Medical Hypotheses 128 (2019) 33–42

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

The sequencing process generated by the cerebellum crucially contributes to social interactions

Frank Van Overwalle[a,*], Mario Manto[b], Maria Leggio[c,d], José María Delgado-García[e]

[a] Department of Psychology, Vrije Universiteit Brussel, Belgium
[b] Service de Neurologie, CHU-Charleroi, Belgium & Service des Neurosciences, Université de Mons, Belgium
[c] Department of Psychology, University of Rome 'Sapienza', Rome, Italy
[d] Ataxia Laboratory, IRCCS Fondazione Santa Lucia, Rome, Italy
[e] Division of Neurosciences, Pablo de Olavide University, Seville, Spain

ARTICLE INFO

Keywords:
Social
Internal models
Forward controller
Cerebellum

ABSTRACT

The capacity to understand another person's emotions, intentions, beliefs and personality traits, based on observed or communicated behaviors, is termed social cognition. During the last decade, social neuroscience has made great progress in understanding the neural correlates of social cognition. However, because the cerebellum is traditionally viewed as only involved in motor processing, the contribution of this major part of the brain in social processing has been largely ignored and its specific role in social cognition remains unclear. Nevertheless, recent meta-analyses have made its crucial contribution to social cognition evident. This raises the question: What is the exact function of the cerebellum in social cognition? We hypothesize that the cerebellum builds internal action models of our social inter-actions to predict how other people's actions will be executed, what our most likely responses are to these actions, so that we can automatize our interactions and instantly detect disruptions in these action sequences. This mechanism likely allows to better anticipate action sequences during social interactions in an automatic and intuitive way and to fine-tune these anticipations, making it easier to understand behaviors and to detect violations. This hypothesis has major implications in neurological disorders affecting the cerebellum such as autism, with detrimental effects on social functionality, especially on more complex and abstract social cognitive processes. Because the fundamental anatomical organization of the cerebellum is identical in many species (cerebellar microcomplexes), this hypothesis could have major impacts to elucidate social interactions in social animals.

Introduction

When maneuvering through the social environment, it is crucial to understand "the mind" of other persons and to form coherent representations about the self. The capacity to capture another person's emotions, intentions, beliefs and personality traits, based on observed or communicated behavior, is termed social cognition, whereas representations of one's own life experiences is referred to as autobiographical knowledge. Both concepts are intimately related, because they involve knowledge about others and the self, using largely similar inference processes and inputs [1]. During the last decade, neuroscience has made great progress in understanding the neural correlates of social and self-cognition, but research predominantly focused on the role of the cerebrum. Two main cortical networks implicated in social cognition have been identified: (1) the mirror network recruited when we observe the actions of other persons (i.e., "body" reading), and (2) the mentalizing network when we imagine the mental state of another person or reflect on the self (i.e., "mind" reading; for reviews see [2,3]). Stated differently, mirroring reflects lower-level processes of immediate perception (e.g., biological mouth, arm and leg moves and gestures), while mentalizing involves higher-level inference about non-observable mental entities such as intentions, beliefs and traits, a unique capacity of humans. These two routes to social cognition operate largely independently from each other [4]. An autobiographical network has also been identified in relation to various forms of self-representations [1] and partly overlaps with the mentalizing network. Although the cerebellum is traditionally regarded as a coordinator of sensorimotor function, its contribution to social and autobiographical processing has been largely ignored and remains unexplored.

Recent insights in the cerebellum as a crucial modulator of a variety

* Corresponding author.
E-mail addresses: Frank.VanOverwalle@vub.ac.be (F. Van Overwalle), mmanto@ulb.ac.be (M. Manto), maria.leggio@uniroma1.it (M. Leggio), jmdelgar@upo.es (J.M. Delgado-García).

https://doi.org/10.1016/j.mehy.2019.05.014
Received 22 February 2019; Accepted 12 May 2019

of cognitive and affective functions [5–7] have strongly increased the interest of the scientific community for the cerebellum in social cognition. A large-scale meta-analysis on social cognition and the cerebellum that included over 350 functional magnetic resonance imaging (fMRI) studies [8], consistently found activation of the cerebellum. Cerebellar activity was present in about one third of most mirror and mentalizing studies, and in about all studies that involved more complex and abstract social inferences [9]. Abstract mentalizing involves, for instance, person trait judgments as opposed to visual descriptions of the same behaviors (e.g., respectively judging “why” versus “how” a person is reading a book [10]; and inferences about the past or future as opposed to the present [11]. Intriguingly, autobiographical memory and future thinking were among the functions that most consistently engaged the cerebellum, being involved in 75% of studies (see also [12]).

In addition, Buckner et al. [13] investigated the large-scale organization of circuits between the cerebrum and cerebellum using resting-state connectivity for a total sample of 1000 participants, resulting in a complete topography of the cerebellum in relation to major networks of the cerebrum [14]. This topography revealed network structures in the cerebellum that are similar to the network structures of the cerebrum, spanning approximately the same relative volumes. Most importantly, Buckner et al. [13] clearly identified distinct mentalizing and mirror networks (part of the larger default and somatomotor networks respectively) in the cerebellum that were directly connected to homologue networks in the cerebrum (see Fig. 1).

Despite the substantial progress in the neurobiology of social cognition, the investigation of the neural underpinnings of the role of the cerebellum in social and autobiographical knowledge is still in its infancy. To our knowledge, no published neuroimaging studies directly investigated the specific role of the cerebellum in lower-level mirroring on the basis of observed behaviors, nor in higher-level mentalizing reflecting basic (e.g., false beliefs) or complex social and self-judgments (e.g., causal and trait attribution). While non-invasive brain stimulation methods such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are increasingly used to investigate cerebellar function, research did not investigate their effect on social and autobiographical tasks. Likewise, (high-level) social and autobiographic processes have seldom been investigated in patients with cerebellar disorders, although clinical observations suggest that impairment in these domains might be important.

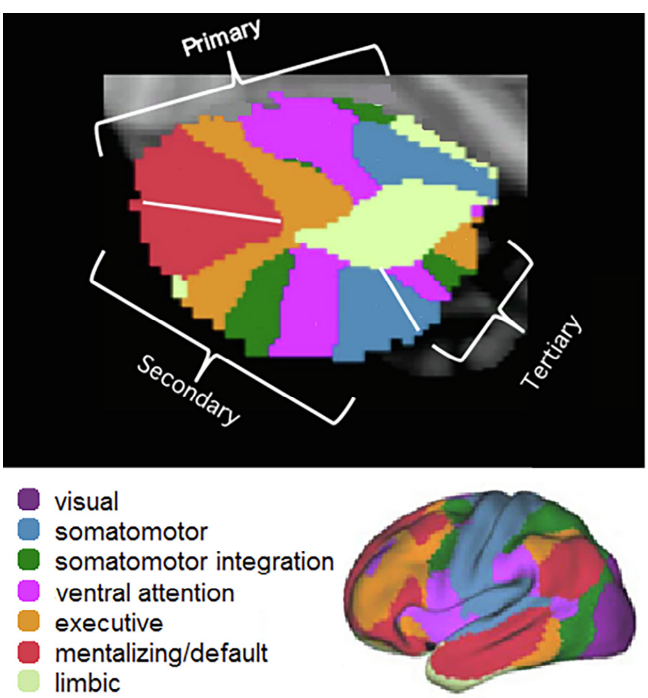

Fig. 1. Parcellation of the cerebellum based on connectivity with the cerebrum [14], showing three distinct representations, labeled the primary, secondary, and tertiary representations. Networks are color-coded with their function as proposed by Buckner et al. (p. 2332) [13], showing the mentalizing/default (red) and mirror/somatomotor (blue/green) networks. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Yet, recent studies provided preliminary evidence pointing to the important role of the cerebellum in social cognitive abilities. For instance, in a study [15], an ad hoc social cognition battery was administered to 27 patients with degenerative cerebellar pathology and 27 healthy controls. In addition, 3D T1-weighted and resting-state fMRI scans were collected to characterize the structural and functional changes in cerebello-cortical loops. The results demonstrated that the patients were impaired in lower-level processes of immediate perception as well as in more complex conceptual levels of mentalizing. Furthermore, they revealed a pattern of grey matter reduction in cerebellar portions that are involved in the social domain such as crus I-II, lobule IX and lobule VIIIa. These areas showed decreased functional connectivity with cerebral areas involved in specific aspects of social cognition [15].

As mentioned earlier, the role of the cerebellum in social and self-cognition remains unclear and underexplored. To elucidate its functional role in social understanding, one theoretical perspective on the general function of the cerebellum is of particular relevance. Several authors have put forth the view that the primary function of the cerebellum is to support sequence learning and memories that underpin skilled motor acquisition, which develops slowly with practice and is inaccessible to consciousness [16–18]. In this respect, the cerebellum constructs internal models of motor processes involving sequencing and planning of action in order to automate and fine-tune voluntary motor processes. These internal models are highly automatized copies from the event implications generated in the cerebrum that continuously sends signals to check whether an anticipated event sequence fits with current behavior and its somatosensory consequences. In this sense, the cerebellum is a “forward controller”. Interestingly, the idea has been put forward that during evolution a more advanced function developed which allowed the cerebellum to construct internal models of pure mental processes in the form of event sequences, without involvement of overt movements and somatosensory responses [17–19]. Thus, the cerebellum regulates non-motor mental operations in much the same way as it regulates movements [20–22]. In particular, the cerebellum may contribute to social cognition by constructing internal models of social interactions and related mental processes in which the prediction of sequential events plays a critical role, allowing to anticipate the other person’s behavior or one’s own reactions [15].

Hypothesis

Our hypothesis is that the sequencing process engendered by the cerebellum crucially contributes to social and autobiographical cognition, by providing internal models that support various representations and judgments about others and the self. Recent data suggests that the role of the cerebellum is most evident and prominent in mental (re) constructions of autobiographical past, future or hypothetical events, and in abstract trait inferences [8]. One might argue that the construction of meaningful sequences of actions and events is a key process in autobiographical and trait inferences. The cerebellum might play a cardinal role in this sequencing processes during social and self-cognition, and in particular in learning and automatizing these sequences in internal models that function as forward controllers during actual social inter-action. This mechanism likely allows humans to better anticipate action sequences during social interactions in an automatic and intuitive way and to fine-tune these anticipations, making it easier to understand the social strategies behind behaviors and to detect violations. Furthermore, this sequencing mechanism may also play an important role in the organization of autobiographical events and self-representations.

We hypothesize that the cerebellum acts as a "forward controller" of social, self-action and interaction sequences. We hypothesize that the cerebellum predicts how actions by the self and other people will be executed, what our most likely responses are to these actions, and what the typical sequence of these actions is. This function of forward controller allows people to anticipate, predict and understand actions by the self or other persons and their consequences for the self, to automatize these inferences for intuitive and rapid execution, and to instantly detect disruptions in action sequences. These are important social functions. Consequently, if neurological disorders affect the cerebellum, detrimental effects on social functionality might be found, especially on more complex and abstract social cognitive processes. The cerebellum would be a "forward controller" that not only constructs and predicts motor sequences, but also takes part in the construction of internal models that support social and self-cognition. In this respect, the cerebellum crucially adds to the fluent understanding of planned and observed social inter-actions and contributes to sequencing mechanisms that organize autobiographical knowledge. Because the fundamental organization of the cerebellar circuitry is identical in many species adopting social behaviors, our hypothesis can also be valid throughout the animal kingdom.

Approach to test the hypothesis

Social cerebellum and other persons

A recent study by Van Overwalle, Heleven, Ma and Mariën [23] provided preliminary support for our sequencing hypothesis during mentalizing. Evidence was found that the cerebellum is strongly recruited and connected to the cortex when novel behaviors have to be integrated with prior behavioral information in order to arrive at an overarching trait inference. Another study by Van Overwalle et al. [24] tested patients with generalized cerebellar degenerative lesions on several tests of social understanding. The cerebellar patients performed similar to matched healthy volunteers on classic social tests which did not involve sequencing. In contrast, they showed clear deficits on a picture sequencing task where each story began with 4 pictures in a random order, and participants had to line the pictures up like a comic-strip in the correct order [25]. Performance was substantially impaired for cartoons depicting false belief stories and was relatively normal for overlearned mechanical stories and social scripts (Fig. 2B). False stories are a key task of social mentalizing and depict a change of location of objects during the absence of a protagonist, so that this person holds the "false" belief that the object is still where it was left earlier (Fig. 2A).

A subsequent fMRI study on neurotypical volunteers using the same picture sequencing task as well as a verbal version of it (extended from the faux-pas task by Baron-Cohen et al. [26]), confirmed that there was stronger activation of the posterior cerebellum (Crus I & II) during false and true belief stories [27] (Fig. 2C). This posterior cluster was considered a key area of the mentalizing network of the cerebellum in several connectivity studies based on resting state [13] and mentalizing inference tasks [28]. To the best of our knowledge, no other studies have been conducted in which the focus of investigation is specifically directed to the sequential role of the cerebellum in the mirror or mentalizing network. Our hypothesis implicates that the role of the cerebellum during social mirroring and mentalizing might be relatively automated during the processing of typical events – thus revealing minimal neural activity but becomes increasingly more activated while constructing novel or complex events, or when violations of typical action sequences occur.

Mirroring

Identifying mirroring in the cerebellum

Mirror neurons are activated both during observation and execution of biological movement and action. Consequently, to identify mirror neurons in the cerebellum, it is necessary to compare brain activation during an observation and an execution task, while controlling for learning (since the cerebellum is known to be involved in learning). An fMRI paradigm could be used with an observation, an imitation, and an execution block, while participants observe a sequence of human behaviors aimed at a common goal. To show evidence of goal-directed behavior (e.g., in the face of obstacles that block the goal) and in close parallel with animal research, we would constrain behavior through physical limitations such as searching a goal in a maze varying in difficulty. Next, the mazes would be presented in a second run and human actions would be observed again (avoiding a strong learning effect), and in a third run the participants would imitate and execute the solution. We expect to observe overlapping "mirror" activations in the cerebellum during the observation and execution of a difficult goal-seeking maze sequencing task, and less so during a simple maze task.

Identifying the importance of a goal in the identification of a mirror network

It is assumed that the mirror network has evolved beyond mere biological motion processing and that part of the mirror system (i.e., the pre-motor cortex) responds more actively when movement is directed towards basic goals and needs (e.g. grasping for an apple to still hunger). To investigate the impact of the presence of a clear goal for understanding action sequences and activation of the cerebellum, the fMRI experiment described in the previous section could be repeated in two groups, with or without the use of a goal (e.g., monetary award) in a maze. We expect that the cerebellum is more involved in goal-directed actions and less so in the same actions without a goal, or in mere sequences of meaningless actions (e.g., walking control task).

Specific role of the cerebellum within the mirror network

Another way to test whether clear goals are critical for understanding action sequences is pretended action, in which the absence of objects makes the goal less obvious so that it must be actively retrieved from internal memory. Research has shown that cerebellar activation is systematically triggered when participants are misled by pretended behavior, such as when pretending to put a book on a shelf (although the book is absent [29]) or to lift a heavier or lighter box than its actual weight [30,31]. An fMRI experiment can be set up in which (a) observation of a goal-directed grasping or placing movement is compared to (b) observation of the same pretended movements (i.e., with an invisible object). If the cerebellum is especially involved in interpreting pretended behavior, there should be stronger cerebellar involvement in the pretended as compared to the actual behavior conditions.

The three fMRI studies in this section on "Mirroring" could be conducted on neurotypical participants (n = ± 40) as well as on a matched patient population with cerebellar lesions (n = ± 30 with left and right hemispheric impairments; preferentially in the posterior cerebellum). The activations observed in the neurotypical participants would be compared with those of the patients to explore their functional differences.

Mentalizing

As noted earlier, a hallmark of mentalizing is that it involves an element of false belief, for instance, when an agent is unaware of changes in object locations during his or her absence. To explore the role of sequencing in mentalizing, various social cognitive tasks can be considered, being validated in earlier neuroimaging research and/or in earlier clinical work with patient groups, covering both visual and verbal inputs. Most often, these tasks would be adjusted for the novel purpose of investigating our sequencing hypothesis. This can be easily

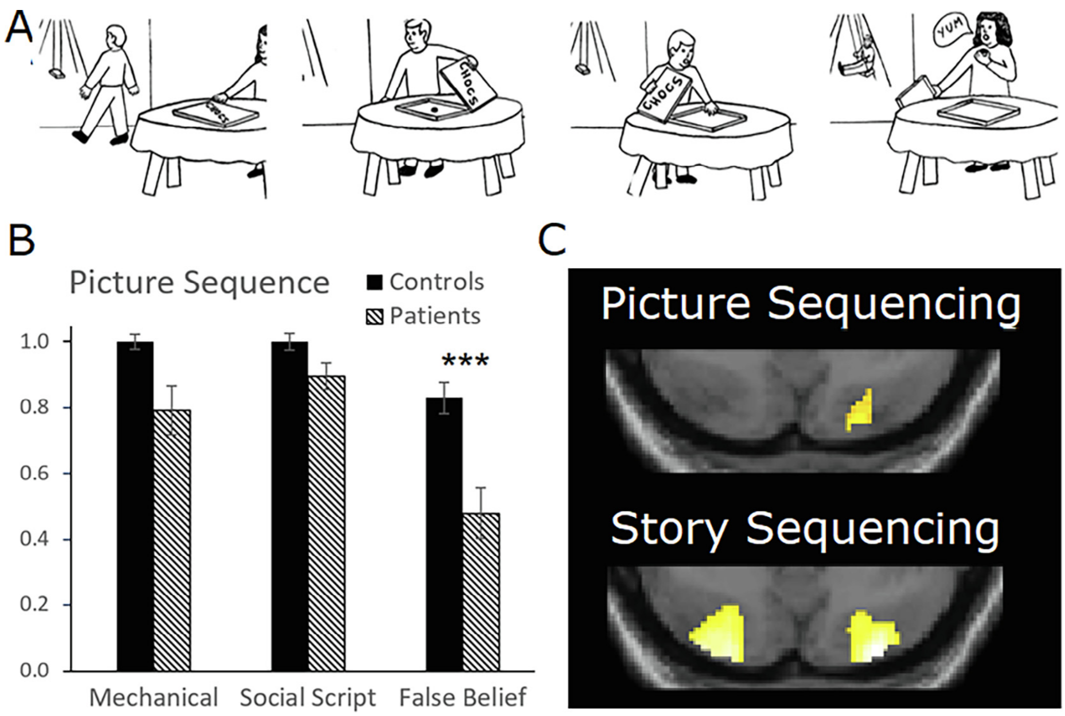

Fig. 2. A: An example of a false belief sequence in the Picture Sequencing task [25] (the correct order is 2 – 1 – 4 – 3). Participants had to select, in the correct order, the first picture on the screen, then the second picture, and so on. Each time, the pictures moved in the order indicated by the participant. Reproduced by permission of the first author. B: Comparison of 11 degenerative cerebellar patients in comparison with 9 healthy controls on the Picture Sequencing tasks. Error bars reflect standard errors. ***$p < .002$ (one-sided *t*-test). C: Transverse view of activation in the posterior cerebellum in the Picture and Story Sequencing tasks for true + false belief > mechanical comparisons ($z = -36$) shown at an uncorrected threshold of $p < .001$.

done if we do not only consider the key cerebellar mechanism of sequence processing, but also that of error controller when the expected sequence does not occur. Specifically, the typical sequencing of events can be altered, or inconsistent actions can be added. We hypothesize that these alterations or inconsistencies will recruit the social areas in the cerebellum much more strongly than the regular execution of consistent sequences or non-sequence controls.

Sequencing when holding false beliefs – spatial belief task

This is a spatial false belief task developed recently by Van Overwalle's laboratory [32]. Participants watch animations on the screen that involve true or false beliefs. In order to investigate violations of sequencing, the task is adapted in such a way that at the end of each trial, the true or false belief of an agent is given in a thought balloon. Half of the thought balloon are consistent with the agent's thinking and knowledge, while the other half is not (inconsistent).

Sequencing when holding false beliefs – verbal belief task

A Dutch version of a verbal belief task [33] was developed and used recently [32]. Participants read short vignettes on the screen. The vignettes describe a protagonist's action and require participants to represent the protagonist's (false) belief. To investigate violations of sequencing, the task is adapted so that stories involve a typical (everyday) sequence followed by a consistent/true or inconsistent/false event. We do this by altering the critical time period in which the event happens so that it occurs either before or after the change-of-object (rendering the protagonist's belief true or false respectively).

Sequencing when inferring human traits – trait attribution

This trait inference task comes from a study with vmPFC patients by Kestemont et al. [34]. Participants read 20 pairs of two or more sentences, each describing a behavior that implies the same trait of a person performing the behavior. After reading the first sentence(s), participants are asked to choose between the most logical sequence of actions (implying the same trait of the target person; based on Kestemont et al. [34]) versus distractor sequences that imply different traits. To investigate violations of sequencing, we can use a similar approach as above, that is, provide sequences with congruent versus incongruent actions with respect to a trait, and measure the impact on cerebellar activation.

Implicit learning of mentalizing sequences

It has been assumed that the cerebellum plays a critical role in the automatization of behaviors, like riding a bike. This goes beyond the mere explicit knowing how to ride a bike, since movement execution and automatization is crucial. Is this also the case for mentalizing? Can humans acquire and/or apply social knowledge on mental beliefs implicitly and automatically? This can be investigated using a serial reaction time task [35,36]. In an adapted serial reaction time task using mentalizing sequences, participants respond rapidly to a series of beliefs like in the visual false belief task mentioned earlier [32]. Unbeknownst to the participants, as in typical serial reaction time experiments, there is a fixed sequence in the location on screen which shows the relevant information for true and false beliefs. In addition, there are also fixed sequences in the transition of true and false beliefs, as well as in the agents involved. These sequences can be relevant for rapid responding, but it is unclear yet which sequence is more task-relevant and which can be learned implicitly. We hypothesize that at least sequences of true and false belief transitions can be learned implicitly, and that this learning covaries with stronger cerebellar activity (e.g., higher activation at the start of implicit learning and when unexpected random sequences are introduced).

Autobiographical knowledge

Recent meta-analyses have shown that the representation of autobiographical knowledge (e.g., judgments about past and future personal events) most reliably activates the cerebellum [8,12]. However, the exact function of the cerebellum in the processing of autobiographical knowledge remains largely unknown. Based on the sequencing hypothesis outlined above, our hypothesis is that the cerebellum may contribute to the sequential organization of autobiographical knowledge at different levels of abstraction and timescales. Research in cognitive psychology and neuroscience has shown that autobiographical knowledge is organized in partonomic hierarchical knowledge structures [37]: representations of specific events (e.g., snorkeling in the Mediterranean) are structured in higher-order themes and event sequences (e.g., my vacation in Italy), which are both organized in more abstract and extended autobiographical periods (e.g., my high school years). Temporal sequences play a central role in the organization of autobiographical representations at these different levels of hierarchical knowledge. In line with our hypothesis, neuroimaging studies revealed higher activation in the cerebellum when processing the temporal order of past and future events compared to simply processing their content [38], and when thinking about past and future events that are organized in themes and sequences [39].

Segmenting event components

A fundamental process in the representation of autobiographical episodes is the need to break the continuous stream of perception and action into meaningful units or event components—a process that has been referred to as event segmentation [40]. To investigate the role of the cerebellum in this process, a typical event segmentation task could be used in which participants have to segment movies depicting actors engaged in everyday activities (e.g., making breakfast) into meaningful event units [41]. One can also assess event segmentation processes for personally experienced events, using movies recorded from a first-person perspective by a wearable camera while participants are engaged in everyday activities [42]. We expect stronger cerebellar activity when movies have to be segmented from a self-perspective as opposed to an other-perspective depicting other actors, or as opposed to movies that are watched passively from the same perspective. In addition to measuring segmentation capacities, these tasks would allow to assess dimensions of participants' experience that determine the perception of event boundaries (e.g., agents, goals, causality, and time).

Sequencing event components

Beyond event segmentation, the formation of coherent autobiographical representations requires that event components are organized in meaningful sequences (based on the chronological order of successive units) that represent specific life episodes [43]. To assess the contribution of the cerebellum in this sequential organization, one can use a timed production paradigm that requires participants to list event components in forwards chronological order, backwards chronological order, or free order [43].

Sequencing events in clusters

Recent research has shown that many autobiographical events are not represented in isolation from each other, but instead are organized in meaningful themes and sequences—referred to as event clusters [44]. The prevalence and nature of such clusters of past and future events has been assessed using an event-cueing paradigm in which participants are asked to produce chains of related events; the types of relational dimensions that characterize event chains are then used to infer the organizational principles underlying autobiographical knowledge [44]. To investigate the role of the cerebellum in this organization of autobiographical events, an event-cueing paradigm can be applied, in which demands on sequencing processes by experimentally manipulating the number of events presented within clusters (from 2 to 5 events) are varied.

Sequencing autobiographical periods

Autobiographical periods refer to temporally defined life periods (e.g., my college years) and include general knowledge about the people, places, activities, and objects characterizing these periods [45]. These autobiographical periods help to integrate and locate specific past and future events in one's life story, thereby playing an important role in the construction of personal identity. The structure of autobiographical periods has been assessed by asking people to identify chapters in their life story [46]. This task can be used to measure the number of autobiographical periods, as well their temporal coherence and duration.

The autobiographical sequencing tasks described above can be adapted in four fMRI studies involving healthy young adults (n = ± 40 per study). In addition to examining changes in activity within the cerebellum (using univariate analyses), this approach allows to assess how the cerebellum interacts with the typical autobiographical network (using functional connectivity analyses) during autobiographical sequencing.

Furthermore, whether the cerebellum plays a causal role in each of the fundamental sequencing processes described above in this section on "Autobiographical knowledge" can be tested by temporarily disrupting information processing in this region in healthy individuals using TMS (n = ± 40 per study). TMS would be applied to the right and left posterior cerebellum where the largest cerebellar mentalizing and autobiographical areas have been located and its effect on autobiographical sequencing will be compared to sham (control) TMS.

To our knowledge, no reports of autobiographical memory deficits exist in patients with cerebellar lesions, but these patients are not routinely tested for autobiographical functions and they may present with subtle impairments. To address this issue, possible deficits in the representation of autobiographical knowledge in patients with cerebellar lesions can be looked for using typical autobiographical memory tasks [47], as well as tasks specifically assessing autobiographical sequencing (described above). Patients with neurodegenerative or acute vascular cerebellar disorders (n = ± 30) can be compared against healthy controls (n = ± 30) matched for age, education and other cognitive/executive capacities.

Autism

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition typically characterized by deficits in social communication and interaction and repetitive behavior or restricted interests [48]. The main behavioral hallmark is an impairment in the ability to recognize and attribute mental states to others to explain and predict their behavior [49]. We speculate that behavioral alterations of ASD individuals are a consequence of a complex of modifications of neuronal networks in which the cerebellum participates. In support of this hypothesis, abnormalities in cerebellar grey matter volume emerged as one of the biomarkers to discriminate individuals with ASD from typically developing individuals [50,51]. Furthermore, abnormalities in functional connectivity between the cerebellum and cortical regions of the social brain have been described in individuals with ASD [52–54]. The underconnectivity theory of ASD proposed by Just et al. [55] attributes the psychological impairment, such as social cognition, to disrupted connectivity within different functional networks [56,57], which have structural and functional relationships with the social cerebellum [51,53].

A recent study with ASD adults analyzing anatomical and structural changes in the cerebellum [58] provided evidence for the social role of the cerebellum in ASD dysfunctions. The results showed decreased cerebellar grey matter volume in the right Crus II, a region showing extensive connections with cerebral areas related to social functions. This grey matter reduction was correlated with the degree of autistic traits as measured by the autism-spectrum quotient [59]. Interestingly, altered functional connectivity was found between the reduced cerebellar Crus II and contralateral cerebral regions, such as frontal and temporal areas [58]. These data suggested that adults with autism spectrum disorder suffer from specific cerebellar structural alterations

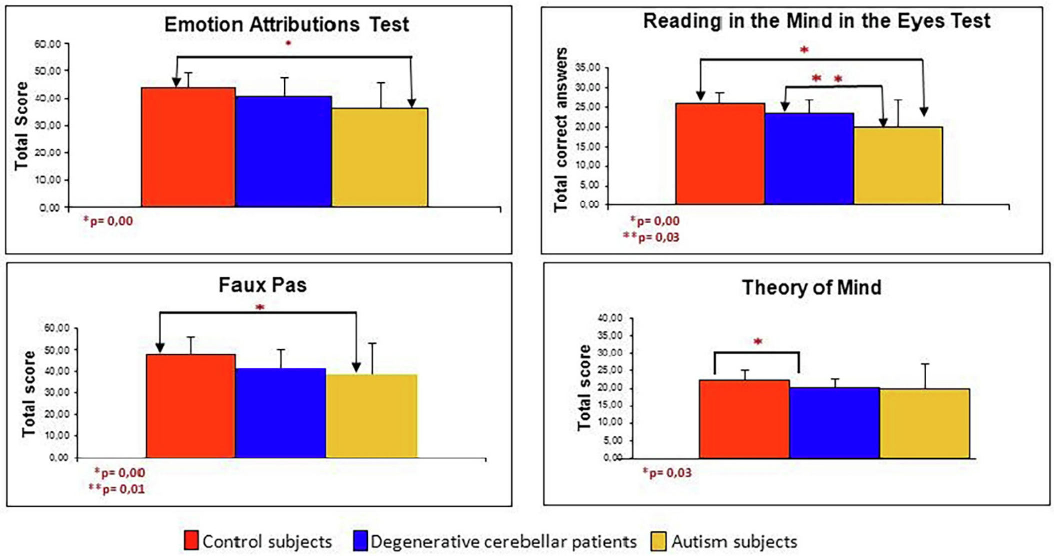

Fig. 3. Comparison of the performances of 25 degenerative cerebellar patients, 13 ASD participants, and 55 control participants on 4 social cognition tasks. Error bars reflect standard errors.From Clausi et al. [60].

that may affect functional connectivity within cerebello-cerebral modules relevant to social processing, and this may account for their autistic traits [58].

In line with this, the involvement of the cerebellum in social cognition was also observed in a pilot study with 25 degenerative cerebellar patients, 13 ASD participants, and 55 control participants [60]. All participants were tested on 4 social cognition tasks: the Emotion Attributions task [61], the Faux Pas task [62], the Advanced ToM task [63], and the Reading the Mind in the Eyes test [59]. The results showed that both cerebellar and ASD groups had a very similar profile in that they revealed weaker performance on these tests than the control group, although not always significantly so (see Fig. 3). These data, although preliminary, suggest that the cerebellum may contribute to the processing of various social cognition components and that cerebellar dysfunctions may affect social cognition abilities of individuals with ASD.

Social and non-social sequencing

Social cognitive impairments of participants with ASD, and the specific role of the cerebellum in this process, can be tested in adults affected by ASD (n = ± 20; inclusion criteria: ADOS scores ≥ 7 and IQ above 70) by means of tasks requiring sequencing processing in social situations and non-social situations (see Sections above on "Mirroring" and "Mentalizing"). The performance of the ASD patients can be compared with healthy controls (n = ± 20), matched for gender, age, and education, as well as with patients affected only by cerebellar disorders

Cerebello-cerebral social networks

Resting-state fMRI can be used to identify the cerebello-cerebral networks involved in social cognition processing, and to compare the pattern of functional connectivity within these networks between participants with ASD (n = ± 20) and matched neurotypical participants (n = ± 20). First, networks-based statistics [64] or dynamic causal modelling [65,66] can be used in ASD patients to isolate the two major mirror and mentalizing networks. Next, topological properties (shape and efficiency) of the connectivity of the extracted subnetworks can be estimated and compared between ASD and neurotypical participants, before and after application of TMS or tDCS over the cerebellum. We hypothesize that there will be changes in network connectivity before and after brain stimulation as attested in previous research [67], and that these changes will differ between ASD and neurotypical populations because their neural connectivity patterns are different to begin with. In addition, it is possible to target a focal area of the cerebellum with TMS or tDCS, and we can explore how this affects other areas in the cerebellum and cerebral cortex through their neural connections. This latter application may highlight the therapeutic potential of cerebellar neuromodulation with TMS or tDCS.

Analogies and discrepancies between social and motor sequencing

Activities of daily life require an accurate integration of spatiotemporal information in the millisecond range. This millisecond accuracy is also required for fluent social interaction and coordination (e.g., talking). Cerebellar lesions such as ataxia encompasses errors in force production and timing [68]. It is speculated that (a) the coding of sequences of motor commands is impaired in cerebellar patients and (b) fundamental errors in motor coordination and social cognition share similar mechanisms. This assumption is based on one major neuroanatomical feature of the cerebellum: for all lobules, cerebellar circuitry is composed of very similar microzones arranged as narrow strips oriented perpendicular to the cortical folds. However, we also predict that depending on the precise location and connectivity with the cerebral cortex, either motor or social performance will be more impaired. There is already some preliminary data from cerebellar patients [24] indicating that there are significant correlations between the degree of motor ataxia and performance on several cognitive and social tests. More robust evidence can be obtained from studies conducting tests encompassing both motor and social performance on larger patient samples, or applying varying levels of brain stimulation (facilitatory or inhibitory) using TMS or tDCS which may impact both motor and social performance.

Basic functionality of the cerebellum: fundamental signatures of social interactions in rats

Studies on the cognitive, affective and social role of the cerebellum have been carried out in humans, and suggestive evidence as also available on non-human animals. For instance, connections between cortical prefrontal areas and cerebellum (mostly lateral cerebellum/dentate nucleus) have been described in non-human primates [69]. In addition, a recent study suggested the putative involvement of the cerebellum in reward processing and in the control of social behavior of mice [70].

The rat is an excellent laboratory animal for operant conditioning

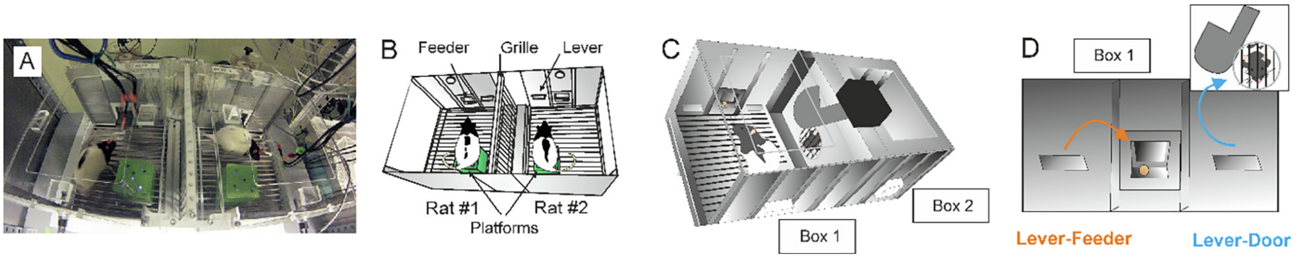

Fig. 4. Two different experimental designs for the study of motor and cognitive processes in alert behaving rats. A, B: A panoramic photograph and a diagrammatic representation of the experimental set-up for the study of cooperative behavior between rats obliged to climb onto a (green) platform and to remain on it simultaneously (0.5–5 s) to obtain a food reward [72]. C, D: A rat located in the box 1 must decide whether pressing the lever to the left to obtain a food pellet or to press the right lever to open a metal door and interact with a rat located in the box 2 for 10 s [73]. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

tasks and the solution of unpredictable environmental situations [71]. Rats can develop prosocial behaviors aimed to interact for the joint solution of complex operant conditioning tasks [72] and to select between food or social rewards [73]. For example, we have already shown that local field potential (LFPs) recorded in the medial prefrontal cortex increase the spectral power in delta and gamma bands during proper social interactions in pairs of rats [72,73]. We therefore hypothesize that rats can be used to elucidate the cerebellar code during social activities.

Social cooperation to obtain alimentary rewards

To study rat's mirroring behaviors while carrying out instrumental learning tasks [72], pairs of rats can be trained in adjacent Skinner boxes to obtain a pellet of food when jumping on a platform in front of a hidden lever. The same rats can be trained to jump simultaneously on the platform to release a lever to obtain the pellet (Fig. 4A, B). The aim is to determine coherence between LFPs and unitary activities from prefrontal and cerebellar cortices when behaviors are synchronized to obtain the reward. In particular, we expect an increase in coherent activities in LFPs and unitary firing between prefrontal cortex (decision making), accumbens septi (positive reinforcing), and lateral cerebellar cortex (VI-VII layers) and dentate nucleus (attentional and cognitive). In addition, to test more specifically the sequential nature of cerebellar involvement, we might manipulate the learning of temporal intervals for coordination tasks requiring joint motor actions.

Decision making between prosocial and food rewards

As a basic physiological need, food is a natural reward used in many experimental procedures with rodents to study learning processes or decision-making abilities. Social interactions also play an important role in the development of these species and can therefore be used as a positive reinforcement. To determine rat's preferences for food or social contact, and to study the involvement of cerebral and cerebellar structures, we can present rats with these two types of reinforcements [73]. For this aim, we will use two modified and adjacent Skinner boxes separated by a guillotine door (Fig. 4C, D). One of these Skinner boxes will have two available levers: pressing one lever provides access to food pellets, and pressing another lever allows 10 s of visual and partial physical contact with another rat located in the adjacent box. In this situation, we expect differential LFP and unitary activities in both cerebral (prefrontal cortex, accumbens septi and ventral tegmental area) and cerebellar areas (lateral cerebellum and dentate nucleus) depending upon the alimentary or social nature of the reward. Moreover, as an initial test of the sequential nature of cerebellar involvement, we might manipulate the learning of temporal intervals for food versus social rewards.

Decision making tasks involving active and passive behavioral responses

In the context of the present hypothesis, it is very important to design animal experiments in which animals perform motor responses as opposed to operant conditioning tasks in the absence of any over intentional movement. Go/No-Go tasks allow to assess decision making processes and, in addition, the ability to suppress a specific action according to the context, or the ability to cancel an action in progress when an unpredictable cue indicates that it should be avoided. In the proposed experiments, rats have to discriminate between two visual stimuli shown on a computer tablet (Go or No-Go). In this situation, the execution (Go) or non-execution (No-Go) of the selected action (to touch or not the visual display) would be reinforced (Fig. 5). Rats will be trained in a modified Skinner box, equipped with a tablet where the visual stimuli will appear [74]. LFPs and unitary responses will be recorded from cerebral (prefrontal cortex, accumbens septi and ventral tegmental area) and cerebellar structures (lateral cerebellum and dentate nucleus). Since this is a rather complex associative learning test, we expect differential cerebellar activity when performing Go (cognitive processes involving motor responses) and no-Go tasks (cognitive processes in the absence of motor responses).

Pharmacological, viral, and transcranial direct-current manipulations of social interactions

The activity in the above-mentioned cerebral and cerebellar cortex and nuclei can be disrupted by local administration of agonists/antagonists of dopamine (medial prefrontal cortex), GABA (cerebellar nuclei), and lidocaine (cerebellar cortex) [75]. For longer lasting effects (days or weeks), cerebellar nuclei can be injected with recombinant adeno-associated viral system (rAAVs and INSIST systems) releasing a variant of the tetanus neurotoxin [76] or tDCS (transcranial direct current stimulation) of selected cerebellar cortical areas [77,78]. These experimental procedures will provide more insight in the cerebellar circuitry involved in social coordination among rodents.

Implications of the hypothesis

A strong neural interaction between the cerebellum and cerebrum during social cognition has recently been confirmed in a meta-analytic connectivity study on social cognition consisting of 34 fMRI studies and 578 participants [79] as well as in an effective connectivity study of individual participants pooled across five fMRI studies containing 91 participants [28]. These studies revealed strong evidence for robust functional cerebro-cerebellar links during social cognition, involving the mirror and mentalizing network. In particular, connections were found between the mentalizing network in the cerebellum and the cerebrum, including core cerebral mentalizing areas such as the temporo-parietal junction and the medial prefrontal cortex. These data have been also confirmed by behavioral and neuroimaging evidences from patients with degenerative cerebellar atrophy [60]. In addition, recent evidence revealed that the posterior cerebellum is functionally connected to the autobiographical network during autobiographical memory retrieval [12].

Our hypothesis has major implications for life sciences and human

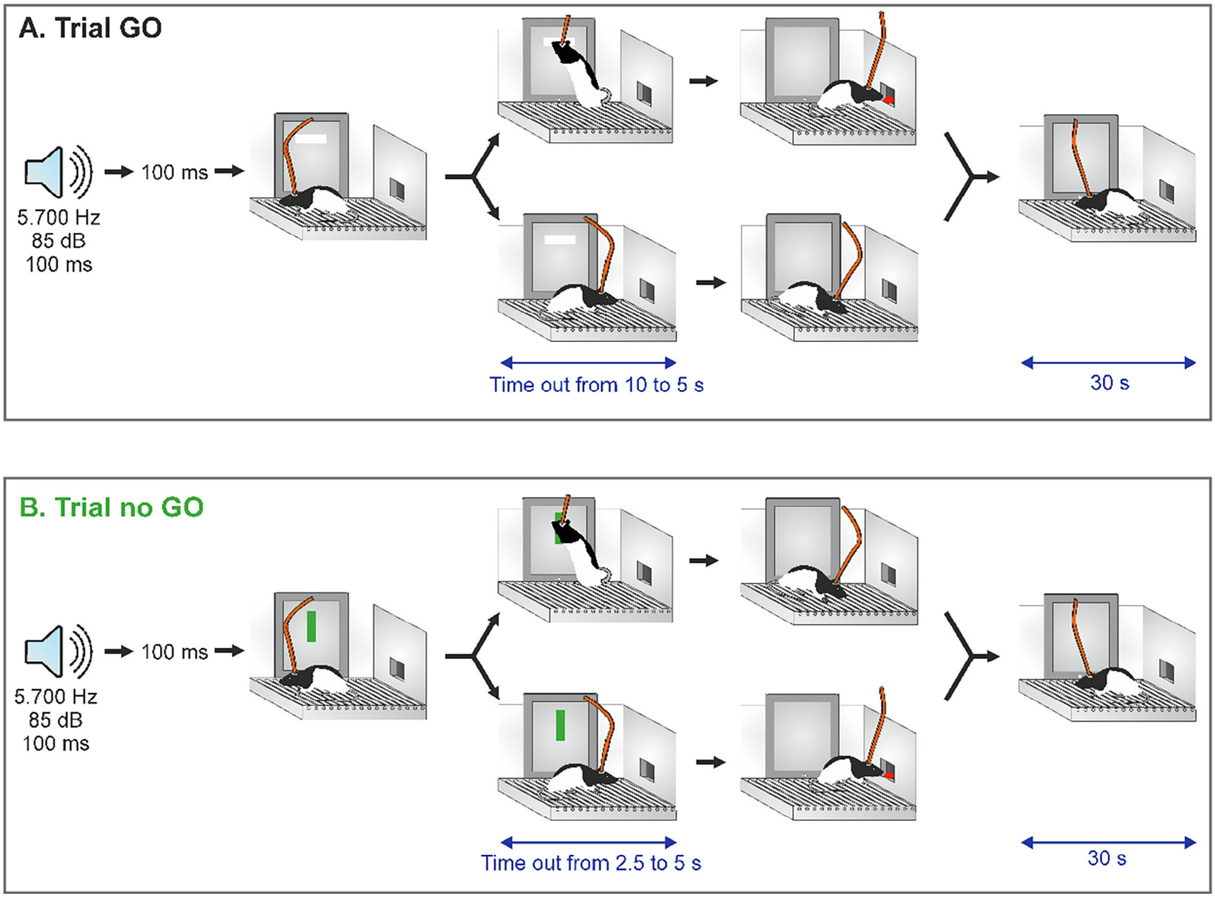

Fig. 5. Go/no-Go experiment. A: For the Go situation, and following a tone, the rat has to touch a white horizontal rectangle on a tablet screen to collect a pellet of food from the dispenser (indicated in red) [74]. The visual stimulus is presented for a short (10–5 s) time. B: For the no Go condition, and following a tone, the rat has to avoid touching the green vertical rectangle displayed on the tablet (for 2.5–5 s) to obtain the food reward. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

disorders characterized by defects in social interactions. Many studies have shown that the cerebellum is crucially implicated in the pathophysiology of a broad range of neuropsychiatric and neurodevelopmental disorders such as autism spectrum disorders, attentional deficit and hyperkinetic disorder, depression, and schizophrenia [80–82]. For instance, in more than 90% of individuals with ASD well-defined cerebellar anatomical abnormalities have been identified [83]. Identification of the role of the cerebellum in the social characteristics of these disorders may open novel and innovative avenues for future research, clinical diagnostics and treatment. Up till now, the investigation of social skills does not constitute an inherent part of the diagnostic workup and treatment of cerebellar impairments, and patients may receive inadequate guidance because of ignorance of cerebellar involvement in these pathologies.

After decades of hesitation, evidence has emerged that attributes key higher functions to the cerebellar circuitry. From an anatomical point of view, the structural organization of the cerebellum as a mantle of grey matter surrounding white matter with embedded nuclei is found in many species, from reptiles and birds to human [84]. The cerebello-thalamo-cortical tract represents an excellent candidate as the major highway involved in social cognition that is impaired especially in autism spectrum disorders, leaving the cerebellum insufficiently connected with the cerebral cortex [53]. Indeed, the functional connectivity between the dentate nucleus and the cerebral cortex is altered in ASD patients, and potentially also in other psychopathologies involving social deficits. There is a defect in the connectivity between the left dentate nucleus and cerebral regions implicated in specific networks, which might be involved in specific aspects of action observation, social mentalizing, and emotional processes [53]. Our hypothesis might also have a potential impact on basal ganglia disorders such as Parkinson's disease and dystonic disorders, given the established anatomical link between cerebellar circuitry and basal ganglia [85]. This is relevant for both motor and non-motor deficits in basal ganglia disorders. There is a consensus that neuronal dysfunction originating in the cerebellum can drive dystonic movements in rodents [86]. The identification of the neural code underlying social interactions is thus a major challenge for the scientific community.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mehy.2019.05.014.

References

[1] Martinelli P, Sperduti M, Piolino P. Neural substrates of the self-memory system: new insights from a meta-analysis. Hum Brain Mapp Mar. 2012;000.
[2] Schurz M, Radua J, Aichhorn M, Richlan F, Perner J. Fractionating theory of mind: a meta-analysis of functional brain imaging studies. Neurosci Biobehav Rev 2014;42:9–34.
[3] Van Overwalle F. Social cognition and the brain: a meta-analysis. Hum Brain Mapp Mar. 2009;30(3):829–58.
[4] Van Overwalle F, Baetens K. Understanding others' actions and goals by mirror and mentalizing systems: a meta-analysis. Neuroimage Nov. 2009;48(3):564–84.
[5] Adamaszek M, D'Agata F, Ferrucci R, Habas C, Keulen S, Kirkby KC, et al. Consensus paper: cerebellum and emotion. Cerebellum Apr. 2017;16(2):552–76.
[6] Baillieux H, De Smet HJ, Paquier PF, De Deyn PP, Mariën P. Cerebellar neurocognition: insights into the bottom of the brain. Clin Neurol Neurosurg Oct. 2008;110(8):763–73.

[7] Mariën P, Ackermann H, Adamaszek M, Barwood CHS, Beaton A, Desmond J, et al. Consensus paper: language and the cerebellum: an ongoing enigma. Cerebellum 2014;13(3):386–410.
[8] Van Overwalle F, Baetens K, Mariën P, Vandekerckhove M. Social cognition and the cerebellum: a meta-analysis of over 350 fMRI studies. Neuroimage Mar. 2014;86:554–72.
[9] Trope Y, Liberman N. Construal-level theory of psychological distance. Psychol Rev Apr. 2010;117(2):440–63.
[10] Baetens K, Ma N, Steen J, Van Overwalle F. Involvement of the mentalizing network in social and non-social high construal. Soc Cogn Affect Neurosci 2013(6).
[11] Van Hoeck N, Ma N, Ampe L, Baetens K, Vandekerckhove M, Van Overwalle F. Counterfactual thinking: an fMRI study on changing the past for a better future. Soc Cogn Affect Neurosci 2013;8(5):556–64.
[12] Addis DR, Moloney EEJ, Tippett LJ, Roberts RP, Hach S. Characterizing cerebellar activity during autobiographical memory retrieval: ALE and functional connectivity investigations. Neuropsychologia 2016;90:80–93.
[13] Buckner R, Krienen F, Castellanos A, Diaz JC, Yeo BT. The organization of the human cerebellum estimated by intrinsic functional connectivity. J Neurophysiol 2011;106:2322–45.
[14] Yeo BTT, Krienen FM, Sepulcre J, Sabuncu MR, Lashkari D, Hollinshead M, et al. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol Sep. 2011;106(3):1125–65.
[15] Clausi S, Olivito G, Lupo M, Siciliano L, Bozzali M. The cerebellar predictions for social interactions : theory of mind abilities in patients with degenerative cerebellar atrophy. Front Cell Neurosci 2019;12.
[16] Ferrucci R, Brunoni AR, Parazzini M, Vergari M, Rossi E, Fumagalli M, et al. Modulating human procedural learning by cerebellar transcranial direct current stimulation. Cerebellum 2013;12(4):485–92.
[17] Ito M. Control of mental activities by internal models in the cerebellum. Nat Rev Neurosci Apr. 2008;9(4):304–13.
[18] Pisotta I, Molinari M. Cerebellar contribution to feedforward control of locomotion. Front Hum Neurosci 2014;8:1–5.
[19] Leggio MG, Chiricozzi FR, Clausi S, Tedesco AM, Molinari M. The neuropsychological profile of cerebellar damage: the sequencing hypothesis. Cortex 2011;47(1):137–44.
[20] Andreasen NC, Pierson R. The role of the cerebellum in schizophrenia. Biol Psychiatry Jul. 2008;64(2):81–8.
[21] Bower J. Control of sensory data acquisition. Int Rev Neurobiol 1997;41:489–513.
[22] Schmahmann JD. Dysmetria of thought: clinical consequences of cerebellar dysfunction on cognition and affect. Trends Cogn Sci Sep. 1998;2(9):362–71.
[23] Van Overwalle F, Heleven E, Ma N, Mariën P. Tell me twice: a multi-study analysis of the functional connectivity between the cerebrum and cerebellum after repeated trait information. Neuroimage 2017;144(A):241–52.
[24] Van Overwalle F, De Coninck S, Heleven E, Manto M, Mariën P. The role of the cerebellum in reconstructing social action sequences: a pilot study. Unpubl Manuscr 2018.
[25] Langdon R, Coltheart M. Mentalising, schizotypy, and schizophrenia. Cognition 1999;71:43–71.
[26] Baron-Cohen S, O'Riordan M, Stone V, Jones R, Plaisted K. Recognition of faux pas by normally developing children and children with asperger syndrome or high-functioning autism. J Autism Dev Disord 1999;29(5):407–18.
[27] Heleven E, van Dun K, Van Overwalle F. The posterior cerebellum is involved in constructing social action sequences: an fMRI study. Manuscr Submitt Publ 2018.
[28] Van Overwalle F, Van de Steen F, Mariën P. Dynamic causal modeling of the effective connectivity between the cerebrum and cerebellum in social mentalizing across five studies. Cogn Affect Behav Neurosci 2018.
[29] German TP, Niehaus JL, Roarty MP, Giesbrecht B, Miller MB. Neural correlates of detecting pretense: automatic engagement of the intentional stance under covert conditions. J Cogn Neurosci Dec. 2004;16(10):1805–17.
[30] Grèzes J, Frith C, Passingham R. Inferring false beliefs from the actions of oneself and others: an fMRI study. Neuroimage 2004;21:744–50.
[31] Grèzes J, Frith C, Passingham R. Brain mechanisms for inferring deceit in the actions of others. J Neurosci 2004;24(24):5500–5.
[32] Özdem C, Brass M, Van der Cruyssen L, Van Overwalle F. The overlap between false belief and spatial reorientation in the temporo-parietal junction: the role of input modality and task. Soc Neurosci 2017;12(2):207–17.
[33] Saxe RR, Kanwisher N. People thinking about thinking people – The role of the temporo-parietal junction in 'theory of mind'. Neuroimage Aug. 2003;19(4):1835–42.
[34] Kestemont J, Ma N, Baetens K, Clément N, Van Overwalle F, Vandekerckhove M. Neural correlates of attributing causes to the self, another person and the situation. Soc Cogn Affect Neurosci Jan. 2015;10(1):114–21.
[35] Geiger A, Cleeremans A, Bente G, Vogeley K. Social Cues Alter Implicit Motor Learning in a Serial Reaction Time Task. vol. 12: May 2018; p. 1–12.
[36] Coomans D, Deroost N, Zeischka P, Soetens E. On the automaticity of pure perceptual sequence learning. Conscious Cogn 2011;20(4):1460–72.
[37] Conway MA. Memory and the self. J Mem Lang 2005;53(4):594–628.
[38] D'Argembeau A, Jeunehomme O, Majerus S, Bastin C, Salmon E. The neural basis of temporal order processing in past and future thought. J Cogn Neurosci 2015;27(1):185–97.
[39] Demblon J, Bahri MA, D'Argembeau A. Neural correlates of event clusters in past and future thoughts: how the brain integrates specific episodes with autobiographical knowledge. Neuroimage 2016;127:257–66.
[40] Zacks JM, Speer NK, Swallow KM, Braver TS, Reynolds JR. Event perception: a mind-brain perspective. Psychol Bull Mar. 2007;133(2):273–93.
[41] Sargent JQ, Zacks JM, Hambrick DZ, Zacks RT, Kurby CA, Bailey HR, et al. Event segmentation ability uniquely predicts event memory. Cognition Nov. 2013;129(2):241–55.
[42] Silva AR, Pinho MS, Macedo L, Moulin CJA. A critical review of the effects of wearable cameras on memory. Neuropsychol Rehabil 2016:1–25.
[43] Anderson RJ, Peters L, Dewhurst SA. Episodic elaboration: investigating the structure of retrieved past events and imagined future events. Conscious Cogn May 2015;33:112–24.
[44] D'Argembeau A, Demblon J. On the representational systems underlying prospection: evidence from the event-cueing paradigm. Cognition 2012;125(2):160–7.
[45] Thomsen DK. Autobiographical periods: a review and central components of a theory. Rev Gen Psychol 2015;19(3):294–310.
[46] Holm T, Thomsen DK, Bliksted V. Life story chapters and narrative self-continuity in patients with schizophrenia. Conscious Cogn Oct. 2016;45:60–74.
[47] Piolino P, Desgranges B, Eustache F. Episodic autobiographical memories over the course of time: cognitive, neuropsychological and neuroimaging findings. Neuropsychologia 2009;47(11):2314–29.
[48] American Psychiatric Association, Diagnostic and statistical manual of mental disorders, 5th ed. Washington DC: Author, 2013.
[49] Baron-Cohen S, Wheelwright S, Skinner R, Martin J, Clubley E. The autism-spectrum quotient (AQ): evidence from asperger syndrome/high-functioning autism, males and females, scientists and mathematicians. J Autism Dev Disord 2001;31(1):5–17.
[50] Ecker C, Rocha-Rego V, Johnston P, Mourao-Miranda J, Marquand A, Daly EM, et al. Investigating the predictive value of whole-brain structural MR scans in autism: a pattern classification approach. Neuroimage 2010;49(1):44–56.
[51] D'Mello AM, Stoodley CJ. Cerebro-cerebellar circuits in autism spectrum disorder. Front Neurosci 2015;9.
[52] Khan AJ, Nair A, Keown CL, Datko MC, Lincoln AJ, Müller RA. Cerebro-cerebellar resting-state functional connectivity in children and adolescents with autism spectrum disorder. Biol Psychiatry 2015;78(9):625–34.
[53] Olivito G, Clausi S, Laghi F, Tedesco AM, Baiocco R, Mastropasqua C, et al. Resting-state functional connectivity changes between dentate nucleus and cortical social brain regions in autism spectrum disorders. Cerebellum 2017;16(2):283–92.
[54] Ramos TC, Balardin JB, Sato JR, Fujita A. Abnormal cortico-cerebellar functional connectivity in autism spectrum disorder. Front Syst Neurosci 2019;12.
[55] Just MA, Cherkassky VL, Keller TA, Minshew NJ. Cortical activation and synchronization during sentence comprehension in high-functioning autism: evidence of underconnectivity. Brain 2004;127(8):1811–21.
[56] Redcay E, Moran JM, Mavros PL, Tager-Flushberg H, Gabrieli JD, Whitfield-Gabrieli S. Intrinsic functional network organization in high-functioning adolescents with autism spectrum disorder. Front Hum Neurosci 2013.
[57] Washington SD, Gordon EM, Brar J, Warburton S, Sawyer AT, Wolfe A, et al. Dysmaturation of the default mode network in autism. Hum Brain Mapp 2014;35(4):1284–96.
[58] Olivito G, Lupo M, Laghi F, Clausi S, Baiocco R, Cercignani M, et al. Lobular patterns of cerebellar resting-state connectivity in adults with Autism Spectrum Disorder. Eur J Neurosci 2018;47(6):729–35.
[59] Baron-Cohen S, Wheelwright S, Hill J, Raste Y, Plumb I. The 'Reading the Mind in the Eyes' Test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. J Child Psychol Psychiatry 2001;42(2):241–51.
[60] Clausi S, Olivito G, Lupo M, Laghi F, Siciliano L, Baiocco R, et al. The cerebellar involvement in social behavior an in autism-like symptoms: a clinical neuroimaging study in patients with cerebellar and subjects with autism spectrum disorder. Manuscr. Prep. 2019.
[61] Blair RJR, Cipolotti L. Impaired social response reversal. A case of 'acquired sociopathy'. Brain 2000;123(Pt 6):1122–41.
[62] Stone VE, Baron-Cohen S, Knight RT. Frontal lobe contributions to theory of mind. J Cogn Neurosci Sep. 1998;10(5):640–56.
[63] Happé FGE. An advanced test of theory of mind: understanding of story characters' thoughts and feelings by able autistic, mentally handicapped, and normal children and adults. J Autism Dev Disord 1994;24(2):129–54.
[64] Zalesky A, Fornito A, Bullmore ET. Network-based statistic: identifying differences in brain networks. Neuroimage 2010;53(4):1197–207.
[65] Friston K, Zeidman P, Litvak V. Empirical bayes for DCM: a group inversion scheme. Front Syst Neurosci 2015;9.
[66] Friston KJ, Litvak V, Oswal A, Razi A, Stephan KE, Van Wijk BCM, et al. Bayesian model reduction and empirical Bayes for group (DCM) studies. Neuroimage 2016;128:413–31.
[67] van Dun K, Bodranghien FCAA, Mariën P, Manto MU. tDCS of the cerebellum: where do we stand in 2016? technical issues and critical review of the literature. Front Hum Neurosci 2016;10.
[68] Manto M, Bower JM, Conforto AB, Delgado-García JM, da Guarda SN, Gerwig M, et al. Consensus paper: roles of the cerebellum in motor control–the diversity of ideas on cerebellar involvement in movement. Cerebellum 2012;11(2):457–87.
[69] Kelly RM, Strick PL. Cerebellar loops with motor cortex and prefrontal cortex of a nonhuman primate. J Neurosci 2003;23(23):8432–44.
[70] Carta I, Chen CH, Schott AL, Dorizan S, Khodakhah K. Cerebellar modulation of the reward circuitry and social behavior. Science 2019;363(6424):eaav0581.
[71] Fernández-lamo I, Sánchez-campusano R, Gruart A, Delgado-garcía JM. Functional states of rat cortical circuits during the unpredictable availability of a reward-related cue. Nat. Publ. Gr. 2016:1–17.
[72] Gruart A, Conde-Moro A, Rocha-Almeida F, Sánchez-Campusano R, Delgado-García J. Coding for interactive behaviors of medial prefrontal areas during joint operant conditioning in male rats. In: SfN Meeting; 2017.
[73] Rocha-Almeida F, Conde-Moro A, Delgado-García J, Gruart A. A 4-Hz oscillation in

the prefrontal cortex and in the accumbens nucleus characterizes prosocial, but not food rewards in rats. In: SfN Meeting; 2018.
[74] Hernández-González S, Andreu-Sánchez C, Martín-Pascual MÁ, Gruart A, Delgado-García JM. A cognition-related neural oscillation pattern, generated in the prelimbic cortex, can control operant learning in rats. J Neurosci 2017;37(24):5923–35.
[75] Almeida F, Conde A, Delgado-García JM, Gruart A. The role of medial prefrontal cortex in cooperative behaviors and decision making in rats. In: FENS Meeting; 2016.
[76] Hasan MT, Hernández-González S, Dogbevia G, Treviño M, Bertocchi I, Gruart A, et al. Role of motor cortex NMDA receptors in learning-dependent synaptic plasticity of behaving mice. Nat Commun 2013.
[77] Márquez-Ruiz J, Ammann C, Leal-Campanario R, Ruffini G, Gruart A, Delgado-García JM. Synthetic tactile perception induced by transcranial alternating-current stimulation can substitute for natural sensory stimulus in behaving rabbits. Sci Rep 2016;6(1):1–12.
[78] Márquez-ruiz J, Leal-campanario R, Sánchez-campusano R, Molaee-ardekani B. Transcranial direct-current stimulation modulates synaptic mechanisms involved in associative learning in behaving rabbits. PNAS 2012;109(17):6710–5.
[79] Van Overwalle F, D'aes T, Mariën P. Social cognition and the cerebellum: a meta-analytic connectivity analysis. Hum Brain Mapp Dec 2015;36(12):5137–54.
[80] Bauman ML, Kemper TL. Neuroanatomic observations of the brain in autism: a review and future directions. Int J Dev Neurosci 2005;23(2–3):183–7.
[81] D'Mello AM, Crocetti D, Mostofsky SH, Stoodley CJ. Cerebellar gray matter and lobular volumes correlate with core autism symptoms. NeuroImage Clin. 2015;7:631–9.
[82] Penn HE. Neurobiological correlates of autism: a review of recent research. Child Neuropsychol Mar. 2006;12(1):57–79.
[83] Carper RA, Courchesne E. Inverse correlation between frontal lobe and cerebellum sizes in children with autism. Brain 2000;123:836–44.
[84] Colin F, Ris L, Godaux E. The cerebellum and its disorders. Cambridge: Cambridge University Press; 2001.
[85] Caligiore D, Pezzulo G, Baldassarre G, Bostan AC, Strick PL, Doya K, et al. Consensus paper: towards a systems-level view of cerebellar function: the interplay between cerebellum, basal ganglia, and cortex. Cerebellum 2017;16(1):203–29.
[86] Shakkottai VG, Batla A, Bhatia K, Dauer WT, Dresel C, Niethammer M, et al. Current opinions and areas of consensus on the role of the cerebellum in dystonia. Cerebellum 2017;16(2):577–94.