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Cerebellar patients demonstrate preserved implicit knowledge of association strengths in musical sequences

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Abstract

Recent findings suggest the involvement of the cerebellum in perceptual and cognitive tasks. Our study investigated whether cerebellar patients show musical priming based on implicit knowledge of tonal-harmonic music. Participants performed speeded phoneme identification on sung target chords, which were either related or less-related to prime contexts in terms of the tonal-harmonic system. As groups, both cerebellar patients and age-matched controls showed facilitated processing for related targets, as previously observed for healthy young adults. The outcome suggests that an intact cerebellum is not mandatory for accessing implicit knowledge stored in long-term memory and for its influence on perception. One patient showed facilitated processing for less-related targets (suggesting sensory priming). The findings suggest directions for future research on auditory perception in cerebellar patients to further our understanding of cerebellar functions.

Keywords

nonverbal auditory perception/music perception; implicit knowledge; music cognition; cerebellum; cognitive priming; neuropsychology

Numerous neuropsychological and neuroimaging findings suggest that the function of the cerebellum is not restricted to movement and motor control, but extends to perceptual and cognitive capacities. A seminal fMRI paper by Gao et al. (1996) reported that the dentate nuclei of the cerebellum were more active during manual tasks that emphasized sensory discrimination, rather than during movement per se. Neuroimaging studies have shown increased activation of the cerebellum during auditory tasks (Petacchi et al., 2005), such as frequency, intensity and duration discrimination (Belin et al., 2002), the processing of complex nonspeech sounds over pure tones (Vouloumanos et al., 2001), as well as for auditory attention (Janata, Tillmann, & Bharucha, 2002) and the perception of musical structures (Parsons, 2001; Tillmann, Janata, & Bharucha, 2003). Work in auditory perception is just one piece of a larger emerging picture that suggests potential cerebellar contributions to higher cognitive functions involving memory and language (see Fiez, 1996; Justus & Ivry, 2001 for reviews). Although the cerebellum seems to be implicated in perceptual and cognitive functions, no

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strong consensus has been reached regarding the cerebellum's precise role in these tasks. Possible, but not mutually exclusive, candidates include the regulation of sensory acquisition (Bower, 1997), temporal processing (Ivry & Keele, 1989), forward modeling and prediction (Wolpert, Miall, & Kawato, 1998) and associative/sequential learning (Tillmann et al., 2002; Shin & Ivry, 2003).

One domain that might give further insights into cerebellar function is music perception: music perception involves processing of a rich auditory temporal structure, associative/sequential learning of harmonic and other structures, and predictions based on previous experience with the musical system. Through mere exposure to music, even nonmusicians acquire implicit knowledge of music with its underlying structures, relations and strengths of associations between events. This implicit knowledge influences subsequent music perception (e.g., Tillmann, Bharucha, & Bigand, 2000). Studying music perception in patients with cerebellar damage allows us to investigate whether knowledge of sequential relationships and strength of associations between tones in the tonal-harmonic system, which was acquired prior to cerebellar damage, can still be accessed after damage to this subcortical structure. The involvement of the cerebellum in auditory processing and attention, and also in associative and sequential learning, led us to speculate on the cerebellum's role in the reactivation of stored sequential representations and their influence on auditory processing.

In the present study, we used the musical priming paradigm, which is an implicit investigation method of listeners' knowledge about tonal relations and its influence on musical event processing (e.g., Bharucha & Stoeckig, 1986). Each trial consists of a prime context (i.e., a chord sequence) and a target event (i.e., a chord). The musical relations between prime and target are systematically manipulated on the basis of music theory, opposing related and less-related targets. In reference to the musical system, related targets are more likely to complete the sequence than less-related targets, even though they are equally probable within the experimental session. Participants perform a simple perceptual task on the target chord (i.e., not an explicit judgment of the musical relations) with the goal of measuring processing time for musical events depending on the musical context. Behavioral priming data have shown that responses to related targets (being more strongly associated to events of the prime context) are facilitated in comparison to less-related targets.

In Bigand et al. (2001), for example, the task was a speeded phoneme identification on the target chord in sequences of sung artificial syllables. The behavioral data showed that phoneme identification was faster when the phoneme was sung on a chord related to the musical context. The slowed-down phoneme identification for less-related targets reflects the cost of processing for a musically less-expected event (i.e., based on listeners' musical knowledge).

Processing costs for less-prototypical ending chords have also been reflected in functional imaging data of musical priming, showing increased neural resources for less-related targets relative to related targets; activation increased in inferior frontal regions and -among other frontal and parietal regions - the cerebellum (Tillmann et al., 2003; 2006). The coordinates of the reported cerebellum activation (i.e., -19 -41 -20 for weaker musical relations (Tillmann et al., 2003), and -32 -57 -23 for the same musical relations¹ (Tillmann et al., 2006)) were close to those reported in an activation likelihood estimate meta-analysis for a wide range of auditory tasks (-44 -50 -32 (crus I) and -20 -50 -22 (lobule V) (Petacchi et al., 2005)). Beyond being part of a network supporting increased auditory processing, the increased cerebellar activation might be linked to a cerebellar role in generating musical expectations based on knowledge of prototypical sequences and association strengths in music.

¹This activation was not reported in the original report (Tillmann et al., 2006) since it only reached the statistical threshold of $p < .005$ (instead of $p < .001$ used in the report).

The involvement of the cerebellum in these processes is suggested by its involvement in learning of associative relations, developing predictions and temporal processing (e.g., Timmann et al., 2002; Wolpert et al., 1998). However, the functional imaging data on musical priming do not inform us whether the cerebellum is mandatory for musical structure processing, as suggested recently for inferior frontal areas (Patel, 2003). For patients with Broca's aphasia (showing lesions in frontal and temporal lobes), behavioral musical priming effects were reduced: musically unrelated events did not result in increased processing times in comparison to related events on the group level (Patel, Iversen & Hagoort, 2004; Patel, 2005). Our present study investigated whether this would also be the case for patients with cerebellar dysfunction. This rationale is thus in parallel to recent observations on language processing: deficits on grammaticality judgments, which have been observed for Broca's aphasics, have now similarly been reported for cerebellar patients (Justus, 2004).

Method

Participants

Eight English-speaking patients with cerebellar dysfunction (see Table 1 and Figure 1) and eight matched controls (c1 to c8) participated after having given written informed consent, following experimental procedure approved by the UC Berkeley Committee for Protection of Human Subjects. Four patients had bilateral degeneration (B1, B2, B3, B5) and four patients showed focal lesions, two of which were due to tumor (left-hemisphere patient L1 and midline patient M1) and two of which were due to infarction (right-hemisphere patients R1 and R3).

Material

The 48 chord sequences of (Bigand et al., 2001) were used. Eight-chord sequences ended on either the tonic chord (related target) or the subdominant chord (less-related target). These chord sequences were composed in such a way that the target never occurred in the previous context. The number of pitch classes² shared with the prime chords was slightly higher for less-related targets (14.75) than related targets (12.5); this rules out the possibility of pitch repetitions driving the priming effect. The sequences were sung on CV-syllables by sampled voice sounds. The succession of the synthetic phonemes did not form a meaningful, linguistic phrase (e.g., /da fei ku jo fa to kei/), and the last phoneme (i.e., of the target) was either /di/or /du/to define the experimental task³. The experiment was run on Psyscope software (Cohen et al., 1993).

Procedure

Participants were asked to decide as quickly and as accurately as possible whether the last chord of each sequence was sung on /di/or /du/by pressing one of two keys. Incorrect responses were accompanied by a feedback signal and a correct response stopped the target. A short random tone sequence was presented after each response. After four practice sequences, the 48 sequences were presented in random order twice in two blocks, separated by a short break⁴. Patients and controls were asked to choose the hand of their preference for responding, with the restriction to use only one hand (with index and middle fingers being used to respond for the two syllables). Accordingly, two patients responded with their left hands, as did two of the controls.

²A pitch class is defined by a set of pitches at different pitch heights that are separated by octaves (i.e., an interval defined by multiples of the fundamental frequency of a tone), for example the tones A at 220 Hz, A at 440 Hz, and A at 880 Hz all belong to the pitch class of A.

³The experimental session consisted of 50% of sequences ending on the related tonic target (25% being sung with/di/, 25% with/du/) and 50% ending on the less-related subdominant target (25% with/di/, 25% with/du/).

⁴With the exception of c2, who stopped the experiment after the first block.

Pretest

Given that French students were used in Bigand et al. (2001), a pretest replicated the musical relatedness effect with American students, also to test whether the sung phonemes were easily judged by native English speakers. 13 students of Dartmouth College (musical expertise in years of instrument, mean of 7.1; std = 3.6; ranging from 0 to 11 with median of 8) participated in the pretest (i.e., based on one block). Accuracy was high overall (98.2%). Correct response times (Figure 2) were analyzed with a 2×2 ANOVA with Musical Relatedness (related/less related) and Target Phoneme (di/du) as within-participant factor. Only the main effect of Musical Relatedness was significant, with faster response times for related than for less-related targets ($F_1(1,12) = 32.28$, $MSE = 1333.72$, $p < .001$; $F_2(1,11) = 12.13$, $MSE = 3317.76$, $p < .01$). While mean response times of each participant were faster for related than for less-related targets, individual analyses with sequences as random factors revealed that this difference reached significance only for four participants ($ps < .05$).

Results

Percentages of correct responses were high overall, with 97% for patients (ranging from 94.8% to 100%) and 88% for controls (ranging from 64% to 98%)⁵. Mean correct response times were longer for patients (1782 ms) than controls (884 ms) and both groups showed inter-subject variability (377 ms to 2976 ms for patients and 537 ms to 1612 ms for controls). To tease apart general differences between patients and controls (i.e., leading to overall differences in response speed) from condition-specific changes in response time patterns (see Faust, Balota, Spieler & Ferraro, 1999; Ober, 2002), the absolute response times were individually normalized to z-scores with a mean of 0 and a standard deviation of 1 (Figure 3 top). Z-scores were analyzed with a 2×2 ANOVA with Musical Relatedness (related/less related) and Target Phoneme (di/du) as within-participant factors and Group (patients/controls) as the between-participants factor. Only the main effect of Musical Relatedness was significant, $F(1,14) = 20.14$, $p < .001$, with faster processing for related targets than for less-related targets. The main effect of Group and its interaction with Relatedness or Target Phoneme were not significant ($ps > .28$).

Figure 3 bottom displays differences between related and less-related conditions (averaged over target phonemes) for each participant. Facilitated processing for related targets (positive values) was observed for all participants, except R3. For the control group, the main effect of Musical Relatedness was significant, $F(1,7) = 33.06$, $p < .001$. For the patient group, the main effect of Musical Relatedness was marginally significant, $F(1,7) = 3.69$, $p = .096$. For the patient group excluding R3, the main effect of Musical Relatedness was significant, $F(1,6) = 8.97$, $p < .05$. Additional analyses with sequences as random factor for each participant revealed that the difference between related and less-related conditions was significant only for two patients ($p < .01$ for L1 and $p < .05$ for B5, but $p = .11$ for B1, $p = .19$ for R3 and $ps > .20$ for B2, B3, M1 and R1) and for one matched control ($p < .05$ for c5, but $p = .09$ for c3 and c7, $p = .10$ for c6 and $ps > .20$ for c1, c2, c4, and c8).

Discussion

The present study demonstrated musical priming effects for cerebellar patients and matched controls as has been observed for healthy college students (in the pretest and in Bigand et al., 2001): Phoneme identification was faster when the phoneme was sung on a chord that was

⁵The lower accuracy for the control group was due to two controls (i.e., 64% and 67%); the mean accuracy of the remaining controls was comparable to the patient group (96%). These two matched controls (c3, c6) found the task overall more difficult, as suggested by their response times (i.e., 1327 and 1470 ms), which were slower in comparison to the mean response time of the remaining controls (i.e., 688 ms). A supplementary analysis on correct response times excluding these two controls confirmed the main effect of Musical Relatedness reported below, $F(1,12) = 13.71$, $p < .01$.

related to the preceding musical context. This outcome suggests that the cerebellum may not be essential for processing sequential structures that involve previously acquired association strengths. For music perception, this concerns listeners' knowledge about association strengths between chords and how chords are used in sequential progressions in tonal-harmonic music. It is worth emphasizing that the musical priming effects cannot be explained by sensory components, such as facilitation of specific tones due to repetition: target chords never occurred in the prime context and less-related targets shared even more tones with the prime contexts than did related targets (Bigand et al., 2001). Musical priming reflects the influence of listeners' abstract knowledge, which has been acquired via prior experience with musical material and without explicit musical training (e.g., instruction in an instrument or music theory). Based on this musical knowledge, listeners develop implicit expectations about the musical events that are most likely to occur next in the sequence and these expectations influence event processing. The patients and matched controls participating in the present study ranged in musical expertise from inexperienced to only moderately experienced (as measured by years of explicit musical instruction; see Table 1). Their musical priming data provide converging evidence for implicit musical knowledge in nonmusician listeners (see Tillmann et al., 2000; Bigand & Poulin-Charronnat, 2006 for reviews).

The patients' musical priming data suggest that musical knowledge, which was acquired prior to cerebellar damage, can still be accessed after this damage. In contrast to accessing previously formed knowledge, cerebellar patients have difficulty in forming new associative knowledge (Tillmann et al., 2002; Shin & Ivry, 2003). Studies investigating reflex behavior support this distinction between the spared use of associative/sequential knowledge formed prior to cerebellar damage and the impaired learning of new associative/sequential knowledge after cerebellar damage (Bracha et al., 1997): Cerebellar patients cannot acquire new classically conditioned responses (i.e., eyeblink response), but retain and express eyeblink responses conditioned before the brain damage (i.e., in reaction to a visual object approaching the face). Alternatively, learning impairment due to cerebellar damage might depend on whether learning requires movement. Deficits were observed in serial reaction time tasks requiring a motor output mapping (e.g., Shin & Ivry, 2003), while implicit learning of artificial grammars (instantiated with visually presented letter strings) remains intact in cerebellar patients (Witt, Nuhsman, & Deuschl, 2002). Future research could investigate this hypothesis by studying whether cerebellar patients can acquire representations of *new* musical associative/sequential relationships (not requiring overt movement during acquisition) - as for example, shown by Bigand, D'Adamo and Poulin (2003) for implicit learning of twelve-tone regularities in healthy adult nonmusician listeners (see also Dienes & Longuet-Higgins, 2004).

Although the cerebellum has been shown to be active during music perception (Parsons, 2001) and more specifically to be sensitive to musical priming manipulations (Tillmann et al., 2003; 2006), our present data suggest that an intact cerebellum may not be necessary for the (behavioral) musical priming effect. The cerebellar activation observed during musical priming might reflect increased auditory processing or attention in response to unexpected events, rather than playing a direct role in mediating the expectations themselves. In contrast to cerebellar damage, lesions causing Broca's aphasia were associated with reduced musical priming effects (Patel et al., 2004; Patel, 2005), with frontal brain areas suggested to be more directly involved in the processing of musical relations (Patel, 2003).

Although our patient group as a whole suggests preserved cognitive priming with a processing advantage for related targets, mean response time differences for patient R3 showed a processing advantage for less-related targets. Even if R3's difference was not significant in the individual analysis, it is worth pointing out because, among all patients, matched controls and pretest students, it is the only difference favoring less-related targets. Faster processing for less-related targets suggests that responses are driven by sensory priming (i.e., repetition of

tones) rather than by abstract knowledge of associative/sequential relationships. Patient R3 has a small, circumscribed lesion in the superior right cerebellar hemisphere (in lobus simplex (VI) and the anterior lobe (IV/V) in the superior planes), which slightly encroaches on the superior portions of the dentate nucleus (see Figure 1). Even if this lesion location possibly implies some deterioration of the connection between the cerebellum and the frontal lobe (Allen et al., 2005), our data set cannot assert its implication in musical structure processing, since other patients of the group also showed dentate impairments (i.e., R1 and degenerative patients). However, R3's behavioral data suggest a unique lesion pattern that might have resulted in impairment in processing relatedness and association strengths between musical events.

Interestingly, this lesion pattern was also associated with impaired language processing: R3 was particularly impaired for grammaticality judgments requiring subject-verb agreement in aurally presented sentences (Justus, 2004). This language task requires access of syntactic (or morphosyntactic) structures of language, which seems to be impaired in R3. The musical priming effect requires access of syntactic structures in music, which also seems to be impaired in this patient. Musical syntax refers to the structural organization of musical events evolving over time and this organization is based on rules specific to the musical system. The comparison between the processing of syntactic structures in language and in music has raised the hypothesis of shared neural resources (see Patel et al., 1998; Patel, 2003; Koelsch et al., 2005). For R3, the two data sets on language and music thus suggest that the particular lesion pattern impairs sequential processing mechanisms that are necessary for syntax processing and that seem to be shared across these two domains.

With this caveat in mind, we suggest that despite damage to the cerebellum listeners remain able to develop expectations in music based on associative/sequential relationships between tones and chords. In addition to such tonal expectations (what event will occur next), listeners also develop temporal expectations (when this event will occur). Given that the cerebellum has also been associated with processing of temporal features (Ivry & Keele, 1989), we are currently investigating whether cerebellar patients are sensitive to temporal manipulations in the musical priming task (cf. Tillmann & Lebrun-Guillaud, 2006, for healthy listeners).

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Figure 1.

The location of cerebellar damage for six of the patients is shown, excepting B5 and M1 for whom reconstructions were not available. B5 had cerebellar degeneration, confirmed by genetic testing (SCA type 3). M1 had a lesion due to resection of a medially located tumor. For the six patients, seven horizontal slices through the pons and the cerebellum are shown, with the most superior slice at the top. The corresponding sections in the atlas by Schmahmann, Doyon, Toga, Petrides, and Evans (2000) are approximately: $z = -9, -17, -25, -33, -41, -49$, and -57 . The left side of each slice corresponds to the patient's left side. Lighter color indicates tissue degeneration, whereas darker color indicates a lesion. For further details on these reconstructions, see <http://socrates.berkeley.edu/~ivrylab/facilities/recons.html>.

Figure 2.

Correct response times obtained in the pretest for related and less-related targets presented as a function of the target phoneme (di/du). Response times were averaged over the sequence set and participants (i.e., healthy college students). Error bars indicate standard errors (over participants).

Figure 3.

Top) Correct response times (transformed into z-scores) for related and less-related targets presented as a function of the target phoneme (di/du) for patients (left) and controls (right). Response times were averaged over the sequence set and participants. Bottom) Differences between related and less-related targets (averaged over target phonemes) for patients (left) and controls (right), with G representing group averages. For patients, B1, B2, B3 and B5 represent bilateral degeneration and M1, L1, R1 and R3 represent focal lesions (along the midline M, left-sided L and right-sided R). Positive and negative values indicate facilitated processing for related and less-related targets respectively. Error bars indicate standard errors (over participants for G and over sequences for each participant).

Table 1

Cerebellar patients participating in the experiment.

Actiology	Age	Ed.	Hand.	Sex	Language	Music	WAIS- FSIQ	ICARS*	
Patients									
B1	bilateral degeneration (SCA6, age 29-)	42	16	right	F	Spanish, English	7 yrs., piano	109	54
B2	bilateral degeneration (unknown, age 30-)	72	12	right	M	English	none	91	45
B3	bilateral degeneration (unknown, age 61-)	63	20	right	M	English	none	108	17.75
B5	bilateral degeneration (SCA3, age 27-)	44	13	right	F	English	choral experience	111 (est.)	31 (est.)
M1	midline tumor (age 28)	37	19	right	M	English	8 yrs., violin, trumpet	120	1
L1	left hem. tumor (age 47)	58	12	right	M	English, Spanish	1 yr., trumpet, horn	83	19.25
R1	right hem. infarction (age 66)	77	18	right	M	English	4 yrs., piano, violin	107	34
R3	right hem. infarction (age 55)	66	12	right	M	English	none	89	4.25
Mean values ± standard deviation:		57 (± 15)	15.3 (±3.4)			3.1(±3.3)			
Controls (mean values ± standard deviation)		65 (±10)	16.4 (±1.8)	6 right, 1 left, 1 mixed	4 M, 4 F	all native English	2.6 (minimum 0, maximum 10) (±4)		

* International cooperative ataxia rating scale (Trouillas et al., 1997). Total ICARS score ranges from 0 (no ataxia) to 100 (most severe ataxia)