonance theory. Greater integration between neuroscience and modelling will be critical to continue moving beyond functional localization and measurement of neural correlates to delineation of specific neurobiological timing components and mechanisms. Advances in data acquisition and analysis techniques are already proving promising in expanding the richness of neuroscientific data. With continued cross-disciplinary endeavors and communication between different fields of music, movement and language research, the next twenty years of neuroscientific research into music should be even more interesting and informative than the last twenty.

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