Neural correlates of music recognition in Down syndrome

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A B S T R A C T

The brain mechanisms that subserve music recognition remain unclear despite increasing interest in this process. Here we report the results of a magnetoencephalography experiment to determine the temporal dynamics and spatial distribution of brain regions activated during listening to a familiar and unfamiliar instrumental melody in control adults and adults with Down syndrome (DS). In the control group, listening to the familiar melody relative to the unfamiliar melody, revealed early and significant activations in the left primary auditory cortex, followed by activity in the limbic and sensory-motor regions and finally, activation in the motor related areas. In the DS group, listening to the familiar melody relative to the unfamiliar melody revealed increased significant activations in only three regions. Activity began in the left primary auditory cortex and the superior temporal gyrus and was followed by enhanced activity in the right precentral gyrus. These data suggest that familiar music is associated with auditory–motor coupling but does not activate brain areas involved in emotional processing in DS. These findings reveal new insights on the neural basis of music perception in DS as well as the temporal course of neural activity in control adults.

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1. Introduction

Music is present in some form in all human cultures and the ability to respond to music and recognize a familiar tune is present early in infancy (Saffran, Loman, & Robertson, 2001; Trainor, Wu, & Tsang, 2004). Although music perception and appreciation does not require formal training and is acquired implicitly during the course of development (Peretz, 2006), little is known about how cognitive and social impairments influence the perception of music. The study of populations with developmental disabilities can therefore provide a richer understanding about the role of music in human development.

Down syndrome (DS) is a developmental disorder resulting from the presence of an additional whole or part copy of chromosome 21. The consequence is a disruption of many aspects of cognitive and sensorimotor development. In addition to these deficits, individuals with Down syndrome also have difficulties in interpreting social and emotional cues and understanding mental states of others (Abbeduto et al., 2001; Williams, Wishart, Pitcairn, & Willis, 2005; Iarocci, Yager, Rombough, & McLaughlin, 2008). In a recent review, Cebulam, Moore, & Wishart (2010) noted that there are key differences in early nonverbal interactions between the infant with DS and caregivers. For example, the ability to look at the caregiver’s face and make eye contact is slower to emerge in infants with DS. When this skill does emerge, it is maintained at a high level into the middle of the first year, a time when typical infants begin to pay more attention to the wider social environment. Infants with DS tend to fixate on the caregiver at the expense of objects, and the environment. This reduced ability in joint attention, which is critical for communication and learning, has a significant impact on the development of language and higher-level social and cognitive skills. In addition, children with DS are less able than typical peers to accurately perceive the complex motor actions that frequently accompany emotional expression, leading to less accurate interpretation of social cues (Virji-Babul, Kerns, Zhou, Kapur, & Shiffrar, 2006).

Children with DS find it difficult to accurately recognize certain facial expressions with improvement being unrelated to either developmental or chronological age (Kasari, Freeman, & Hughes, 2001; Wishart & Pitcairn, 2000). Tasks using photo-matching or puppet paradigms to explore emotion recognition have shown that in comparison to typically developing children of a similar level of cognitive ability, children with DS may experience difficulties in recognizing some of the core facial expressions of emotion. The recognition of fear, surprise and anger appear to be particularly
problematic (Kasari et al., 2001; Williams et al., 2005; Wishart, 2007; Wishart & Pitcarrow, 2000), with similar findings recently reported in a study with adults (Hippolyte, Barinsnikov, & Van der Linden, 2008; Virji-Babul, Watt, Nathoo, & Johnson, 2012). Adults with DS not only show difficulties with pure facial emotion but also have difficulties in extracting the appropriate cues within a social context to determine the construct of friendship (Watt, Johnson, & Virji-Babul, 2010).

Given the evidence for social-affective deficits in relation to emotional facial processing in DS, we considered whether and how these deficits would manifest in musical emotion processing. For over a century, it has been reported that individuals with DS show high levels of interest, and particular ability in music (Shuttleworth, 1900; Stratford & Ching, 1989; Tredgold, 1908). Anecdotally, parents of children with DS also report that their children are emotionally responsive to music. However, to date, behavioral studies have only tested information processing skills related to music cognition and no studies have evaluated the neural basis of how individuals with DS perceive emotions conveyed in music.

Music is known to induce strong emotions in typical individuals (Koelsch, Fritz, von Cramon, Müller, & Friederici, 2006; Mitterschiffthaler, Fu, Dalton, Andrew, & Williams, 2007). In particular, recognition of familiar music involves a network of brain areas including the superior temporal sulcus (STS), the supplementary motor area (SMA), inferior frontal gyrus, ventral striatum (Peretz et al., 2009) and the cingulate and parahippocampal gyrus (Satoh, Takeda, Nagata, Shimosegawa, & Kuzuhara, 2006). This suggests that listening to familiar music activates not only areas involved in auditory-perceptual transformation and memory retrieval, but also engages the limbic and paralimbic system related to emotional processing (Blood, Zatorre, Bermudez, et al., 1999).

The goal of our study was to use magnetoencephalography (MEG) to establish the temporal dynamics and spatial distribution of brain regions activated during emotional processing within the context of music listening, in control adults and adults with DS. Given the cognitive impairments in DS, we chose to use a passive music listening task in which individuals were simply required to listen to familiar/pleasurable and unfamiliar instrumental melodies. Participants were not required to make any judgments regarding the emotional quality of the music. We chose a familiar melody that all the participants were familiar with and enjoyed listening to. In addition, the participants with DS all had exposure to this melody from a previous music program and had expressed their pleasure in listening to the melody. Given the conflicting reports of a strong interest in music combined with the social-affective impairment in this population, we hypothesized that music perception in DS would activate brain areas related to auditory-perceptual processing but with decreased activity in brain regions related to processing of emotional states.

2. Materials and methods

2.1. Study participants

Nine healthy right-handed control adult subjects (aged 20–40 years; six females, three males) and eight right-handed adults with Down syndrome (aged 17–38 years; five females, three males) participated in this study. The parents/guardians of the DS participants filled in the Salk/McGill Music Inventory Questionnaire of Music Ability and Interest (Levitin et al., 2004). The questionnaire contained 33 multiple-choice questions with responses rated on a 1–7 Likert scale. The questions were clustered into the following categories: demographics, interest in music, emotional responses to music, musical creativity and reproduction and musical training. The parent/guardian of each of the DS participants completed this questionnaire, and the percentages are reported in Table 1. The percentage refers to the total number of participants who selected each level of the Likert scale. In some cases, levels of the Likert scale were grouped together – for example, on the first question referred to in the table, “very accurate” refers to responses of 5 or 6 on the Likert scale (with four being average and seven being extreme). Table 1 provides a summary of the characteristics of the individuals with DS in terms of their overall cognitive ability based on the Peabody Picture Vocabulary Test (Dunn & Dunn, 2007) and musical interest.

All participants provided informed, written consent and had normal or corrected to normal vision. This study was approved by the Down Syndrome Research Foundation and Simon Fraser University and conducted in accordance with the Declaration of Helsinki.

2.2. Task

Participants listened to two different melodies played by a professional musician on a piano: a familiar melody called “Mamma mia” and an unfamiliar piece by Bach called “Musette” (BWV Anh. 126). Both pieces consisted of melodies and accompanying harmonic part and were played in D major at the same tempo. Twenty easily recognizable 2 s segments (ten different segments cut from each melody) were randomly presented through headphones. All subjects had previously heard “Mamma mia” and were asked to listen to this melody for 10 min prior to data collection. None of the subjects were familiar with “Musette”. The participants with Down syndrome had all completed a 6 week music program called “Music in motion” within the past week in which they had been exposed to “Mamma mia”. The program was 2 h in length each week and was led by professional musicians who lead participants through a variety of musical instruments (keyboard, guitar, maracas, shakers, drums, etc.). This program consisted of reciprocal conversation about music, show and tell, and a sing-along. “Mamma mia” was a favorite of all the participants with DS and they all expressed their pleasure in listening to this piece during the experiment. During the collection, segments of each melody were presented about 100 times in random order with randomized time intervals. Participants were asked to be seated quietly during the presentation and to refrain from talking or singing when they heard the music.
2.3. MEG data acquisition

The MEG data was acquired using a 151-channel whole head MEG system (VSM Medtech, Coquitlam, Canada) installed within a magnetically shielded room. Fifteen minutes of continuous data were initially collected at a rate of 600 samples per second with a 150-Hz low pass filter, using third-order gradiometer noise cancelation. The data was manually inspected for artifacts and corresponding segments were marked as bad.

2.4. Data processing

Given a set of data that is obtained from the external sensors, the major technical issue in MEG analysis is to estimate the sources within the brain that give rise to these signals. This is referred to as the inverse problem. There are a number of assumptions, models, and signal processing techniques that are used to estimate the location of these sources. Before these estimates can be made, the exact shape of each participant’s head surface is obtained using Polhemus FASTRAK digitizer. After the head shape is digitized a multiple-sphere approximation of the scalp surface is used to create an electromagnetic model of the head. This head model is co-registered with anatomical data by matching the measured head shape to the participant’s MRI image, found by computer-assisted fitting of a best matching MRT from a database of about one hundred images. To solve the inverse problem, a spatial filter is applied that uses statistical techniques to discriminate the signals arriving from a location of interest, and those signals that originate from other locations in the brain. The specific filter applied in this analysis is known as the SAM(erf) event-related beamformer (Robinson, 2004) specifically tailored for identifying event-related signals that have stable, consistently repeating time courses with respect to the stimulus. Such responses are usually referred to as the phase-locked activity. The SAM(erf) beamformer calculates the ratio of RMS amplitude of the source waveforms, averaged over epochs, to that of the plus–minus average waveform, for a selected time window. Thus, SAM(erf) yields a specific form of a signal-to-noise ratio (SNR) where the signal part is the RMS of the phase-locked response, and the noise part is the RMS of the background brain noise, estimated as the plus–minus average over the epochs (Robinson, 2004). In our case, spatial distributions of this SNR were computed over a three-dimensional grid with a 5 mm step, using a full-band signal. SAM(erf) beamforming was performed for 40 overlapping time intervals, 100 ms long each, positioned in 50 ms steps from 0 to 1.95 s relative to the start of the music segment. Thus 80 SAM(erf) distributions per subject (40 for the familiar and 40 for the unfamiliar music) were obtained. Then differential (familiar minus unfamiliar) distributions were created and spatially normalized to a standard brain space, using SPM99 software. For each of the 40 time intervals, differential distributions were group-averaged then extrema (i.e. minima and maxima) of the mean distributions were examined. Only those exceeding 95% threshold obtained by bootstrap – that is, by randomly permuting the “familiar” and “unfamiliar” labels – were retained for further processing. These extrema are referred to as the “group peaks”. Each group peak was characterized by its magnitude and latency relative to the stimulus, which is that of the corresponding time interval. The time resolution achieved this way roughly corresponds to the length of the interval – that is, around 100 ms. The p-value of each group peak was obtained by applying a t-test based on the values of the individual distributions at the peak’s location. Finally, we corrected the p-values for multiple comparisons (i.e. for the total number of peaks found for a given time interval) and retained only peaks with false discovery rates (FDRs) not exceeding a specified threshold. For many of the 40 time intervals processed, there were no peaks that survived this screening process.

3. Results

3.1. Salk/McGill Music Inventory Questionnaire of Music Ability and Interest

Table 1 displays the results from the Salk/McGill Music Inventory Questionnaire of Music Ability and Interest. Overall, parents reported that their children with DS showed a very high level of interest in music related activities and experienced high levels of emotional responses to music compared with individuals of the same age. However, as a group they were not very accurate in reproducing complex music and reproduced simple music less frequently in comparison with individuals of the same age.

3.2. Group averaged volumetric standard deviations

In order to characterize the overall measure of brain activity for each condition and for each group, we calculated the volumetric standard deviations (STDs) of the group-averaged images corresponding to different time windows. Because of its lack of spatial specificity, the volumetric STD is less affected by the within group variability making the between-group comparisons possible. The overall time courses of the STDs are displayed in Fig. 1. The plot on the left shows the response to the familiar condition for both groups. Statistically significant intervals were observed at the following time points: .1 s, .45 s, .8 s and 1.6 s. The plot on the right shows the response to the unfamiliar condition for both groups. Statistically significant differences were observed at .1 s, .45 s and 1.4 s. In both conditions, the control group showed a larger amplitude response with an earlier latency in comparison with the DS group.

3.3. Differential spatial distributions of brain areas

Due to the large variability in the DS group, we were unable to find specific spatial locations that showed statistically significant differences between groups. In particular, maxima of the between-group differential images for either condition typically were below the 90% threshold obtained by randomly assigning group labels for each subject (1000 reassignments were used to estimate the null-distributions). In addition, the spatial structure of the group-averaged response was very similar. In order to extract the qualitative differences in the spatial locations, we therefore calculated the spatially normalized and group-averaged beamformer differential distributions for time intervals that yielded significant locations for at least one of the groups. These locations are shown in Fig. 2. In this figure, all the active voxels in the 3D space are orthogonally projected onto the plane of the figure, as if the brain were completely transparent. The pixels with magnitudes within (–2, 2) dB range are explicitly set to 0. This corresponds to approximately 3% significance threshold obtained by bootstrap (exact threshold values of course depend on the time interval). The white circles mark significant locations listed in Tables 2 and 3. Peaks separated by less than 100 ms are shown in the same plot (for example, peaks #2, 3 and 4 with latencies 0.6 s and 0.65 s for the control group).

Table 2 lists all the significant peaks obtained from the familiar vs. unfamiliar differential analysis in the control group. Positive values indicate areas of activation that were stronger for the familiar condition and negative values indicate areas of activation that were weaker for the familiar condition. Listening to the familiar melody relative to the unfamiliar melody thus revealed increased significant activation primarily in the left hemisphere with activations in the primary auditory cortex, parietal, limbic and sensory-motor regions. In the right hemisphere only two locations were
identified – the insula and the postcentral gyrus. Areas of activation that showed weaker responses in the familiar condition compared to the unfamiliar condition included bilateral auditory cortices, limbic regions, dorsolateral prefrontal cortex and somatosensory regions.

Table 3 lists all the significant peaks obtained from the familiar vs. unfamiliar differential analysis in the DS group. Listening to the familiar melody relative to the unfamiliar melody thus revealed increased significant activation in three regions: left primary auditory cortex, the left superior temporal gyrus (STG) and the right
The present MEG study investigated the spatial–temporal pattern of brain activation during passive listening to a familiar and unfamiliar instrumental melody in typical adults and adults with DS. In relation to the control group, we found that neural activation of familiar music vs. unfamiliar music was associated with a task-specific temporal pattern involving distributed cortical, limbic and paralimbic areas. These findings are discussed below.

### 4.1. Spatial–temporal activation of music recognition in control adults

As expected, in the familiar vs. unfamiliar condition, the earliest activation was observed in the left primary auditory cortex, starting at .25 s following the onset of the melody. Activations in the right insula and right somatosensory areas began at approximately .6 s, followed by activation in the left premotor and SMA regions at .8 s. From 1 s until 1.45 s, activations were observed in the left cingulate, primary auditory region and premotor regions. Relative to familiar music, unfamiliar music led to later activations with activity beginning in the left primary auditory cortex and left dorsolateral prefrontal cortex at .8 s followed by activations in the right anterior cingulate, right somatosensory and left insula. Further significant peaks were observed later between 1.15 s and 1.4 s in the right sensorimotor regions, left insula and right primary auditory regions (Fig. 2 top).

In the DS group, familiar music relative to unfamiliar music led to the earliest activation in the left primary auditory cortex and the left STS beginning at .3 s, followed by activation in the right premotor region at .6 s. Unfamiliar music relative to familiar music also led to later activations beginning in the left STG at .4 s and the left inferior frontal gyrus at approximately 1.4 s (Fig. 2 bottom).

### 4.2. Discussion

The present MEG study investigated the spatial–temporal pattern of brain activation during passive listening to a familiar and unfamiliar instrumental melody in typical adults and adults with DS. In relation to the control group, we found that neural activation of familiar music vs. unfamiliar music was associated with a task-specific pattern of neural activation involving the left auditory, right limbic and left motor related regions.

### Table 2

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<th>X (left–right)</th>
<th>Y (posterior–anterior)</th>
<th>Z (inferior–superior)</th>
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<th>T (s)</th>
<th>Amp</th>
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### Table 3

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in relation to past emotional experiences and a secondary network related to auditory experiences in relation to past action experiences (e.g. singing, dancing etc.).

In contrast, unfamiliar music showed a different temporal–spatial pattern of activation. First, in comparison with familiar music, unfamiliar music led to later activity beginning in the left primary auditory cortex and left dorsolateral prefrontal cortex (DLPFC) at .8 s followed by activations in the right anterior cingulate, right somatosensory and left insula. In this comparison, the pattern of activation highlights the processing required for unfamiliar music. In particular, unfamiliar music vs. familiar music involved greater activation of the left dorsolateral prefrontal cortex, an area whose function remains controversial. Functions associated with the DLPFC involve motor planning, attention and working memory, selection of action (Lau, Rogers, Ramnani, & Passingham, 2004), comparing consecutive stimuli (Petrides, 1995) as well as rhythmic synchronization (Stephan et al., 2002). The early activation of the DLPFC may reflect any of these processes related to processing an unfamiliar melody or may be specific to processing musical structure of a novel melody in concert with the right sensorimotor areas. Activation of bilateral limbic areas may reflect general processing of affective information elicited by the unfamiliar melody. In this task, the neural activation may again reflect task specific networks – one related to processing the structural information in the melody and a second overlapping network related to processing affective information. The differentiation of these networks in relation to emotional processing of musical information will be critical for future studies.

4.2. Spatial–temporal activation of music recognition in Down syndrome

In the DS group, there are only three areas that showed significant activation in the familiar vs. unfamiliar condition. It is possible that the smaller number of locations may be due to higher variability in this population. These were the left primary auditory region, left STS and the right premotor region. Comparison of familiar music relative to unfamiliar music showed earliest activation in the left primary auditory cortex and the left STS beginning at .3 s, followed by activation in the right premotor region at .6 s. The STS is thought to be critical in musical memories (Peretz et al., 2009). The enhanced activation of this region in combination with the right premotor region suggests that there is tight auditory–motor coupling related to previous action based experiences (i.e. singing, dancing) with this melody. It is particularly noteworthy that there was no significant activity in limbic or paralimbic areas suggesting that the networks related to processing the emotional content of the musical melodies were not activated.

While this was not unexpected in light of the social–emotional impairments in this population, the fact that all participants reported that they enjoyed the familiar music, were clearly able to differentiate the familiar and unfamiliar melodies and remembered their previous experiences in music class with great pleasure may appear puzzling. However, it should be kept in mind that the significant locations we observed were produced in relation to subtraction between conditions. We did in fact observe limbic loca-
tions in both conditions, however these did not reach statistical significance following subtraction. This may be related to a combination of the small number of participants in this study and the fact that there is some neuroanatomical evidence that the temporal–motoric system is disproportionately reduced in volume and complexity (Jernigan, Bellugi, Sowell, Doherty, & Hesselink, 1993; Pinter et al., 2001) in DS. How these structural changes relate to emotional functioning clearly requires more detailed study.

The motor activation we observed is somewhat surprising given the perceptual–motor impairments present in this group. In studies examining perceptual–motor coupling, we found that during observation of tasks, there was a lack of motor activity. We have previously reported that there is a diminished correspondence between the networks involved in action execution and action observation in individuals with Down syndrome indicating a dysfunction in the mirror neuron system in this group in relation to visual action representation (Virji–Babul et al., 2010a, 2010b). Movement execution during a grasping task (picking up a coffee cup) was characterized by activity in bilateral motor, frontal, and parietal regions. However, observation of the same motion was characterized by activity primarily in the right frontal, parietal, and mid temporal regions with a conspicuous lack of activity in the motor regions suggesting a dysfunction in the relationship between visual/perceptual and motor processes in adults with Down syndrome. The results from our study show that deficits in the visual recognition of actions do not parallel deficits in audio–motor coupling suggesting that the visual and auditory representation of action may be mediated by independent networks in DS.

The findings from this study suggest that at the simplest level of music recognition, there may be at least two overlapping brain networks – one related to processing auditory information in relation to past emotional experiences that is activated early during stimulus processing, and a secondary network related to auditory experiences in relation to past action experiences. In individuals with DS who have a known impairment in social–emotional processing, we observed activation of only one brain network related to auditory–motor coupling. This provides preliminary evidence that emotional recognition in social and non-social contexts may share overlapping brain circuits.

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References


Further reading
