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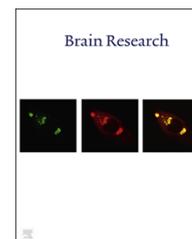
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Research Report

Brain responses to altered auditory feedback during musical keyboard production: An fMRI study



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ARTICLE INFO

Article history:

Accepted 3 February 2014

Available online 7 February 2014

Keywords:

Altered auditory feedback

Music performance

Sequence production

Perception and action

Piano

ABSTRACT

Alterations of auditory feedback during piano performance can be profoundly disruptive. Furthermore, different alterations can yield different types of disruptive effects. Whereas alterations of feedback synchrony disrupt performed timing, alterations of feedback pitch contents can disrupt accuracy. The current research tested whether these behavioral dissociations correlate with differences in brain activity. Twenty pianists performed simple piano keyboard melodies while being scanned in a 3-T magnetic resonance imaging (MRI) scanner. In different conditions they experienced normal auditory feedback, altered auditory feedback (asynchronous delays or altered pitches), or control conditions that excluded movement or sound. Behavioral results replicated past findings. Neuroimaging data suggested that asynchronous delays led to increased activity in Broca's area and its right homologue, whereas disruptive alterations of pitch elevated activations in the cerebellum, area Spt, inferior parietal lobule, and the anterior cingulate cortex. Both disruptive conditions increased activations in the supplementary motor area. These results provide the first evidence of neural responses associated with perception/action mismatch during keyboard production.

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1. Introduction

Music performance is a highly complex sensorimotor task, involving coordinated sequential movements of many effectors with high temporal precision (Gabrielsson, 1999, 2003; Palmer, 1997). Arguably the primary goal of music performance is to create sound patterns. The coordination between

the sounds the performer creates and the movements that he/she plans and executes is highly important and involves a complex neural network of sensory and motor areas (Zatorre et al., 2007). The importance of this perception/action coordination is demonstrated by the disruptive effects of alterations to auditory feedback (AAF), such as delayed auditory feedback (first demonstrated in speech by Black (1951), in music by

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Havlicek (1968), Lee (1950)). The disruptive effects of delayed auditory feedback include slowing of production, increases in error rates, and increased variability of timing.

Previous neuroimaging research concerning the effects of AAF has focused on vocal-motor associations during speaking and singing. Delayed auditory feedback (DAF) during speech increases activations in auditory areas, including superior and middle temporal gyri, relative to speaking with normal feedback (Hashimoto and Sakai, 2003; Takaso et al., 2010; Watkins et al., 2005). Speaking or singing with frequency shifted feedback has likewise been associated with increased activations in the superior temporal gyrus (Watkins et al., 2005; Zarate and Zatorre, 2008), and singing with frequency-shifted feedback is accompanied by increased activation in the anterior cingulate cortex (Zarate and Zatorre, 2008). A neuroimaging study of speaking with shifted formants likewise revealed activations in posterior temporal areas, as well as right prefrontal and Rolandic areas (Tourville et al., 2008).

However, it is unclear whether similar effects would occur in piano performance, given that keyboard perception/action associations may be based on more flexible contingencies than the auditory-vocal associations in speech (Howell et al., 1983; Pfordresher and Mantell, 2012). Previous neuroimaging research on perception/action associations in keyboard production has focused on how musical training affects neural audio-motor associations. Musical keyboard training leads to effector-specific motor associations while listening to music (activates the “hand area” of the primary motor cortex, as well as Broca's area and its right-hemisphere homologue (Bangert and Altenmüller 2003; Bangert et al., 2005; Lahav et al., 2007). In addition, musical training causes activations in auditory areas during silent keyboard production (Bangert and Altenmüller 2003). Although motor areas were not present in the aforementioned studies of AAF during vocal

production, one study did find increased activation during DAF in the vicinity of the left inferior frontal gyrus (Hashimoto and Sakai, 2003). Taken together, these results suggest that AAF may influence a network of auditory-motor associations mediated by activations in the inferior frontal gyrus.

An important issue from behavioral research on the role of auditory feedback not addressed in previous neuroimaging research on AAF effects has to do with effects from different kinds of AAF. Specifically, the effects of AAF vary depending on the timescale at which perception/action relationships are altered. Consider, for instance, a feedback delay short enough that feedback from event i happens after the action associated with that event (here, a key press) but before the action associated with event $i+1$ (see Fig. 1A). Under such circumstances, perception and action are misaligned with respect to *onset synchrony*. By contrast, consider a manipulation in which each key press is synchronized with a pitch associated with a previous or future serial position. Such a manipulation operates at the timescale of event sequencing and is a manipulation of feedback contents. Fig. 1B shows a *lag-1 serial shift* of pitch contents. These two manipulations yield qualitatively different effects on production. Whereas asynchronous feedback disrupts the production of timing (inter-response intervals become slower and more variable), the accuracy of event sequencing remains unperturbed. By contrast, serial shifts of feedback contents disrupt the accuracy of sequencing (errors increase) but spare event timing. This pattern of results has been termed a *sequencing/timing dissociation* in auditory-motor interactions (Pfordresher, 2003, 2006; Pfordresher and Kulpa, 2011). In the research reported here, we tested whether this behavioral dissociation reflects an underlying neural dissociation in the networks linking perception and action. If so, the network of brain activations associated with AAF manipulations of synchrony versus

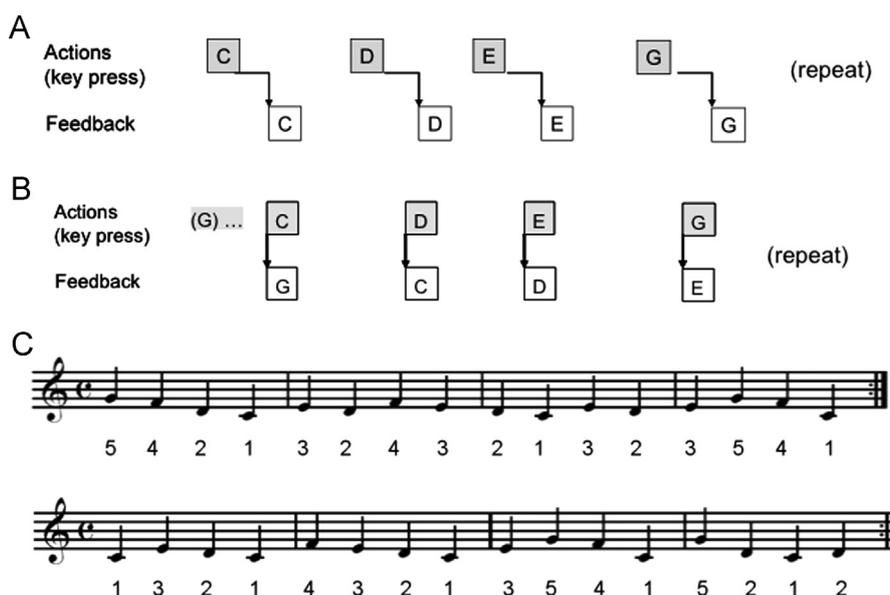


Fig. 1 – Illustrations of the effects of asynchronous AAF (A) and serially shifted AAF (B), with grey boxes indicating the timing and pitch contents associated with actions (key presses on a piano keyboard), and white boxes indicating the timing and pitch contents of auditory feedback. Notation from melodies used in the experiment (C), numbers below the notation indicate fingering, where 1=thumb and 5=pink of the right hand.

contents may be distinct, just as their effects on behavior are distinct.

In the experiment reported here, pianists memorized an unfamiliar melody while hearing normal feedback and then performed this melody from memory in the scanner under one of the following conditions: no auditory feedback (the “silent” performance condition), normal auditory feedback, asynchronous AAF, serially shifted AAF, or AAF with randomly selected pitches. A final “listen only” condition was included in which participants heard the intended melody but did not move their fingers. We were primarily interested in the pattern of activations during asynchronous and serially shifted AAF. We reasoned that areas common to these conditions, but distinct from activations during normal feedback, represent neural responses to the disruptive effect of AAF, whereas areas distinct across asynchronous and serially shifted conditions represent neural correlates of the sequencing/timing dissociation. The random pitch AAF condition is similar to the serial shift condition in that only feedback contents are manipulated; however, this condition typically does not disrupt production (Pfordresher, 2005) and so contrasts between this condition and other AAF conditions provide further information as to neural correlates of disruptive versus non-disruptive AAF.

2. Results

2.1. Behavioral results

Behavioral results from the five performance conditions (excluding the listen only control) are shown in Fig. 2. These results replicate the effects of AAF on performance reported elsewhere, including the sequencing/timing dissociation (e.g., Pfordresher, 2003). There was a significant effect of condition on mean IRIs, shown in Fig. 2A, $F(4,76)=34.49$, $p<.001$. Post-hoc tests (Tukey's HSD, $\alpha=.05$, critical value=15.42 ms) indicated that asynchronous AAF led to slower IRIs than every other condition. By contrast, no other condition (including serially shifted AAF) increased IRIs relative to normal feedback, although random pitch AAF led to significantly faster IRIs than normal feedback.

Feedback condition also significantly affected error rates, shown in Fig. 2B, $F(4,76)=11.68$, $p<.001$. Post-hoc tests (Tukey's HSD, $\alpha=.05$, critical value=2.3%) indicated that error rates for serially shifted AAF were higher than every other condition except for random pitch AAF. However, random pitch AAF did not lead to significantly higher error rates than normal feedback (difference=1.7%) and thus should not be considered as a “disruptive” AAF condition.

2.2. fMRI results

The top row of Fig. 3 shows contrasts between the normal feedback condition and the silent performance baseline (left) and listening only baseline (right). These plots illustrate brain activations that accompany performance with normal auditory feedback (FDR corrected $p<.05$), and have implications for how the brain processes coordinated auditory and motor activity. Table 1 shows the Talairach coordinates of the significant areas of activation from these contrasts. As can be seen, the normal feedback minus silent performance contrast yielded activations in auditory cortex (Brodmann areas, BA 41, 22), reflecting perceptual processing of auditory feedback, as well as the supplementary motor area (dorsal BA 6, see Table 1). Contrasts between performance with normal feedback and the listening control condition (Fig. 3, top right) revealed significant activations in the primary somatosensory cortex (BA 3) as well as the medial frontal gyrus and cerebellar culmen (see Table 1).

Lower rows of Fig. 3 illustrate areas of activation from the contrasts between disruptive AAF conditions (asynchronous, serially shifted) and performance with normal auditory feedback (FDR corrected at $p<.05$ for asynchronous minus normal, $p=.05$ for serial shift minus normal). Corresponding Talairach coordinates are shown in Table 2. Areas associated with asynchronous AAF, but not serially shifted AAF, included Broca's area (BA 44, see Table 2), and its right homologue (shown in the horizontal slice of Fig. 3). Areas associated with serially shifted AAF but not asynchronous AAF included the thalamus, anterior cingulate cortex, and area Spt (the Sylvian-temporal-parietal junction, Hickok et al., 2003). More cerebellar activations were also apparent during serially shifted than asynchronous feedback (relative to performance normal feedback). One area of activation

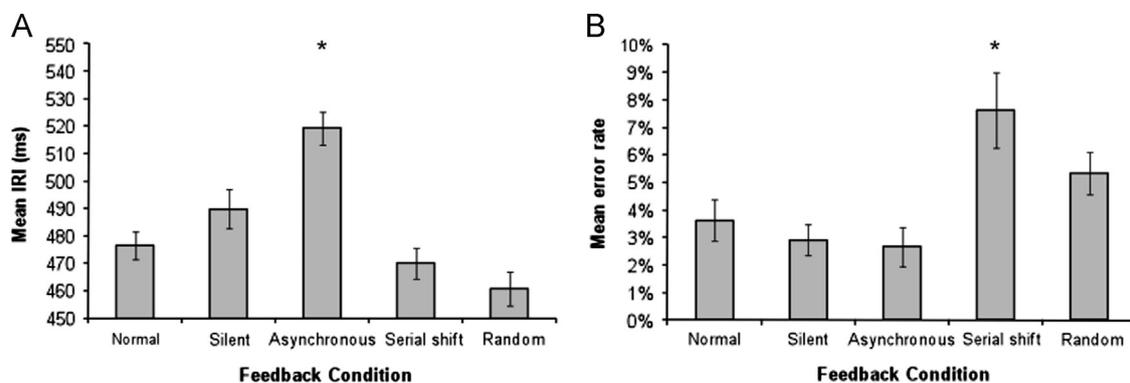


Fig. 2 – Behavioral performance results by feedback condition: Mean inter response intervals (A) and mean error rates (B) averaged across trials and participants. Error bars reflect one between-participants standard error of the mean. Asterisks highlight AAF conditions with means that were significantly higher than the normal feedback condition ($p<.05$, Tukey's HSD).

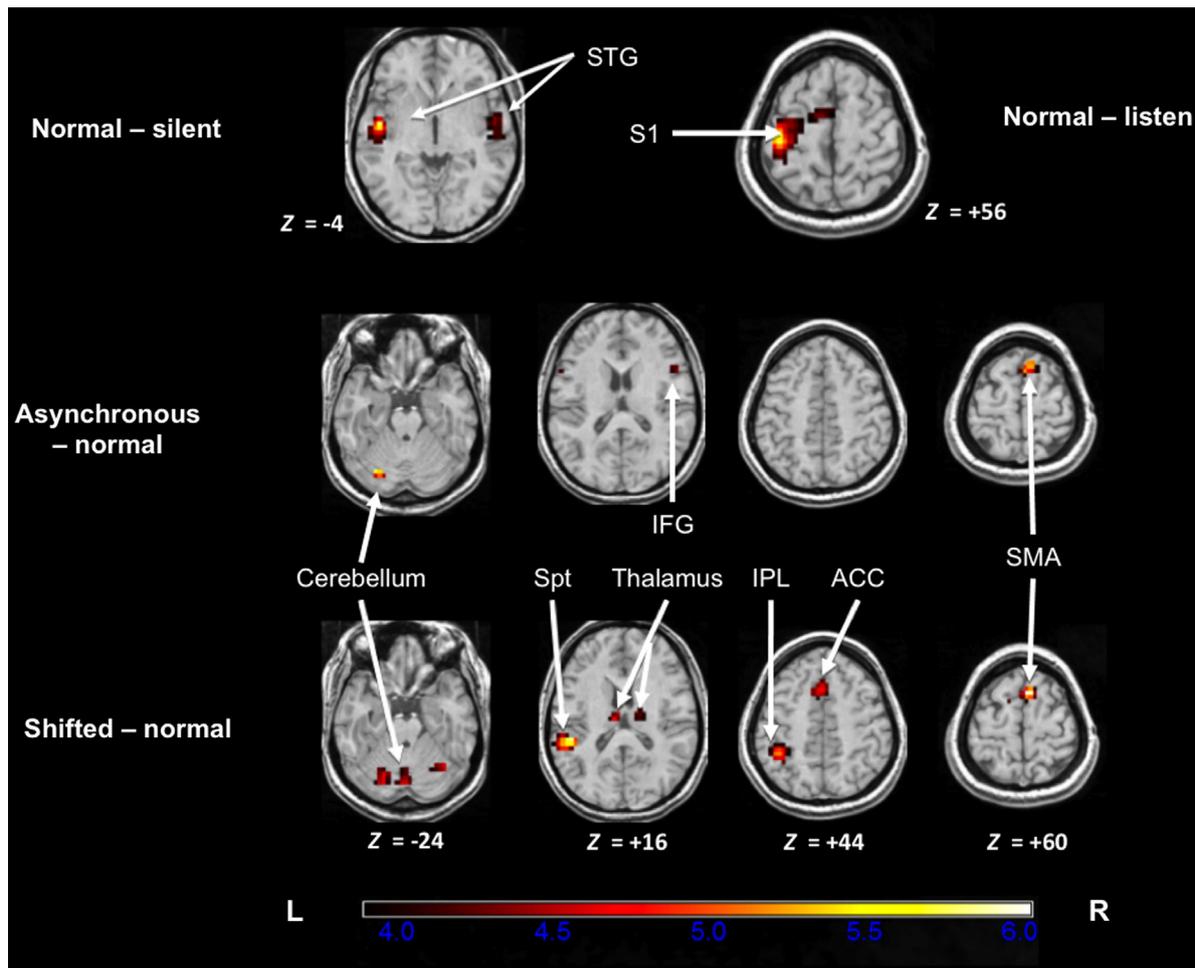


Fig. 3 – Horizontal slides (MNI z-coordinates indicated) showing areas of significant activation for selected contrasts. Activations are superimposed on average anatomical scans. Left is left and right is right. STG=superior temporal gyrus (association cortex), SM1=primary somatosensory cortex, Spt=Sylvian-parietal-temporal junction, IPL=inferior parietal lobule, ACC=anterior cingulate cortex, SMA=supplementary motor area.

Table 1 – Brain regions yielding significant contrasts between performance with normal feedback and two baseline conditions.

Region	BA	Left				Right			
		<u>x</u>	<u>y</u>	<u>z</u>	<u>t</u>	<u>x</u>	<u>y</u>	<u>z</u>	<u>t</u>
Normal—silent									
<i>Frontal</i>									
Precentral gyrus	6					51	–10	8	8.15
<i>Temporal</i>									
Superior temporal gyrus	22	–42	–28	5	9.12				
Transverse temporal Gyrus	41					43	–25	13	6.73
Normal—listen									
<i>Frontal</i>									
Medial frontal gyrus	6	–9	–10	50	4.84				
<i>Parietal</i>									
Postcentral gyrus	3	–42	–21	52	9.82				
Postcentral gyrus	40	–39	–28	48	9.22				
<i>Sub-cortical</i>									
Culmen	*					10	–53	11	6.78

All reported t values are significant at $p < .001$ (FDR corrected at $p < .05$).

Table 2 – Brain regions yielding significant contrasts between AAF conditions and performance with normal auditory feedback.

Region	BA	Left				Right			
		<u>X</u>	<u>Y</u>	<u>Z</u>	<u>t</u>	<u>x</u>	<u>y</u>	<u>z</u>	<u>t</u>
Asynchronous—normal									
<i>Frontal</i>									
Superior frontal gyrus	6					6	8	59	5.26
Precentral gyrus	9					39	6	34	4.80
Inferior frontal gyrus	13	–36	24	7	4.70				
Inferior frontal gyrus	44	–53	9	15	4.32				
Precentral gyrus	44					47	9	10	5.37
<i>Temporal</i>									
Superior temporal gyrus	22	–53	–51	6	4.14				
Insula	13	–38	–11	–6	6.03	43	10	2	5.85
<i>Sub-cortical</i>									
Cingulate gyrus	32					6	17	38	4.11
Declive of cerebellum	*	–23	–67	–20	5.93				
Shifted—normal									
<i>Frontal</i>									
Superior frontal gyrus	6					2	4	59	5.15
<i>Temporal</i>									
Superior temporal gyrus	41	–49	–36	11	5.10				
Anterior insula	13	–38	14	–6	4.56	43	9	6	4.68
<i>Parietal</i>									
Inferior parietal lobule	40	–31	–38	33	4.61				
<i>Sub-cortical</i>									
Declive	*	–5	–76	–21	4.46				
Pyramis	*	–1	–63	–27	3.89				
Thalamus	*	–5	–18	20	4.37	14	–10	11	3.94
Midbrain	*	10	–27	–5	4.26	10	–27	–5	4.26
Random—normal									
<i>Frontal</i>									
Inferior frontal gyrus	44	–53	5	15	4.09				
Middle frontal gyrus	9	–42	30	28	3.32				
Middle frontal gyrus	6	–42	30	28	3.32				
Middle frontal gyrus	6	–31	–6	54	4.05	32	–3	51	3.20
Precentral gyrus	6					36	3	30	3.87
<i>Temporal</i>									
Superior temporal gyrus	22	–57	–28	4	6.69	58	–21	7	4.65
Superior temporal gyrus	13	–49	–41	18	6.60	50	–38	23	4.68
Anterior insula	*					47	6	2	5.64
<i>Parietal</i>									
Parietal sub-gyral	40	–35	–43	39	6.92	35	–43	37	4.11
Precuneus	*					9	–66	45	4.59
<i>Sub-cortical</i>									
Thalamus	*	–1	–11	21	3.78				
Caudate body		14	–15	21	3.57				

Regions of peak neural activity for all feedback-present conditions, compared to the normal feedback control. All reported t values are significant at $p < .001$ (uncorrected). Contrasts of serially shifted feedback with normal are FDR corrected at $p = .05$; other contrasts are FDR corrected at $p < .05$.

common to both asynchronous and serially shifted AAF was the supplementary motor area. We also examined higher-level contrasts between the two AAF conditions mentioned here. None of these contrasts were significant given the FDR correction. However, in uncorrected contrasts, activation of the inferior parietal lobule was significantly higher during serially shifted feedback than during asynchronous feedback ($p < .001$).

Like the serial shift condition, random pitch involves alterations to feedback pitch but not synchrony; unlike the

serial shift condition, the random pitch condition typically does not disrupt performance (as replicated here). Areas associated with this contrast are shown in Table 2. Many areas of activation overlapped with either the asynchronous or serial shift contrasts, with three noteworthy exceptions. First, random minus normal yielded significant activations in the primary auditory cortex. The other two exceptions were that random pitch did not yield significant activations in the cerebellum (unlike the serial shift condition) or the inferior frontal areas found for asynchronous AAF.

One possible limitation of the present design is that brain activations associated with different AAF conditions were also associated with different performance effects. It is important to test whether areas associated with the disruptive effect of a given feedback condition simply reflect measures of performance independent of feedback (e.g., do effects of asynchronous feedback appear simply when pianists play more slowly?). Follow-up analyses that regressed measures of disruption (production rate, errors) during AAF conditions on contrasts between AAF and normal conditions yielded similar areas of activation shown in Fig. 3 for feedback-based contrasts regardless of the performance measures. For instance, right inferior frontal activations associated with the asynchronous minus normal contrast were correlated with both error rates and timing during performances with asynchronous feedback. Thus, brain activations reflect the influence of auditory feedback and were not an epiphenomenon of the observed behavioral tendencies.

3. Discussion

We have reported the first fMRI data concerning the effects of altered auditory feedback (AAF) on piano performance and, more importantly, have presented the first evidence we know of that different neural networks support the integration of perception and action at the timescales of onset synchrony versus sequential organization. The current data thus have important implications for neural auditory-motor associations in the production of action sequences, as well as the hierarchical control of perception and action. In contrast to studies that have examined areas of overlapping activations during temporally separate perceptual and motor tasks (e.g., Bangert et al., 2005), the current study addresses perception/action integration by focusing on areas of activation associated with congruent versus incongruent mapping between perception and action during performance.

3.1. Responses to AAF

Our primary motivation for conducting the present research was to test the hypothesis that the behavioral dissociation between sequencing and timing effects of AAF is related to different patterns of neural activity that accompany these feedback conditions. Although past research hints at certain areas that may be responsible for planning actions along each time scale (cf. Zatorre et al., 2007), there is enough inconsistency in the literature that we considered the identification of candidate areas to be exploratory. As such, we identified areas in the brain via whole-brain analyses rather than by analyzing select regions of interest.

Asynchronies between actions and sound were associated with increased activity in the inferior frontal cortex bilaterally. This area has recently been highlighted as being of potential importance to audio-motor interactions in a study by Lahav et al. (2007), who found activations in these areas when non-musician participants heard melodies comprising pitches that were used in a previous keyboard learning task, as opposed to melodies comprising pitches that were not associated with prior learning. However, in that study,

activations were related to pitch content rather than synchrony. As such, the results of Lahav and colleagues provided an auditory analogue to earlier research showing shared activations in right and left IFG across (visual) observation and imitation of hand gestures, including fingering on the guitar (Buccino et al., 2004). Likewise, activations in the right IFG during the perception of musical tones are increased when non-pianists learn to perform the piano with normal action-pitch mappings than with random mappings (Bangert and Altenmüller 2003). Why, then, were such activations in the current study elicited by feedback asynchronies and not by alterations to feedback contents? It is important to note that the earlier studies summarized here did not examine activations during performance with altered feedback; they instead examined changes in activation associated with auditory perception that follow some kind of learning regime. It may be that the IFG is important for the binding of associations by temporal contiguity during performance, including while learning, and that these fundamentally temporal associations are later activated by the auditory sequence when presented on its own. The fact that we found increased activation based on perturbed auditory/motor relationships, as opposed to increased activations associated with congruent mappings (as in past studies), may reflect the fact that auditory and motor information were presented concurrently here, whereas these modalities were separated in previous studies.

Serially shifted AAF was associated with a distinct pattern of activations that included the cerebellum, thalamus, area Spt, inferior parietal lobule, and anterior cingulate cortex. Activation of the cerebellum is of particular theoretical interest given diverging views on its role (for recent reviews see Buckner, 2013; Manto et al., 2012). One possible role of the cerebellum is in the forward modeling of perception/action relationships (Blakemore et al., 2001; Wolpert et al., 1998). According to this view, the cerebellum is used to generate an anticipated outcome from actions that can then be used during online correction of that action once it is produced. The cerebellum thus may function as a kind of error monitor, and may be activated by serially shifted AAF due to the fact that this kind of alteration is interpreted as an error. Serially shifted AAF also, not surprisingly, leads to errors in behavior. It is these performance errors that may result from the fact that serially shifted AAF leads to increased activity in the anterior cingulate cortex. This region has been characterized as responsible for monitoring errors (Scheffers and Coles, 2000) and/or responding to conflicting commands about which action to select (Carter et al., 1998; MacDonald et al., 2000), which also can lead to errors. Previous research that has measured ERP responses to isolated altered pitch events during piano performance likewise suggests that pianists process such alterations similarly to performance errors (Herrojo-Ruiz et al., 2009; Maidhof et al., 2010). The correlated activations of cerebellum and thalamus, which share many anatomical connections (Glickstein and Doron, 2008; Strick et al., 2009), are consistent with a view that the cerebellum helps modulate sensory inputs in the presence of disruptive pitch information (Gao, Parsons, Bower, Xiong, Li, & Fox, 1996). It is also worth noting that activations in the cerebellum overlap both neocerebellar and spinocerebellar areas, and

thus may broadly involve both sensory and motor functions mediated by the cerebellum. With respect to the parietal lobe, recent research suggests that this region is active during mental transformations of musical sequences (Zatorre et al., 2010). It is possible that performers treat alterations of feedback pitch as transformations of the planned event sequence and try to resolve these transformations during production; these transformations (possibly performed at a non-conscious level) would be most extreme while hearing random pitch sequences.

Past research has suggested that disruptive alterations of AAF during speech are associated with activations in the temporal lobe, including the temporal-parietal junction (BA 40, cf. Hashimoto and Sakai, 2003; Tourville et al., 2008). In the current study, however, activation in this area was specific to alterations of feedback pitch (serial shift, random), but were not found for asynchronous auditory feedback. The present findings are consistent with the role for Spt proposed by Hickok and colleagues, that it is used for audio-motor integration (Hickok et al., 2003, 2011). The current results suggest that area Spt's role may extend to associations between manual gestures and sound, and may not be limited to sensorimotor integration for vocal production as some previous data suggest (Pa and Hickok, 2008). In addition, the temporal-parietal junction has been associated with visual and auditory streams associated with action and spatial localization (Milner and Goodale, 1995; Rauschecker and Tian, 2000). On the surface, it may seem puzzling that this region was not active during asynchronous feedback, whereas it has been found during traditional manipulations of delayed auditory feedback with speech (Hashimoto and Sakai, 2003; Takaso et al., 2010), which likewise lead to asynchronies. However, it is important to note that perception/action relationships in these contexts are not as well controlled as in the current paradigm (as discussed earlier). As such, it is likely that DAF manipulations in these studies led to some overlap between the produced events (syllables) and the content of previous events, as in the present serial shift condition.

Serially shifted and asynchronous feedback conditions both led to increased activations in the supplementary motor area. Thus disruption from AAF may be based largely on auditory encoding of feedback more so than processes related to production. The supplementary motor area is commonly associated with motor planning (Bangert, 2006; Zatorre et al., 2007) and is active during auditory imagery (Halpern, 2001). As such, this area of activation may reflect the fact that AAF conditions interfere with motor planning, based on timing and/or sequencing (Pfordresher, 2006).

For the most part, areas of activation that were associated with disruptive AAF conditions (serial shifts or asynchronies) were also found when participants experienced feedback with randomly selected pitches, a condition that does not significantly disrupt performance: the cerebellum (associated with serial shifts) and the right inferior frontal cortex (associated with asynchronous feedback). Thus these areas may reflect neural responses to the disruptive effects of AAF. By contrast, other areas may respond to perception/action mismatches independent of the interfering effects of feedback on production.

3.2. Implications

These results address important theoretical questions regarding the influence of AAF that have been difficult to address in behavioral studies. First, despite the high reliability of the sequencing/timing dissociation in behavioral studies, questions remain regarding whether this effect truly represents an underlying dissociation in the representation that links perception and action, as opposed to reflecting different points along a single temporal continuum. A lag-1 serial shift, after all, can justifiably be characterized as a delay that is somewhat longer in duration than what we referred to here as asynchronous AAF. The presence of many distinct brain areas that respond to these conditions argues for a neural distinction between sequencing and timing in the regulation of perception and action. Second, a major point of debate in the research on perceptual feedback concerns whether AAF is treated by the production system as an error signal. Early theories concerning the effect of DAF made this suggestion (e.g., Black, 1951; Lee, 1950) but later evidence has not provided support for it (Finney, 1997; Howell and Archer, 1984; Howell et al., 1983). In this context, the presence of activations in the anterior cingulate cortex is informative. The role of this area as a potential monitor for errors and/or response conflict leading to errors suggests that there may be some truth to earlier claims concerning an error monitoring role for auditory feedback (echoed in more recent models such as DIVA; Guenther, 1995).

The present data also suggest a new way of conceptualizing the control of action during sequence production. Theories of action commonly distinguish sequencing and timing as being conceptually distinct (Krampe et al., 2005; MacKay, 1987; Palmer, 1997; Rosenbaum et al., 1983). However, neural evidence to date has been unclear on whether such a distinction exists in the brain, perhaps because it is difficult to distinguish different brain areas during production tasks, when planning and execution at both levels runs concurrently. By using AAF manipulations to selectively disrupt production at different time scales, this paradigm offers a way to revisit the bases of hierarchical control. As such, somewhat surprisingly, the current data suggest that the inferior frontal gyrus may guide behavior at a smaller timescale, whereas longer timescales may be guided by thalamo-cerebellar connections. An interesting avenue for future study would be to explore similar manipulations of auditory feedback among non-musicians who are trained to perform simple melodies (cf. Lahav et al., 2007). Behavioral effects of AAF document similar patterns of disruption for pianists and non-musicians, but with pianists showing more sensitivity to alterations than non-musicians (Pfordresher, 2006, 2012).

4. Conclusion

The current data confirm the view that audio-motor associations during production operate at distinct timescales (Pfordresher, 2003, 2006). As such, alterations of auditory feedback during performance that lead to asynchronies between actions and sound lead to a distinct pattern of disruption and are associated with distinct neural activation

patterns, as compared to alterations of feedback that disrupt perception and action at the level of event sequencing. Patterns of brain activity during these AAF conditions suggest that the regulation of synchrony between perception and action may originate in the right inferior frontal gyrus, whereas the regulation of sequential associations may involve a broader network that includes the cerebellum, thalamus, and anterior cingulate cortex.

5. Experimental procedures

5.1. Participants

Twenty piano players (16 women, 4 men) were recruited for this study. Some had participated in previous research using the AAF paradigm, but none of them were familiar with the stimulus melodies or conditions used in the present study. Participants reported 13.4 years of experience playing the piano on average (range=7–30, data on years of experience for two participants were lost). The mean age was 24 years (range=19–35). One pianist reported being left-handed (the results of this participant did not differ from average trends across participants). The neuroimaging data from one participant were removed due to technical problems.

5.2. Materials

Two melodies were used for this study, with half the participants performing one melody and half performing the other (see Fig. 1C). Each melody was in the key of C-major and was composed exclusively with the first 5 pitch classes of this scale [C4 D4 E4 F4 G4] so that pianists would not have to change hand positions while in the scanner. Each melody was 12 notes long and designed to avoid repeated finger patterns within one repetition of the sequence, so that participants would not engage in stereotyped motor movements. Melodies were designed so that they could be played repeatedly several times during a block without stopping.

5.3. Apparatus

Participants performed melodies on a specially designed MRI-compatible electronic keyboard that contained no ferromagnetic components (Mag Design and Engineering, Sunnyvale, CA) and listened to stimuli on noise-cancelling headphones (Resonance Technology, Northridge, CA). Music notation and instructions (presented during the practice phase and the initial synchronization phase of blocks) were presented to participants via VisuaStim fMRI-compatible goggles (Resonance Technology, Northridge, CA). Manipulations of auditory feedback and behavioral data collection were conducted using the software program FTAP (Finney, 2001) on a Linux computer that ran in parallel with another Linux computer that served as the MRI console.

5.4. Design and conditions

We incorporated a block design in which each 1-min block comprised repeated performances of the stimulus melody

with a single feedback condition, or listening to repeated performances of the melody. This design was used because the behavioral effects of serially shifted AAF accumulate over time and thus may not appear in a short block (Pfordresher and Kulpa, 2011). Because we did not use sparse sampling, scanner noise was present during blocks, but did not interfere with participants' ability to hear auditory feedback. Moreover, behavioral data suggested that the presence of scanner noise did not lead to different behavioral effects of AAF than are observed without background noise.

We incorporated six conditions, comprising three control and three AAF conditions. The three control conditions included performing with normal feedback, performing with no feedback ("silent performance"), and listening to the melody without performing ("listen only"). AAF conditions were implemented by FTAP. The asynchronous AAF condition incorporated delays timed to be 33% of the running average of produced inter-response intervals (IRIs). Thus, asynchronies would maintain consistent relative timing with the performance tempo, while varying in absolute time (cf. Pfordresher and Benitez, 2007). During serially shifted AAF, each key press would trigger the pitch corresponding to the previous key press. During random pitch AAF, each key press would trigger a pitch that was randomly selected from a 1-octave range (from C4-C5) rather than from the more constrained set of five pitches used for melody construction. The six conditions were pseudo-randomly ordered within a single block. Subjects experienced four blocks in total and each block contained a different order of the six feedback conditions.

5.5. Procedure

At the beginning of the session, participants were positioned supine on the scanner bed and the keyboard was placed on their lap. They were allowed to orient the keyboard according to their comfort but were told not to shift the position of the keyboard during blocks. All participants played melodies with the right hand only. After participants identified a comfortable position for the keyboard, their hand was positioned appropriately and they were moved into the scanner. Participants were shown music notation, with fingering indicated beneath the notation (1=thumb, 5=pinky), and given instructions to practice the stimulus at a moderate tempo and to perform without stopping. Participants then performed the melody once or twice to make sure that they understood the music notation (all understood). Following this initial orientation, a 7-min anatomical scan was conducted during which participants were allowed to practice the melody. After the anatomical scan, the experimenter assessed the participant's memory for the melody by removing the musical notation. Melody memorization was defined as the participant's ability to perform three successive error-free repetitions of the melody. Participants were allowed to practice with notation again if necessary.

After memorization, the experiment began. Four separate 6-min scanning runs were conducted and each of the six feedback conditions was presented for 1 min within each block. Individual blocks that involved performance followed a synchronization-continuation structure that is common in

motor control timing tasks (Stevens, 1886). The synchronization phase started at the beginning of a block; in this phase a metronome would establish the performance tempo of 120 beats per minute (500 ms per IRI). Participants listened to at least 4 metronome clicks and then started performing the melody at that rate, always with normal feedback. During this time participants viewed instructions on a screen displaying the melody to play or (in the case of listen only trials) instructions to refrain from playing. Then after 12 key presses (one repetition of the stimulus) the continuation phase began immediately; the metronome would stop, the screen went to black (participants kept their eyes open), and the participant continued performing while experiencing one of the five performance feedback conditions (silent, normal, asynchronous, serially shifted, or random pitch). During listen-only trials, participants first heard a performance of the melody with the metronome, while viewing notation, followed by nine repetitions with no metronome and a black screen.

5.6. Behavioral data analysis

Behavioral performance data were analyzed with respect to performance tempo and key-press error rates. The initial synchronization phase of blocks was not included in these analyses. Performance tempo was computed using the mean of the IRIs during a block, after removing outliers (IRIs outside a window of 2 standard deviations for the block). Error rates were analyzed using software that identifies mismatches between the performed sequence of key presses and the target sequencing, using an algorithm based on the minimum number of changes needed to match the two sequences (Large, 1993; Palmer and van de Sande, 1993, 1995).

5.7. fMRI acquisition and analysis

Brain images were acquired using 3 T GE Signa LX Excite 12.0 scanner with an 8 channel head coil. Functional magnetic resonance images were acquired using gradient echo T2* Echo Planar Imaging (EPI), which generated 29 5 mm thick slices in a cluster. Whole-head scans were taken in the orientation orthogonal to the AC–PC axis (TR=2000 ms, 180 repetitions, TE=35 ms, voxel size $3.75 \times 3.75 \times 5 \text{ mm}^3$, matrix size 64×64 , FOV 24 mm^2 , flip angle=90°). Functional images were overlaid on a structural FSPGR scan (TR=9.2 ms, TE=4.1 ms, voxel size=1 × 1 × 1 mm³, flip angle=20°).

The BOLD response during each block was analyzed starting at the time of the transition from the synchronization to the continuation phase (which is when the AAF condition could be experienced), until the end of the trial. The timing of the continuation phase was determined by the participant's actions, beginning with the 17th key press and continuing until the next 1 min mark. Analyzed segments of the block were, on average, 48.7 s in duration. Brain activity within this window was analyzed using Statistical Parametric Mapping 5 software (SPM5; Wellcome Department of Cognitive Neuroscience, London, UK). Axial images were realigned, slice-time corrected, co-registered, and normalized to a standard template in MNI coordinate space and resampled to $4 \times 4 \times 4 \text{ mm}^3$ voxel size. Images were smoothed using a full-width half maximum (FWHM) 8 mm Gaussian

smoothing kernel. In the first-level analyses, experimental conditions were modeled with a boxcar function convolved with a canonical hemodynamic response function. To reduce motion-related activation artifacts, each subject's motion correction parameters were included as regressors in the model. Resulting individual contrast images of parameter estimates were then submitted to second-level random effects group analyses, in which group level effects were determined by one-sample t-tests.

Acknowledgments

This research was supported in part by NSF grant BCS-0642592. We are grateful to Ece Yildirim, Ryan Coppolo, Anastaysia Kobrina, and John Kulpa for help with behavioral data collection, and to Chris Magnano and Michelle Andrews for help with fMRI acquisition and analysis.

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