Cerebellum, temporal predictability and the updating of a mental model

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We live in a dynamic and changing environment, which necessitates that we adapt to and efficiently respond to changes of stimulus form (‘what’) and stimulus occurrence (‘when’). Consequently, behaviour is optimal when we can anticipate both the ‘what’ and ‘when’ dimensions of a stimulus. For example, to perceive a temporally expected stimulus, a listener needs to establish a fairly precise internal representation of its external temporal structure, a function ascribed to classical sensorimotor areas such as the cerebellum. Here we investigated how patients with cerebellar lesions and healthy matched controls exploit temporal regularity during auditory deviance processing. We expected modulations of the N2b and P3b components of the event-related potential in response to deviant tones, and also a stronger P3b response when deviant tones are embedded in temporally regular compared to irregular tone sequences. We further tested to what degree structural damage to the cerebellar temporal processing system affects the N2b and P3b responses associated with voluntary attention to change detection and the predictive adaptation of a mental model of the environment, respectively. Results revealed that healthy controls and cerebellar patients display an increased N2b response to deviant tones independent of temporal context. However, while healthy controls showed the expected enhanced P3b response to deviant tones in temporally regular sequences, the P3b response in cerebellar patients was significantly smaller in these sequences. The current data provide evidence that structural damage to the cerebellum affects the predictive adaptation to the temporal structure of events and the updating of a mental model of the environment under voluntary attention.

1. Introduction

The cerebellum has featured prominently in past and recent attempts to identify the neural basis of temporal processing and to understand how the brain represents and uses temporal structure [1–5]. However, this line of research is one of many contributing to a growing body of evidence that the cerebellum is engaged in numerous cognitive functions including speech and music [6–9] and the question arises how specific these functions are. One possible way to delineate these functions is to have a closer look at cerebello-cortical connections that may allow specification of their respective contribution to cognition. For example, some of these connections manifest links between the cerebellum and other brain areas associated with temporal processing such as the basal ganglia or the supplementary motor area (SMA) [10–14]. Increasingly more fine-grained anatomical differentiations corroborate assumptions of divergent, and also shared, operations in motor (production) and non-motor (perception, cognition) functions in brain areas such as the cerebellar dentate nucleus and its motor and non-motor sub-compartments, the caudate/putamen of the basal ganglia or the subdivisions of the SMA [15–18].

Temporal processing is considered fundamental to neurocognitive operations underlying motor and non-motor function(s) relevant in domains such as speech and music to optimize overt and covert behaviour. Importantly, optimal timing implies a form of predictive adaptation to the temporal structure of events in the environment to circumvent exclusively reactive behaviour. It is
therefore not surprising that ‘prediction’ is another neurocognitive operation that has been associated with the cerebellum [19–21]. However, efficient prediction and adaptation in behaviour requires adequate internal representations of both the formal structure (‘what’) and the temporal structure (‘when’) of events in the environment. In other words, information pertaining to the form or identity of events has to be encoded alongside information that relates to the rhythm or temporal locus of events [22]. Turning to concrete examples, we can ask how musicians coordinate their play while creating music together. Recognizing the absence of sound in a musical piece marks the start of a pause. Prior information about the duration of a pause allows the musicians to predictively adapt their behaviour and to resume playing together at the right point in time. In the absence of an external reference, such as the arm movement of a conductor, the behavioural benefit granted by temporal prediction is determined by an individual’s ability to exploit regular rhythms and temporal relations such as estimating a pause’s duration. Similarly, we can consider how two people communicate with each other. Here, lengthening of a phrase’s final word or syllable, followed by a pause, may (among other factors) indicate that one social partner signals the opportunity for the other partner to take a turn at talk. The combination of verbal and non-verbal temporal cues as described above allows the communicative partners to predictively adapt to each other and to take turns at the correct point in time to ensure optimized communication flow.

One way to investigate the operations underlying the ability to use temporal structure in order to optimize behaviour is to infer function from pathological dysfunction. Here we considered structural damage to the cerebellum, which should affect precise event-based perceptual encoding of temporal structure [23,24]. Thus, structural damage to the cerebellum should disrupt how one efficiently extracts and uses temporal regularity to generate predictions about the temporal locus of an upcoming event and may further lead to suboptimal performance in a number of cognitive tasks. To explore this potential link between temporal predictability and optimal performance, we tested how temporal predictability influences auditory deviance processing under voluntary attention in patients with cerebellar lesions and healthy controls. Deviance processing provides a relatively simple framework, which should make it possible to probe how patients and healthy controls exploit temporal regularity and the temporal predictability associated with it in optimal tone perception.

Broadly speaking, deviance processing refers to a set of neurocognitive operations associated with change. For example, how does one perceive a change in tone frequency or duration, while expecting a particular tone frequency or duration that has been previously established? Deviance processing is classic in event-related potential (ERP) research. Different stages of deviance processing are reflected in early responses associated with sensory processing and progressively later responses associated with cognitive operations [25,26]. Critically, deviance processing makes it possible to test the interaction of formal and temporal structure by varying formal stimulus properties (e.g. tone frequency) and temporal regularity (e.g. when a tone occurs in a tone sequence) in one single experimental setting. In addition, the impact of temporal regularity on deviance processing (e.g. optimal detection of deviance) is linked to a number of well-established ERP components.

Consequently, we set out to test patients with cerebellar lesions and healthy, age-matched controls using an auditory oddball paradigm, in which frequent standard and less frequent deviant tones are presented in either a temporally regular or irregular context. This particular approach is based on previous work, in which pre-attentive deviance processing as indexed by the P50, N1, mismatch negativity (MMN), P3a and reorienting negativity was contrasted with attentive deviance processing as indexed by the P50, N1, N2b and P3b ERP components [24,27]. Statistically indifferent ERP responses obtained in the pre-attentive context suggest that pre-attentive deviance processing is relatively robust against the manipulation of temporal regularity [24,27], while amplitude modulations in the P3 range for attentive deviance processing may indicate an interaction of formal and temporal stimulus properties at this processing stage [24]. Considering the active experiment task (counting of deviant tones) and the centro-parietal topographical distribution of the effect, this finding was interpreted as an attention-dependent differentiation of the P3b component. More specifically, deviant tones presented in a temporally regular context evoked a larger P3b response (amplitude enhancement) in comparison with physically identical deviant tones presented in a temporally irregular context. Similar findings have been obtained with linguistic stimuli [28], suggesting that the P3b enhancement in response to deviant stimuli in temporally regular stimulus sequences may reflect the impact of temporal structure and temporal predictability on deviance processing. The fact that P3b enhancement is reported for lower level auditory stimuli (tones) as well as more complex linguistic stimuli suggests that these operations in deviance processing apply to a number of cognitive functions including speech and music. As a result, it is important to understand how structural damage to the cerebellar temporal processing system affects the precise encoding of the temporal structure of successive events and how this may affect the efficient adaptation to a dynamic environment.

In this study, participants listened attentively to tone sequences, and counted deviant tones while their electroencephalogram (EEG) was recorded. We focused on two ERP responses in this context. The fronto-centrally distributed N2b response is typically associated with the detection of a deviant event, whereas the predominant theoretical account for the more centro-parietally distributed P3b links this component to the updating of a mental model of the environment in response to a deviant event [29–31]. The exact nature of this mental model remains elusive at this stage. However, the P3b is typically believed to instantiate a neural signature of a change in this model, conceived as a general schema of all available data in the environment and of the stimulus context, in particular [29,31]. With respect to the oddball paradigm used here this suggests that the model established by frequent standard tones has to be transformed (updated) when an infrequent deviant tone is encountered, reflecting the mediation between the participants’ expectations and sensory input [32,33]. We expected that healthy controls would show an N2b response to deviant tones in both types of sequences and a further enhanced P3b response to deviant tones in temporally regular compared with irregular tone sequences [24] reflecting the beneficial effects of temporal regularity on deviance processing and, in turn, effective updating of a mental model of the environment. Patients with cerebellar lesions, who are expected to be less sensitive to temporal regularity owing to increased system noise and uncertainty in the event-based encoding of temporal structure, should not show a similarly beneficial effect of temporal regularity. Thus,
while an N2b response to deviance per se may be comparable with healthy controls, the P3b responses to deviant tones in temporally regular and irregular tonal sequences should be dissimilar, substantiating the idea that temporal predictability cannot be efficiently applied to optimally update the mental model. We therefore addressed two core questions in the current experiment: (i) Does temporal predictability influence deviance processing under voluntary attention in a similar fashion in healthy ageing controls as previously observed in young healthy participants? (ii) How does structural damage to the cerebellum affect the potentially optimizing influence of temporal predictability on deviance processing and the updating of a mental model as indicated by N2b and P3b?

2. Material and methods

(a) Participants

Eleven patients with cerebellar lesions (figure 1 and table 1) and a corresponding number of healthy controls participated in the study. Healthy controls matched the patients in terms of gender (five women), age (mean 43.3 ± 11.9 years), handedness (all right handed) and education (10 ± 1.6 years). All participants gave their informed written consent regarding the experiment and received a compensatory fee. Patients were recruited through the database of the Clinic for Cognitive Neurology at the University Hospital of Leipzig. Healthy controls were recruited from the participant database of the Max Planck Institute for Human Cognitive and Brain Sciences in Leipzig.

(b) Magnetic resonance imaging and lesion mapping

High-resolution T1-weighted magnetic resonance (MR) scans were obtained at 3 T with a Siemens TrioTim (Siemens Healthcare, Erlangen, Germany) or a Bruker BioSpin (BioSpin GmbH, Rheinstetten, Germany) MR system with a 32-channel phased-array head array coil using an MP-RAGE sequence [36]. The resulting images were segmented and spatially normalized to the Montreal Neurological Institute (MNI) space by means of the unified segmentation approach [37] as implemented in SPM (SPM8, Wellcome Department of Imaging Neuroscience, London, UK, http://www.fil.ion.ucl.ac.uk/spm). The MRICron software package [38] was used to manually delineate lesions on axial slices of...
the normalized T1-weighted images and to create binary lesion maps for each patient (average lesion volume 12.61 cc, s.d. 14.16 cc). To visualize overall lesion distribution (figure 1), the lesion maps were superimposed on a scalp-striped T1-weighted single subject template in MNI space (Colin27_T1_seg_MNI.nii, available at http://brainmap.org/ale/index.html).

(c) Stimulus sequences and experimental task

During the EEG recording, stimuli were delivered by Presentation 12.0 (Neurobehavorial Systems). Each oddball sequence (figure 2) consisted of 450 tones in total, corresponding to 360 standard (600 Hz, 300 ms, 10 ms rise and fall times) tones and 90 deviant (660 Hz, 300 ms, 10 ms rise and fall times) tones (4:1 ratio). In the regular condition, the inter-stimulus intervals (ISIs) were fixed to 600 ms, while the ISIs were randomly chosen from a range between 200 and 1000 ms (600 ms on average) in the irregular condition. Randomization constraints ensured that no more than two deviants were presented in a row and that the first four tones of each sequence were standards in order to allow participants to establish a memory trace for these tones. The type of initial sequence presented was counterbalanced across participants. A short excerpt of this sequence was presented to the participants in order to familiarize them with the different tone types. During the experiment, participants listened to the tones presented via loudspeakers and silently counted the number of deviant tones embedded in a sequence. The counting task was employed in order to make sure that the participants directed their attention towards the stimulus sequence. This conforms to a cognitive task with no motor aspect during the recording interval, in which any brain potential confound owing to impaired motor control in the cerebellar patients should be absent or at least minimal. Participants were not informed about the nature of the temporal context that tones could occur in. They reported one final count at the end of each type of sequence to which they had listened. A short pseudo-randomized sequence consisting of 12 additional tones (7 standards and 5 deviants) was attached to the irregular sequence to obtain different correct count values for the two conditions (90 regular versus 95 irregular) in order to prevent accurate task performance being achieved by simply reporting the same value twice. These additional tones were disregarded from all further EEG analyses.

(d) Electroencephalogram recording and analysis

The EEG recordings took place in a dimly lit sound-attenuated booth. Participants sat in front of a computer screen, which displayed a fixation cross throughout the session. The EEG was recorded at a sampling rate of 500 Hz from 25 Ag/AgCl scalp electrodes mounted in an elastic cap and arranged according to the standard 10–20 International System. Additional horizontal and vertical electrooculography was recorded by means of four separate electrodes. The ground electrode was placed on the sternum and electrodes placed on the left and right mastoids served as reference during the recording.

Data pre-processing and ERP analyses were performed using the EEG 3.2 software package (Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, commercially available as EEG Prob, ANT Neuro). Raw data were re-referenced offline to averaged mastoids. Epochs lasting from −100 to 450 ms relative to stimulus onset were averaged for standards and deviants for each condition per participant and across participants. All epochs of tones that immediately followed the presentation of a deviant tone were rejected. Automatic rejection was applied to artefacts exceeding 30 μV at eye-channels or 40 μV at electrode CZ. To increase the number of eligible trials for both groups, prototypical artefacts reflecting eye blinks and saccades identified via electrooculography were used to obtain propagation factors, which were then used to compensate for similar artefacts in the remaining trials via a regression algorithm (Electrooculogram Epoch Classification), implemented in the EEG software.

The ERPs of interest were analysed in four regions of interest (ROIs) to assess both the typical fronto-central and centro-parietal scalp distributions of the N2b and P3b components as well as potential hemispheric differences of component distribution as a result of cerebellar pathology. These ROIs covered left-anterior (F7, F3, F17, FC3), right-anterior (F8, F4, FT8, FC4), left-posterior (T7, C3, CP5, P3) and right-posterior (T8, C4, CP6, P4) electrode positions. A 2 × 2 × 2 × 2 ANOVA with a between-factor group (patients versus controls) and within-factors temporal structure (regular versus irregular), formal structure (standard versus deviant), hemisphere (left versus right) and region (anterior versus posterior) was conducted using SAS 9.3 (SAS Institute Inc.) for a 50 ms time-window lasting from 198 to 248 ms (N2b) and a 130 ms time-window lasting from 298 to 428 ms (P3b) relative to the stimulus onset, respectively. These time-windows were selected after visual inspection of the data and included the peak of each component across groups and conditions. Thus, N2b was analysed from the transition into a negative-going deflection until the earliest crossing into positive voltages (which was found in response to regular deviants in controls; figure 3), while P3b was analysed from the transition into a positive-going deflection until the latest transition into a negative-going deflection (found in response to regular deviants in patients).

3. Results

(a) Behavioural results

Both controls (regular mean value reported 89.36, s.d. 1.29, range 87–91; irregular mean 94.55, s.d. 0.82, range 93–96) and patients (regular mean 88.82, s.d. 2.18, range 86–92; irregular mean 94.45, s.d. 0.82, range 93–96) performed well in the counting task, which is also indicated by comparably high
percentages of accuracy for controls (regular 99%, s.d. 1.1; irregular 99%, s.d. 0.7) and patients (regular 98%, s.d. 1.4; irregular 99%, s.d. 0.7). One-sampled $t$-tests were conducted to test for differences between the values provided by the participants and the actual number of deviants embedded in each sequence (90 regular, 95 irregular). The results were non-significant in the control group (regular: $t(10) = 2.164, p = 0.132$; irregular: $t(10) = 2.184, p = 0.096$) and in the patient group, even though there was a strong trend in the irregular context (regular: $t(10) = 2.184, p = 0.096$; irregular: $t(10) = 2.21, p = 0.052$).

Taken together the behavioural results confirm that both healthy controls and cerebellar patients paid attention to the task requirements and executed the task appropriately.

(b) Event-related potential results

Visual inspection of the averaged group ERP data confirmed the typical component evolution associated with attentive deviance processing, and also suggested qualitative component differences between the two groups (figures 3 and 4). While the N2b and P3b responses (components of empirical interest) to standard tones seemed to be comparable between both groups independent of temporal context, the responses to deviant tones seemed to vary as a function of temporal context. The N2b response to deviants embedded in irregular temporal structure appeared similar across groups, but the difference between regular and irregular temporal structure seemed to be more pronounced in the patient than the control group. The P3b was generally larger for deviants embedded in regular temporal structure, but was much reduced in the patient group compared with the control group.

Further, in comparison to controls, the patient group also appeared to show more pronounced differences between standards and deviants already in the N1 range, with highly similar responses for standards embedded in regular and irregular temporal structure. N1 responses in controls followed a similar pattern as previously reported for younger healthy participants [27]. However, complementary statistical analyses in the N1 range did not confirm any significant group differences.

Likewise, the repeated-measures ANOVA of the N2b time-window did not fully confirm the initial visual inspection. Results showed a strong trend towards a main effect of temporal structure ($F_{1,20} = 4.30, p = 0.051$), while there was a significant main effect of formal structure ($F_{1,20} = 8.63, p < 0.01$). There was a significant interaction of temporal structure $\times$ hemisphere ($F_{1,20} = 6.12, p < 0.03$), indicating a global effect of temporal structure over right ($F_{1,20} = 7.49, p < 0.02$) but not left hemisphere electrode sites ($F_{1,20} = 1.18, p = 0.288$). However, the three-way

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**Figure 3.** Group-averaged EEG data for healthy controls and patients. Data recorded from a representative electrode (CZ) are shown on the left side. A 7 Hz low-pass filter was applied offline for graphical display only. Topographical maps on the right side illustrate the distribution of the corresponding N2b and P3b effects, i.e. voltage differences obtained by subtracting responses to standard events from responses to deviant events in each experimental condition. (Online version in colour.)
interaction of temporal structure × formal structure × hemisphere approached statistical significance ($F_{1,20} = 4.06, p = 0.058$) in accordance with the initial visual inspection. Of note is the lack of a significant main effect of group ($F_{1,20} = 0.54, p = 0.473$) or interaction involving the factor group (all $p > 0.20$). In order to explore a potential relation between the extents of structural damage (i.e. lesion volume) and the electrophysiological response, individual lesion volumes were correlated with individual mean N2b amplitudes obtained at electrode CZ for patients in all four conditions. However, this procedure yielded no significant result for regular standards ($r = 0.06, p = 0.87$) or deviants ($r = 0.12, p = 0.72$) nor for irregular standards ($r = 0.12, p = 0.73$) or deviants ($r = 0.22, p = 0.53$). Thus, the current findings verify the presence of a typical N2b response to deviant tones in both groups independent of temporal context.

Analysis of the P3b time-window revealed significant main effects of temporal structure ($F_{1,20} = 20.66, p < 0.001$), formal structure ($F_{1,20} = 38.26, p < 0.0001$) and region ($F_{1,20} = 11.71, p < 0.01$) but not of group ($F_{1,20} = 2.04, p = 0.169$). However, there was a significant interaction of group × temporal structure × formal structure ($F_{1,20} = 7.59, p < 0.02$). Informed by our hypotheses, a subsequent step-down analysis by the factor formal structure revealed an interaction of group × temporal structure for deviant ($F_{1,20} = 5.25, p < 0.04$) but not for standard tones ($F_{1,20} = 0.08, p = 0.785$). Further resolution of the two-way interaction for deviant tones by the factor temporal structure confirmed that the two groups differed with regard to their deviance response in the regular temporal context ($F_{1,20} = 4.81, p = 0.04$) but not in the irregular context ($F_{1,20} = 1.07, p = 0.312$). Patients showed a smaller P3b response ($2.0\mu V$) relative to healthy controls ($4.5\mu V$). This difference was confirmed by a paired-samples $t$-test ($t(10) = 2.78, p = 0.02$). To further validate this finding and to preclude any disproportional influence of individual patients on the statistical group comparison, identical $t$-tests were conducted with individual patient–control pairings excluded one at a time (N-1 method). However, the result remained significant in each of these cases (minimum $t = -2.37, p = 0.042$). Pursuant to the ANOVA analysis, the P3b amplitude was correlated with the extent of lesion size. Similar to the non-significant N2b correlation results, this P3b correlation was also non-significant for regular standards ($r = 0.15, p = 0.65$) and deviants ($r = 0.06, p = 0.86$), as well

**Figure 4.** Ninety-five percentage confidence intervals for N2b and P3b responses in both participant groups. REG, regular condition; IRR, irregular condition; PAT, patients; CON, controls; STA, standards; DEV, deviants. (Online version in colour.)
as for irregular standards (r = 0.21, p = 0.54) and deviants (r = 0.15, p = 0.66). Thus, independent of lesion size, these P3b results provide evidence for the significant impact of cerebellar pathology on the use of temporal predictability and the updating of a mental model of the environment as reflected in the P3b. Moreover, the fact that deviance processing was most affected in temporally regular, but not irregular context substantiates initial assumptions that structural damage to the cerebellum leads to imprecise encoding and use of temporal structure, and accordingly to the encoding and use of temporal regularity. This, in turn, affects optimized deviance processing in the case of maximal temporal predictability as seen in the control group.

4. Discussion

Testing the proposed role of the cerebellum in precise event-based temporal processing [4,14,39] and attempting to replicate previous findings in healthy young participants [24] in a healthy aging control cohort, this study investigated the impact of cerebellar lesions on the interaction of formal structure (varying stimulus form) and temporal structure (varying temporal regularity in tone sequences) in auditory deviance processing. Both cerebellar lesion patients and healthy aging controls detected deviant tones, as evident in the behavioural and in the N2b results. However, cerebellar patients showed a qualitatively different P3b response to deviant tones embedded in temporally regular sequences as confirmed by statistically significant group differences. Healthy controls showed the expected enhanced P3b deviance response to tones in regular compared with irregular temporal contexts. These data suggest that healthy aging participants display optimized deviance processing with full temporal predictability under voluntary attention. By contrast, while patients with cerebellar pathology detect formal stimulus deviance, they are less capable of using temporal predictability, and presumably, to exploit this information to optimally update a mental model of the environment.

The current results substantiate previous findings on how temporal regularity influences basic neurocognitive operations linked to deviance processing. In earlier reports, deviance processing under voluntary attention was evident in N2b and P3b responses, but deviance processing in the P3b range varied as a function of temporal context [24]. While a strong statistical trend (three-way interaction of temporal structure, formal structure and hemisphere) in the N2b time-window may indicate that temporal regularity impacts deviance processing at this earlier processing stage, the current results remain inconclusive. Clearly, further research has to confirm whether a potential interaction of temporal and formal structure in deviance detection (N2b) is prone to individual differences, as previous results have not reported a similar trend in comparable experimental set-ups (i.e. [24]). Awaiting further evidence, we can therefore only carefully conclude that patients with cerebellar lesions detect deviance comparably to healthy controls as evidenced in a similar N2b response to deviant tones independent of temporal context.

However, we report clear group differences in the P3b response to deviant tones, which confirms that patients with cerebellar lesions cannot benefit in a similar way as healthy controls from temporal predictability. Considering the ‘almost unquestionable’ [33] agreement of P300 theories on the function of this component as an index for the interplay of stimulus expectancies and actual sensory input, it seems appropriate to interpret this finding as an instance of impaired updating of a mental model of the environment. This result substantiates the critical role of the cerebellum in event-based temporal encoding [4,14,39] and the optimized adaptation to change in the environment (e.g. [29–31]).

The current findings further suggest that damage to the cerebellum alters how temporal regularity optimizes the quality of auditory deviance processing. In this context, deviance processing under voluntary attention is but one example of a perceptual process. It remains to be shown to what extent the current findings generalize to other perceptual (e.g. visual, multisensory) or even higher-level cognitive (e.g. natural and emotional speech) processes [14,40,41] and temporally more complex stimulus qualities such as meter and rhythm in speech or artistic forms of language such as poetry or rhetorical speech [40,42].

Importantly, cerebellar lesions diminish the response to deviants in temporally regular tone sequences, whereas no such reduction was found in the irregular tone sequences. While this dissociation of temporal processing as a function of temporal regularity does not speak against the role of the cerebellum in event-based encoding of temporal structure per se, it substantiates assumptions concerning a cerebellar contribution to perceptual processing in those cases in which predictive adaptation is possible. However, most likely, the cerebellar temporal processing system does not perform this function in isolation, but in concert with other structures implicated in temporal processing, namely the basal ganglia and the SMA, as part of an integrative temporal processing network. Importantly, the respective anatomical and functional connections may provide a means to compensate for dysfunction in each structure [13,43,44]. While cerebellar lesions may lead to imprecise encoding of temporal structure, thus reducing the effect of full temporal predictability, the intact basal ganglia temporal processing system may partially compensate for this ‘noisy’ encoding, e.g. by increasing tolerance against temporal variability in the processing of sequences with a regular beat. However, such mechanisms are most likely highly dependent on the specific temporal characteristics of the input, and compensation for cerebellar dysfunction may be more difficult for the timing of the absolute duration of single intervals [45].

We now need to consider what classical functions of the cerebellum (i.e. motor behaviour) and deviance processing in perception may have in common. These functions may converge in a common operation such as an, at least, two-fold response to changes in the environment (e.g. initial deviance detection in the form of an error response when expecting a particular tone quality in a tonal sequence, followed by the updating of a mental or internal model of the environment via adaptation of the expected tone quality in a tonal sequence to a new tone quality induced by the change and initial error response to such change [31,46–48]). Accordingly, precise encoding and subsequent use of temporal structure to optimize performance should be critical in both the motor and non-motor domains when updating of a mental model is required. This line of thinking may therefore be related to the updating of a forward model of cerebellar information processing [47,48]. A forward model receives its input in the form of (efference) copies of motor commands, which are used to predict the sensory consequences of an ideally executed movement, backed up by a comparator, which identifies discrepancies
between the predicted and the actual consequences and signals a corresponding error signal in order to adjust the accuracy of the model [49]. Analogously, the mental model of the environment receives its input in the form of sensory events and may implement a form of error detection and updating in response to unpredicted events. While the forward model relies on cerebellar connections to central motor and somatosensory brain areas, one may speculate that a mental model of expected events in the environment may rely on connections between the cerebellum and sensory areas (e.g. the temporal cortices [50,51]). However, whether implemented at the neural, motor, or non-motor (sensory, cognitive) level, any efficient model of the environment needs to be dynamic in nature. Accordingly, temporal structure should contribute to the continuous generation of hypotheses about the environment by the nervous system as indexed by the P3b [52]. In this context, one of the functional roles of the cerebellum may be the precise encoding of temporal structure, which subsequently is used to generate specific temporal predictions [46]. Kahneman & Tversky [53] remarked: ‘Before an event there are expectations—after an event there may be surprise’. What remains to be resolved is whether the underlying operations of cerebellar function in temporal processing, prediction, or surprise as indexed in the P3b response [54] share common ground as they appear to be intimately tied to each other. Moreover, whether prediction and surprise represent facets of more global cerebellar computation(s) serving a predisposition towards optimal timing and adaptation in motor and non-motor behaviour alike, remains to be addressed in future studies beyond lower level auditory processes.

Finally, the current results raise a more fundamental question about how the component evolution from early to late ERPs relates to formal and temporal stimulus dimensions on the one hand, and the operations speculated to underlie optimization of behaviour on the other. Typically, an ERP suppression effect (i.e. an amplitude reduction) in early ERP components such as the P50 or N1 is considered to reflect efficient sensory gating or successful temporal prediction, while ERP enhancement seems to indicate qualitative processing differences in later components such as the P3b [24,28,55]. Morphologically, this component evolution changes at approximately 200 ms after stimulus onset. In other words, temporal predictability seems to lead to suppression of early components as opposed to an enhancement of late components. While there are indications of reduced N1 suppression effects in cerebellar patients [56], no significant effects were observed in the current set-up. However, the absence of a similar finding does not necessarily contradict these results or imply intact function, as differences in the paradigms used may result in qualitative and quantitative ERP differences, e.g. due to the use of a motor response.

Of note is that early suppression effects reflect temporal predictability, while later enhanced effects are driven by an interaction of temporal and formal structure. We may therefore consider that a change from suppression to enhancement may result from the differential engagement of operations such as successful encoding of temporal properties and the efficient updating/adaptation of a mental model of the environment in the quest to optimize behaviour. Further, while a classical dissociation of exogenous and endogenous ERP components [57] could support such a differentiation of operations, this conceptualization of ERP components seems inappropriate as both so-called ‘pre-attentive responses’ (MMN) and early ‘exogenous’ components are sensitive to attentional (i.e. cognitive) manipulations (e.g. [58]).

In conclusion, we set out to answer two critical questions regarding the functional role of the cerebellum in temporal predictability, deviance detection and the updating of a mental model of the environment. The present results suggest that structural damage to the cerebellum, apparently independent of the extent (across anterior/posterior dimensions) or the lateralization (left, right, bilateral) of the lesion, critically affects temporal predictability and its impact on perceptual deviance processing involving both an error response and updating a mental model of the environment to achieve optimal behaviour. Clearly, more studies with (i) larger patient sample sizes and (ii) temporally more complex stimulus aspects such as meter and rhythm in speech and music (for relevant neuroimaging evidence see [35,39,59–61]) are needed to further delineate whether specific sub-components of the cerebellum contribute to these operations in a function-specific or a domain-general manner.

Ethics statement. The local ethics committee at the University of Leipzig approved the study.

Acknowledgements. The authors thank Anne-Kathrin Franz, Heike Boethel and Ingrid Brilmayer for their support during data acquisition.

Funding statement. This work was support by a DFG KO 2268/6-1 grant to S.A.K.

Endnote

1To validate the impression of potential early group difference in the N1, identical analyses as for the later components were conducted in a 50 ms time-window (88 to 138 ms). This analysis yielded statistically significant main effects of temporal structure (F1,20 = 13.42, p < 0.01), formal structure (F1,20 = 8.66, p < 0.01) and region (F1,20 = 4.45, p < 0.05), as well as a significant interaction of formal structure × region (F1,20 = 4.84, p < 0.04). Resolving this interaction by the factor region yielded significant effects of formal structure in anterior (F1,20 = 10.32, p < 0.01) and posterior regions (F1,20 = 5.91, p < 0.03). However, there was no significant main effect of group (F1,20 = 1.68, p = 0.209) or any interaction involving the factor group (all p > 0.11), and only a non-significant trend for an interaction of temporal structure × formal structure (F1,20 = 3.20, p = 0.089).

References


