



Cerebellum and Emotion in Social Behavior

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Abstract

Accumulating evidence suggests that the cerebellum plays a crucial role not only in the motor and cognitive domains but also in emotions and social behavior. In the present chapter, after a general introduction on the significance of the emotional components of social behavior, we describe recent efforts to understand the contributions of the cerebellum in social cognition focusing on the emotional and affective aspects. Specifically, starting from the description of the cerebello-cortical networks subtending the social-affective domains, we illustrate the most recent findings on the social cerebellum and the possible functional mechanisms by which the cerebellum modulate social-affective behavior. Finally, we discuss the possible consequences of cerebellar dysfunction in the social-affective domain, focusing on those neurological and psychopathological conditions in which emotional and social behavior difficulties have been described as being associated with cerebellar structural or functional alterations.

Keywords

Cerebellar sequencing · Social interactions · Prediction · Cerebro-cerebellar circuits · Social-affective alterations

15.1 General: Emotions in Social Behavior

Emotional processing includes immediate physiological responses and both automatic and intentional behavioral reactions to life events, proving critical to individuals' survival and adaptive social relationships (Lerner et al. 2015). Humans are intrinsically predisposed to perceive and understand their own and others' emotions and are constantly engaged in social interactions (Zaki and Ochsner 2011). One of the most primitive and key processes for successful social interactions is the ability to infer others' emotions from visual and acoustic features, such as facial expressions and vocalizations (Schaller and Rauh 2017). While this ability reflects automatic aspects of emotion recognition, the ability to integrate contextual information with emotional states and to make detailed appraisals based on the interplay between present and past conditions is a reflection of more conceptual aspects of emotion recognition (Siciliano and Clausi 2020). Emotion recognition represents one of the two core components of social cognition, a composite human function defined by Brothers (Brothers and Ring 1990) as

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“the processing of any information which culminates in the accurate perception of the dispositions and intentions of other individuals.” The other component of this complex function is termed mentalizing or theory of mind (ToM), which consists of the advanced capacity to recognize and attribute mental states, such as emotions, intentions, and beliefs, to others (Premack and Woodruff 1978). This human ability allows us to make abstract social inferences in terms of past, future, or hypothetical events to adaptively predict social-affective behaviors (Van Hoeck et al. 2013). Emotion recognition and ToM are two closely linked processes since the recognition of others’ emotional state and related relevant cues culminate in the recognition of intentions (Brothers and Ring 1990). In this framework, social cognition processes could be viewed along a continuum, ranging from more automatic emotional processing to the recognition of complex emotional and mental states. Along this continuum, the ability to recognize the emotional state of others, based on specific situations and contexts, coincides with the capacity to empathize with them and has been defined as the affective component of ToM (Abu-Akel and Shamay-Tsoory 2011). Whereas affective ToM is thought to involve emotional contagion and empathetic appreciation of others’ emotional states, cognitive ToM is believed to require the understanding that others may have beliefs and intentions that differ from ours (Shamay-Tsoory 2011). Although these two components are separate aspects of ToM, their cooperation is needed to guarantee effective social interactions (Shamay-Tsoory et al. 2009). This model is in line with the one proposed by Coricelli (2005), which described a two-mind reading process: an unconscious/automatic process that allows the decoding of others’ intentions by the recognition of action and emotional contagion and a conscious/voluntary process that is linked to the ability to take the perspective of others and to use anticipatory and comparative mechanisms to make assumptions regarding their mental state (Coricelli 2005).

The multifaceted nature of these functions is supported by extended and dynamic neural networks composed of limbic areas, including

the amygdala, hippocampus and insula (Phillips et al. 2003; Kipps et al. 2007; Gu et al. 2012), and cortical and associative areas, such as the anterior cingulate cortex, superior temporal sulcus (STS), temporo-parietal junction (TPJ), medial precuneus, and medial and lateral prefrontal cortex (Kennedy and Adolphs 2012; Van Overwalle et al. 2014). Despite the high specialization of these structures, constant interactions between them are needed to accomplish such complex functions, and overlaps can be found between emotional and social brain (Fossati 2012).

Nevertheless, the large-scale network sustaining all the functions covered under the umbrella term social cognition has yet to be well defined, and the role of the cerebellum is becoming increasingly emphasized (Van Overwalle et al. 2020a). The demonstrated influence of the cerebellar vermis, termed the “limbic cerebellum,” in emotional processing represents a crucial starting point for broadening its role in related affective and social fields (Adamaszek et al. 2015; Leggio and Olivito 2018). Indeed, recent MRI studies have shown cerebellar involvement in different aspects of social-affective behavior (Van Overwalle and Mariën 2016; Van Overwalle et al. 2020b). In particular, it has been highlighted that specific and phylogenetically more recent regions of the cerebellum are activated during complex social cognition tasks and are coupled with brain areas belonging to the mentalizing network (Van Overwalle et al. 2014; Van Overwalle and Mariën 2016). This interesting issue will be described in depth in the following sections.

15.2 The Role of Cerebro-Cerebellar Circuits in Social-Affective Behavior

Consensus is growing on the starring role of the cerebellum in social-affective behavior. Indeed, although this very interesting field is still at its early stages, many research findings point to a better understanding of the involvement of the cerebellum in social-affective domains. Substantial data come from structural and functional

neuroimaging studies, which provide a useful characterization of the cerebellar functional topography for emotional (Stoodley and Schmahmann 2010) and social processing (Van Overwalle et al. 2014, 2015).

The cerebellar vermis has been indicated as the principal target of limbic connections, supporting the modulation of more “primitive” emotions (Schmahmann 1991; Schmahmann 2000) and the processing of stimuli that are critical for the emotional/affective experience (Schmahmann and Sherman 1998). In contrast, more complex emotional processing, such as social mentalizing, recruits specific regions in the posterior cerebellum (Van Overwalle et al. 2014, 2015). Accordingly, in a recent meta-analysis, Van Overwalle et al. (2020b) investigated which areas of the posterior cerebellum are specialized for social mentalizing and found that the Crus II was shown, in approximately 75% of the studies, to support domain-specific social cognition tasks related not only to social mentalizing but also to self-related emotional experience. Interestingly, among the mentalizing tasks, the highest percentages were found in subcategories examining attribution of others’ emotions (27%) and emotional self-experiences (17%). Notably, predominant activity during mentalizing tasks has also been found in the lobule IX of the cerebellum.

Considering that social cognition is a sophisticated mental process, neuroimaging studies on brain functional connectivity (FC) have proven very useful in characterizing the complex brain networks involved in this function. In this field, the findings accumulated within the past decade have proven the presence of segregated cerebellar functional organization that allows the cerebellum to play a crucial role in emotional and social processing through its functional interactions with specific emotional and social brain cerebral regions (Leggio and Olivito 2018). Specifically, a study investigating the pattern of resting-state FC among vermal, paravermal, and hemispheric regions of the cerebellum (Sang et al. 2012) suggested that the cerebellum has a third functional subdivision, beyond the motor and cognitive subdivisions, that is devoted to emotional

processing. Functional coherence was found between the cerebellum and brain limbic structures typically implicated in emotional regulation, such as the hippocampus and the amygdala (Sacchetti et al. 2009; Milner et al. 1998; Phelps and Le Doux 2005). In particular, the vermal I–VI, Crus II–X, hemispheric I–VI, and Crus II and IX regions are functionally connected to the hippocampus, while the vermal I–V, VIIb, VIIIa,b, and IX and hemispheric I–VI and VIIb regions are more functionally connected to the amygdala (Fig. 15.1a).

Further studies investigating cerebellar contributions to cerebral intrinsic connectivity networks reported patterns of functional coherence between the vermal and hemispheric parts of the lobule VI, the adjacent Crus I, and the dentate nuclei with the salience network (Habas et al. 2009). This network includes the dorsal anterior cingulate cortex and the fronto-insular cortex and is involved in interoception, autonomic regulation, and emotional regulation (Seeley et al. 2007). Lateral hemispheric regions of the posterior cerebellum (especially the Crus I/II), which are part of the “executive cerebellum,” also show connectivity with the salience network (Habas et al. 2009; Stoodley and Schmahmann 2010) and are likely to be recruited when more cognitive aspects of emotional processing are in demand.

Several resting-state fMRI studies also proved the participation of the posterior portions of the cerebellum (Crus I/II) in intrinsic connectivity networks related to social mentalizing (Habas et al. 2009; Buckner et al. 2011). In particular, while motion-related mirroring movement tasks have been shown to recruit “somatomotor” networks in the anterior cerebellum (Buckner et al. 2011), nonmotion-related mentalizing tasks have been shown to recruit the “default/mentalizing” network in the posterior cerebellum (Crus II), specifically when a high level of abstraction is required (Van Overwalle and Mariën 2016).

Connectivity fMRI studies have reported participation of the cerebellum in the default mode network (DMN) (Habas et al. 2009; Buckner et al. 2011), highlighting a crucial role of the cerebellar

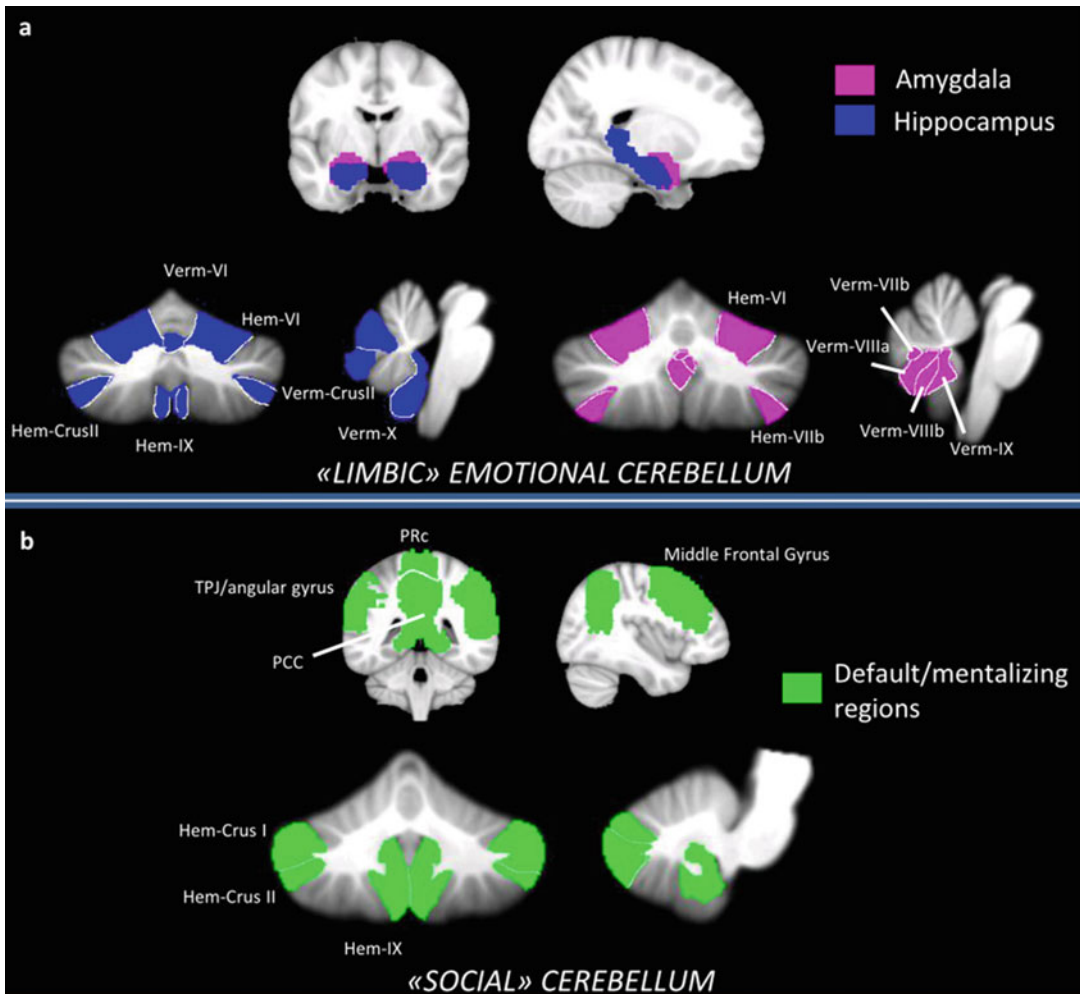


Fig. 15.1 Cerebellar functional topography for affective/emotional and social domains. Cerebellar lobules are segregated by affective/emotional and social mentalizing functions and superimposed on the Spatial Unbiased Infratentorial Template. **(a)** Cerebellar lobules of the limbic/emotional cerebellum having connectivity with limbic

brain regions: amygdala (in violet) and hippocampus (in blue); **(b)** cerebellar lobules of the social cerebellum having connectivity with default/mentalizing brain regions (in green). *Verm* vermal, *Hem* hemispheric, *TPJ* temporo-parietal junction, *PRc* precuneus, *PCC* posterior cingulate cortex

Crus I/II. The DMN is of particular interest in the context of mentalizing functions since it includes a set of cerebral regions that are particularly relevant for the social understanding of others, such as the TPJ, posterior cingulate cortex, precuneus, lateral parietal/angular gyrus, medial prefrontal cortex, and superior frontal gyrus (Schilbach et al. 2008). The cerebellar Crus I/II has been shown to be functionally coupled to default mode regions, while the anterior Crus I is

functionally associated with the cerebral fronto-parietal network (Bernard et al. 2012).

Consistent with these data, altered cerebello-cerebral functional connectivity has been reported in adults with autism spectrum disorder (Olivito et al. 2017a, 2018), a neurodevelopmental disorder typically characterized by an impairment in social mentalizing (Baron-Cohen 1995; Hill and Frith 2003). In particular, altered FC was found between the cerebellar Crus II and cortical

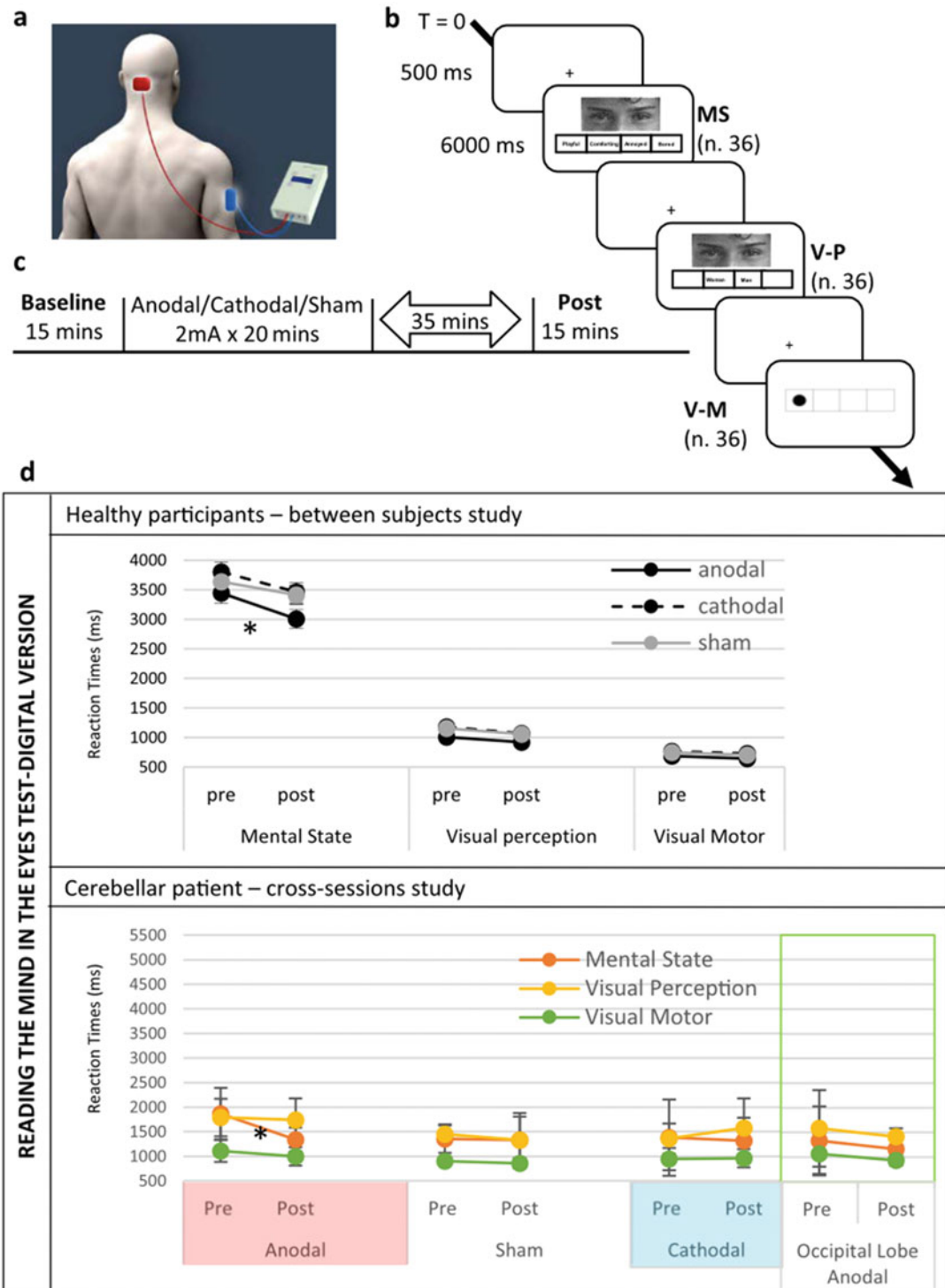


Fig. 15.2 tDCS montage, experimental protocol, stimuli examples and behavioral results. (a) Extra-cephalic montage: the active electrode was placed on the cerebellar vermis and the reference electrode was placed on the

right deltoid; (b) tDCS protocol; (c) Stimuli examples of the digital Reading the Mind in the Eyes Test: mental state (M-S) visual perception (V-P) and visual motor (V-M) stimuli are showed; (d) Study results in healthy

regions belonging to the DMN (Olivito et al. 2018). Interestingly, a meta-analysis of connectivity studies has identified a cerebello-cerebral mentalizing network that is particularly involved when a high level of abstraction is required, such as inferring group stereotypes, a person's traits, or a person's past (Van Overwalle and Mariën 2016). This network included the right posterior cerebellar region corresponding to the Crus II and bilateral mentalizing regions in the cerebrum, such as the bilateral TPJ, precuneus, and medial prefrontal cortex (Fig. 15.1b). A recent study using dynamic causal modeling showed that bidirectional connectivity exists within this network and that cerebral and cerebellar mentalizing areas are effectively connected via closed loops. In particular, the bidirectional (closed-loop) connectivity between the Crus II and bilateral TPJ has been specifically related to high-level social understanding (Van Overwalle et al. 2019a).

Taken together, these data confirm the existence of cerebellar functional segregation for emotional and social processing and suggest that the cerebellum significantly contributes to emotional processing both in the early stages of emotional perception and recognition and in the modulation of more complex social-affective behaviors.

15.3 The Role of the Cerebellum in Emotional Component of Social Cognition

15.3.1 From Emotion Regulation to Mentalizing Abilities: The Advent of the Social Cerebellum

In recent years, different research groups have paid great attention to the contribution of the

cerebellum in emotional processing and social-affective behavior, going beyond its well-known role in the motor and cognitive domains. Early research reports regarded cerebellar involvement in *emotion regulation* and *affective disorders*, such that impaired modulation of affective behavior has been recognized as a part of “cerebellar cognitive affective syndrome” (CCAS) (Schmahmann and Sherman 1998). Subsequent clinical studies in individuals with cerebellar focal or degenerative damage showed symptomatology that ranged from inappropriate affective reactions to external events, such as pathological laughter and crying (Parvizi et al. 2001, 2007), agitation, impulsivity and irritability, to difficulties in processing negative emotions (fear and anger), mood fluctuations or affective flattening and depressive disorders (Richter et al. 2005; Tavano et al. 2007).

Moreover, clinical evidence has reported that the cerebellum also participates in the ability to consciously define our own affective state. Indeed, patients with cerebellar damage presented with difficulties in feeling conscious emotions of regret subsequent to disadvantageous choices in a gambling task (Clausi et al. 2015) and in explicitly recognizing their bad mood in the presence of clinically relevant depressive disorder (Clausi et al. 2019a).

Most of these alterations have been associated with damage to the vermis, which is part of the limbic cerebellum and is well known for its involvement in emotional processing and regulation (Parvizi et al. 2001; Richter et al. 2005; Schmahmann 2001; Stoodley and Schmahmann 2009). Interestingly, animal studies have shown that potentiation of excitatory and inhibitory synapses, which impinge on Purkinje cells at the level of the vermis, correlated with associative learning of fear, an emotion that is endowed with high adaptive value, and has long-lasting

Fig. 15.2 (continued) participants and in one patients affected by cerebellar atrophy. In the healthy participant's study, each subject was assigned to one of three groups in which anodal, cathodal, or sham stimulations was delivered. Instead, in the cerebellar patient, the anodal,

cathodal, and sham stimulations were delivered over the cerebellum in three double-blind sessions (with 1-week interval). Moreover, one occipital lobe stimulation session was performed as further control condition. * $p < 0.005$

effects (Sacchetti et al. 2009; Zhu et al. 2007; Scelfo et al. 2008). These data allow us to hypothesize that learning-related plasticity at the level of the vermis might be crucial for relaying appropriate emotional and motor behaviors in response to external stimuli and maintaining this information for long periods. Thus, through its connections with the limbic system, the vermis may act as the interface between sensory stimuli, emotional state, and behavioral responses.

Since emotion regulation and affective state awareness are crucial abilities in social interaction and in the adaptation to new social contexts, the cerebellum implication in these functions paved the way to further investigation about the social-affective cerebellum.

Studies have primarily focused on the cerebellar contribution in emotional processing from facial expressions (Adamaszek et al. 2015; Schutter et al. 2009; Ferrucci et al. 2012). Facial expressions are crucial for non-verbal social interactions and are markers of internal states and intentions (Phillips and David 1995; Schupp et al. 2004). Recognizing facial expressions is vital in a complex social world, as it permits one to detect the emotional state of another person and provides cues on how to respond in social situations (Frank and Stennett 2001; Grossmann and Johnson 2007).

The contribution of the cerebellum in this domain is supported by studies using non-invasive neuro-stimulation techniques targeting the human cerebellum, such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) (van Dun et al. 2017). Specifically, Schutter et al. (2009) found that repetitive TMS (20 Hz) over the cerebellar vermis increased emotional responsiveness to happy facial expressions with no changes in consciously experienced mood. In the same way, tDCS delivered over the cerebellar vermis significantly reduced the time needed to identify negative facial expressions, such as anger and sadness (Ferrucci et al. 2012). More recently, facilitative effects of tDCS over the cerebellar vermis on the ability to recognize mental states of others through the eyes expression was found in both healthy subjects and patients with

cerebellar ataxia (personal observations) (Fig. 15.2). These studies used the digital version of Reading the Mind in the Eyes (RME) test, an advanced ToM task that involves more implicit emotional processing and requires recognizing complex facial emotions and mental states from photographs of the eye region (Baron-Cohen et al. 2001).

These preliminary findings are in line with clinical observations in patients affected by neurodegenerative cerebellar pathologies in whom low performance on the RME test, difficulties in attributing negative emotion, and impaired performance on advanced mentalization tasks have been reported (D'Agata et al. 2011; Sokolovsky et al. 2010; Clausi et al. 2019b, 2021). Impairments in visual emotional attention and emotional face recognition have also been reported in subjects affected by cerebellar hemisphere damage (Adamaszek et al. 2013, 2015). In this context, the cerebellum has been characterized as an active interface with large-scale cerebral pathways that are involved in emotionally conscious processes. In line with this, fMRI studies have shown that the cerebellum, in addition to the amygdala and prefrontal cortex, is activated during conscious processing of emotional faces (Fusar-Poli et al. 2009). In fact, specific portions of the cerebellum are part of brain networks, including the amygdala–medial prefrontal circuitry, which contribute to determining the meaning of external stimuli and coherently reacting to them (Ghashghaei et al. 2007). Specifically, the medial prefrontal cortex plays a key role in complex aspects of emotional processing, such as social interactions (Rudebeck et al. 2008). Amygdala activation has also been associated with the perception of emotion (Adolphs 2002) and emotional arousing effects (Le Doux 2007; Wallentin et al. 2011).

The cerebellar involvement in emotions and social-affective behavior is strongly supported by neuroimaging meta-analyses in healthy subjects, which show that different areas of the cerebellum can be linked to specific social-cognitive processes, such as mirroring and mentalizing (Van Overwalle et al. 2014, 2015). In fact, as detailed in Sect. 15.2, although the

vermis seems to participate in autonomic and implicit processing of emotions, the posterior portions of the cerebellum (i.e., the Crus I and II) have been proposed to mediate emotional content at higher cognitive levels (Timmann et al. 2010) and social cognition processing (Van Overwalle et al. 2014, 2015). In line with this suggestion, posterior regions of the cerebellum were shown to be activated during conscious feelings and empathy of pain (Singer et al. 2004) and are connected with the temporal, parietal, and prefrontal cortices (Ramnani 2006), which are involved in cognitive elaboration of emotional content (Lane 2008).

Accordingly, the causal role of the posterolateral region of the cerebellum in inferring others' mental states from observation of their body language has also been demonstrated in neurostimulation studies. For example, Ferrari et al. (2018, 2019) showed that TMS over the left posterior cerebellar hemisphere affects the discrimination of emotional facial and body expressions in static pictures of real-life individuals. Overall, the abovementioned data from studies employing non-invasive brain stimulation and neuroimaging techniques converge to the view that the cerebellum acts not only in automatic perceptual processing but also in conscious processing of emotional and mental state information required for adequate social functioning. However, one question remains open: how does the cerebellum participate in processes related to the social-affective domain?

Currently, the most widely accepted hypothesis is that the modulatory actions that the cerebellum exerts on projection areas in the cerebral cortex are crucial not only for motor adaptation to sudden environmental changes but also for the optimization of social interactions and adaptation to the social context in accordance with internal and external emotional changes. This idea has been substantiated by the existence of anatomofunctional circuits (see Sect. 15.2) that allows the cerebellum to exert its function as part of the social-affective brain.

15.3.2 Cerebellar Modulation of Social-Affective Behavior: Theoretical Hypotheses

As illustrated above, the involvement of the cerebellum in social-affective behavior is becoming an accepted notion in the scientific community (Van Overwalle et al. 2020a). In parallel with the interest in defining the emotional and behavioral aspects by which the cerebellum plays a role and with the need to characterize the cerebello-cortical networks involved in the control of these functions, several groups of researchers in recent years have tried to elaborate specific theoretical hypotheses about the way in which this particular brain area influence the social-affective functioning.

15.3.2.1 Universal Cerebellar Transform and Dysmetria of Thought Theories in Social Behavior

One of the theories that has been posited to explain cerebellar functioning in emotional processing and social-affective behavior is the "uniform cerebellar transform" (UCT) hypothesis (Schmahmann 1991, 1998, 2000). It states that the cerebellum contributes to different domains by a singular neurological computation due to the repeating cytoarchitecture of its cortex and to the topographical organization of the extensive reciprocal anatomical connections between specific regions in the cerebellum and the sensory-motor and associative cortices (Schmahmann 2001; Schmahmann and Pandya 1997). Although the cerebellar cortex has an essentially uniform, monotonously repetitive architecture, immunohistochemistry has shown that it contains anatomically identifiable parasagittal bands (Hawkes et al. 1993) that appear to have connective and physiological specificity (Hallem et al. 1999). Thus, the functional specificity of each cerebellar module is determined by the cortical brain region to which it is connected. Indeed, there is anatomical specificity linking each cerebral cortical area with unique patterns of termination in the basilar pons, which in turn is linked with specific regions of the cerebellar cortex. The

cerebellar cortico-nuclear projections are then transmitted to specific areas of the thalamus before returning to those cerebral areas from which the projection originated (Kelly and Strick 2003). Based on its characteristic anatomical organization, the authors suggested that the cerebellum performs a universal cerebellar transform on the information to which it has access (Schmahmann 1991, 1998, 2000).

Following this idea, the uniform structure of the cerebellar cortex enables a unique computation that modulates the processing of multiple streams of information not only in sensorimotor and cognitive domains but also in emotional and social-affective domains. The cerebellum may serve as an oscillation damper, smoothing out performance in all domains and modulating behavior (Schmahmann 1998). Specifically, with respect to social-affective behavior, it has been hypothesized that the cerebellum acts to compare the consequences of actions with the intended outcomes, that is, to match reality with perceived reality. This is possible through existing cerebellar anatomical links with systems that control these functions, such that the vermis, fastigial nucleus and flocculo-nodular lobe are linked with the limbic system, whereas the cerebellar posterior areas are linked with paralimbic areas and association cortices concerned with the integration of emotional experiences into the repertoire of perceptions and behaviors required for social interactions (see Sect. 15.2 for further details).

The UCT theory is supported not only by neuroimaging findings on cerebro-cerebellar circuits but also by evidence on the significant relationships between social behavior and other motor and non-motor domains (Schmahmann 2000; Schmahmann and Sherman 1998; Schmahmann et al. 2019). Indeed, a new line of inquiry has examined general organizational principles that are shared between social and other motor and non-motor domains and has provided evidence that cerebellar social neuroanatomy can be contextualized within a larger triple representation principle that is common

across numerous non-motor domains in the cerebellar cortex. Specifically, similar to the well-established descriptions of a double motor representation in lobules I–VI and VIII (Snider and Eldred 1952), it has been demonstrated that all non-motor processes in the cerebellar cortex might simultaneously engage some aspects of lobules VI/Crus I (first non-motor representation), lobules Crus II/VIIIB (second non-motor representation), and lobules IX/X (third non-motor representation) (Buckner et al. 2011; Guell et al. 2018). In the same way, social processing exhibited a first and contiguous second representation in lobules Crus I/II and a third representation in lobule IX (Guell et al. 2018). This organization allows the parallel processing of complex information such as that required in social-affective behavior.

As a corollary of the UCT hypothesis, the same authors defined the ‘dysmetria of thought’ theory according to which the symptoms consequent to cerebellar damage can reflect universal cerebellar impairment, namely, dysmetria. In line with this, cerebellar malfunctioning can also lead to dysmetria in the cognitive and affective domains, which refers to the concept of dysmetria of the movement typical of patients with ataxia (Schmahmann 1991; Schmahmann and Sherman 1998). Indeed, in the motor domain, it is well known that a cerebellar lesion results in impairments of coordination, precision, and fluidity of motor control; in the same way, in the cognitive and affective domains, a cerebellar lesion leads to impaired coordination, precision, and fluidity of thought and emotion, including social processing (Schmahmann 2000; Schmahmann and Pandya 1997; Schmahmann et al. 2019). Impaired modulation of affect and mismatches between reality and perception of reality are central and defining features of psychoses, including schizophrenia and related disorders, bipolar affective disorders and related illnesses. Therefore, the role of the cerebellum in the pathophysiology of these conditions becomes plausible in the context of the dysmetria of thought hypothesis.

15.3.2.2 Cerebellar Sequencing and Prediction in Social Interactions

Increasing evidence on the functional diversity of structurally similar cerebellar modules has also enlarged the perspectives for hypothesizing other possible functional processes underpinning cerebellar influence in social-affective behavior. Within this framework, another theory was recently applied to explain the mechanisms by which the cerebellum is involved in non-motor processes, including social-affective domains, and is referred to as the “sequence detection theory” (Van Overwalle et al. 2020a; Leggio et al. 2008, 2011; Leggio and Molinari 2015). Sequencing is defined as the ability to perceive, represent, and execute spatio-temporal relations among events that follow a particular order. It can be considered a supra-modal function encompassing all human activities and crucial to the predictive processing of the brain (Savalia et al. 2016).

The “sequence detection theory” posits that the cerebellum plays a central role in sequencing (Leggio et al. 2008, 2011; Braitenberg et al. 1997). The cerebellum receives patterns of sequential temporal or spatial events via the pontine nuclei and compares them with information conveyed by climbing fibers. This interaction provides data regarding previously encountered sequences and consequently generates internal models useful in making predictions. Because of these mechanisms, the cerebellum can recognize sequential events and identify possible errors in the expected sequence, thereby acting as a feedforward controller that guarantees anticipatory actions (Molinari et al. 2009; Sokolov et al. 2017).

In the traditional view, the cerebellum has been related to motor processes, where internal models are considered to be responsible for the construction, detection, and application of motor sequences (Ito 2008). Through feedback and feedforward control, individuals become capable of predicting and adjusting movements in accordance with sudden environmental changes. More recently, Leggio et al. (2008) and Van Overwalle

et al. (2019b) proposed that during human evolution, the cerebellum advanced and began engaging in similar processes for purely mental sequences. The authors argued that the cerebellum is also involved in the construction of internal models of mental processes during social interactions, in which the prediction of sequential events plays a central role (Clausi et al. 2019b; Van Overwalle et al. 2019b). Specifically, in the social-affective domain, as in the sensorimotor domain, the cerebellum may act by matching external information (social inputs) with the internal model of a specific social event linked to previous experiences, contributing to the formation of judgements on the mental state of others and predicting the consequences of social actions based on an individual’s beliefs and the social norms (Koster-Hale and Saxe 2013). Thus, to accomplish these functions in a fluid and automated manner, the cerebellum might modulate higher-order cortical areas by detecting socially predictable sequences (e.g., internal model of a social action) and promoting optimized feedforward control over activity (Sokolov et al. 2017; Van Overwalle et al. 2019b; Middleton and Strick 2000). This allows us to anticipate and understand the consequences of others’ actions and to recognize deviations in the predicted outcomes of social interactions to modify future social expectations. When cerebellar damage occurs, fast and continuous information comparisons between external stimuli and internal model results are affected; thus, subjects fail to recognize deviations/errors in social interactions and to adjust their response according to social expectations, as recently observed in patients with cerebellar neurodegenerative diseases (Clausi et al. 2021; Van Overwalle et al. 2019c).

Strong support for these theoretical hypotheses also comes from recent fMRI studies in healthy subjects (Heleven et al. 2019), in which activation of regions in the posterior cerebellum was observed during the construction of sequences of social actions that required understanding of the mental state of the protagonist (e.g., involving false or true beliefs) or when social predictions

were violated (e.g., violations of social norms) (Berthoz et al. 2002).

Overall, the role of the cerebellum in predictive coding and adaptive control could be crucial in the social cognition domain because anticipation, adaptation, and learning are indispensable for successful social interactions and adaptive social behavior. This brain area could assist in learning and understanding social action sequences, supporting optimal predictions about imminent or future social interactions. In line with this theory, impaired sequencing and prediction mechanisms could be considered possible functional substrates of emotional and social-affective alterations in pathologies characterized by cerebello-cerebral dysfunctions.

15.4 Social-Affective Behavior in the Presence of Cerebellar Structural and Functional Alterations

The characterization of cerebellar involvement in specific aspects of emotional processing and social cognition and deeper knowledge of the mechanisms by which the cerebellum participates in social-affective domains assume strong significance in those pathological conditions that present both maladaptive social-affective behavior, and cerebellar structural and functional alterations. In the present section, we will focus on specific neurodegenerative diseases and psychiatric and neurodevelopmental conditions.

15.4.1 Social-Affective Behavioral Alterations in Patient with Cerebellar Pathologies

Evidence in the clinical field has shown that difficulties in recognizing basic emotions and difficulties with social behaviors are present in patients with focal and degenerative cerebellar pathologies (Adamaszek et al. 2014, 2015; Sokolovsky et al. 2010). Indeed, since the identification of emotional and affective changes found in patients with focal lesions of the cerebellum

leading to the description of the CCAS (Schmahmann and Sherman 1998), the number of studies assessing emotional and social competences in cerebellar patients has exponentially grown. Indeed, difficulties in empathizing and mentalizing abilities have been described in a patient with cerebellar stroke involving the vermis and the posterior regions of the cerebellar hemispheres (Gerschovich et al. 2011). Moreover, clinical studies have evidenced specific patterns of social-affective alterations in patients with different types of cerebellar degenerative pathologies. For example, difficulties in the recognition of emotions were found in individuals with complex cerebello-cerebral degeneration and patients with isolated cerebellar degeneration (Sokolovsky et al. 2010; Hoche et al. 2016), while patients with spinocerebellar ataxia type 1 showed selective difficulties in the attribution of mental states (Sokolovsky et al. 2010).

Interesting findings have come from a recent behavioral and neuroimaging study with patients affected by various forms of cerebellar ataxia (Clausi et al. 2019b). In this study, patients presented with difficulties in basic aspects of social behavior, such as emotional contagion and recognition of the emotions of others, and in its more complex aspects, such as the ability to simulate, anticipate, and predict mental states of others. Intriguingly, cerebellar patients also have gray matter reductions localized in specific portions of the cerebellum (vermis and bilateral Crus I/II), which showed decreased functional connectivity with cerebral areas involved in mirroring and mentalizing processes (Abu-Akel and Shamay-Tsoory 2011; Clausi et al. 2019b).

In a more recent anatomo-functional study in a homogeneous cohort of SCA2 patients (Clausi et al. 2021), alterations in social cognition were found to be associated with structural damage to specific cerebellar lobules and microstructural alterations in the cerebellar peduncles, which are involved in different aspects of social-affective processing. Specifically, the correlational analyses evidenced that impairments in anger attribution were mainly related to the degree of gray matter atrophy in right lobules VIIIB and IX. This finding is consistent with increasing

evidence that vermal and paravermal cerebellar areas are involved in the processing of ‘primitive’ emotions (Bauman and Mattingley 2012), such as fear of dangerous stimuli and anger towards aggressors (Schmahmann 1991), and participate in detecting, integrating, and filtering emotional information as a part of a cerebello-cortical-limbic network (Habas et al. 2009). In contrast, patients’ impairments in more complex components of social cognition were associated with atrophy in specific posterior cerebellar regions (right Crus II). As reported above, this cerebellar area is associated with complex brain networks involved in mentalizing abilities (Van Overwalle et al. 2014; Habas et al. 2009; Sokolov et al. 2017).

Moreover, the scores of the patients on the Reading the Mind in the Eyes test were related to the cerebellar peduncle microstructural damage reported in an SCA2 cohort (Olivito et al. 2017b). These data have been explained with consideration of the well-known function of the cerebellum as a predictor (Sokolov et al. 2017; Ito 2008). Indeed, since the abovementioned task requires determination of the meaning of the expression in the eyes and an automatic and rapid inference of another person’s mental state (Baron-Cohen et al. 2001), the cerebellum might act by matching the external information (i.e., expression of the eyes) with the individual’s internal model of eye region expression linked to previous experiences, thus contributing to an immediate judgment about the other’s mental state. Notably, the middle and posterior peduncles are the feedback and feedforward limbs of the cerebello-cortical system, respectively, through which the cerebellum receives information and sends information back to cerebral regions (Ramnani 2006). Therefore, it is reasonable to assume that fiber degeneration within the cerebellar peduncles could interfere with the communication between the cerebellum and the cortical projection areas involved in the more automatic mentalizing processes.

Considering the complexity of information processing in the social cognition domain and the cerebellar interplay with the brain networks involved in these processes, it is reasonable to infer that neuroanatomical damage that occurs in

cerebellar patients may account for their behavioral impairments and also alter cerebello-cortical interactions. Accordingly, in a recent study, altered inter-nodal connectivity between the right Crus II and cerebral areas involved in more complex aspects of mentalization, such as the dorsomedial prefrontal cortex and the TPJ, was found in SCA2 patients (Olivito et al. 2020).

In summary, the findings reported above offer a new point of view regarding specific symptomatology in patients with cerebellar ataxia, where the importance of links between social behavior difficulties and cerebellar damage has often been underestimated or neglected, with direct consequences on clinical practice.

15.4.2 Cerebellar and Social-Affective Alterations in Neurodegenerative Disorders and Psychiatric and Neurodevelopmental Conditions

Several studies have described impairments in social functioning and mentalizing processes not only in patients affected by cerebellar pathology (D’Agata et al. 2011; Sokolovsky et al. 2010; Clausi et al. 2019b) but also in individuals affected by neurodegenerative disorders (Poletti et al. 2012), such as Alzheimer’s and Parkinson’s diseases (Wu and Hallett 2013; Jacobs et al. 2018) and behavioral variants of frontotemporal dementia (Van den Stock et al. 2019), that have often been associated with cerebellar alterations.

A recent study suggested that the impaired cerebellar modulation described in sporadic Alzheimer’s disease may be predictive of the onset of cognitive and neuropsychiatric deficits (Jacobs et al. 2018). With this disease, cerebellar gray matter reductions have been found to progressively evolve, beginning with early involvement in the vermis and the posterior cerebellar lobe and extending to the anterior cerebellar lobe in more advanced stages (Jacobs et al. 2018; Toniolo et al. 2018). As both structural and functional cerebellar modifications progress in parallel with pathological changes in the cerebral cortex,

social-affective behavioral alterations evolve as well. Moreover, in people with Parkinson's disease, cognitive, behavioral, and mentalizing impairments arise after the onset of motor symptoms; this progression of disease parallels the degree of structural and functional changes occurring in both the cerebellum and cortical areas involved in higher-order functions (Wu and Hallett 2013; Camicioli et al. 2009; Nishio et al. 2010). Difficulties in the mentalizing domain have often been reported in patients affected by behavioral variants of frontotemporal dementia (Pardini et al. 2013; Desmarais et al. 2018), who show correlations between task performances and atrophy in posterior regions of the cerebellum (Crus I and II) (Van den Stock et al. 2019; Synn et al. 2018).

A specific role for the cerebellum has been hypothesized in the onset of emotional and mentalizing difficulties described in some psychiatric and neurodevelopmental disorders (Corcoran et al. 1995; Fatemi et al. 2012; Bora et al. 2016; Bora and Berk 2016). Indeed, a number of neuroimaging studies in individuals affected by schizophrenia, depressive and bipolar disorders, and ASD have shown structural and functional alterations in regions of the "social cerebellum" and in cerebello-cerebral mentalizing networks (Adler et al. 2007; Becker and Stoodley 2013; Kim et al. 2014). Specifically, microstructural disruptions in cerebro-cerebellar pathways (Kanaan et al. 2009) and intracerebellar white matter (Kim et al. 2014) were found in schizophrenic individuals, who often present with difficulties in the automatic process of mentalizing and fail to select the appropriate behavioral representation for understanding the actions and intentions of others (Das et al. 2012; Martinez et al. 2019). In these patients, alterations in cerebellar forward modeling have been considered to be the cause of hallucinations because of the inability to distinguish between internal states and external events (Frith et al. 2000; Ford and Mathalon 2012).

Moreover, altered functional connectivity between the posterior cerebellum and mentalizing regions, such as the TPJ, medial prefrontal cortex, and posterior cingulate, has been reported in

individuals with a diagnosis of bipolar disorder (Liu et al. 2012; Wang et al. 2015) and in those with depressive states. In particular, reduced volumes and decreased activity in the vermis and posterior cerebellar lobes (Adler et al. 2007; Mills et al. 2005; Narita et al. 2011; Kim et al. 2013; Sani et al. 2016) and reduced functional connectivity between the posterior cerebellum and the amygdala, inferior frontal gyrus (orbital), and striatum have been described in patients with bipolar disorder (Shaffer et al. 2018; Wang et al. 2016; Li et al. 2015). Likewise, decreased functional connectivity between the cerebellum and temporal and parietal regions has been shown in individuals with major depressive disorder (Guo et al. 2013).

In these clinical populations, including individuals in both manic and depressive states (Bora et al. 2016; Bora and Berk 2016) and remitted patients with bipolar disorder (Bora et al. 2005; Bora and Pantelis 2016), alterations in mentalizing are thought to affect social behavior. Accordingly, preliminary studies in patients affected by type 1 or type 2 bipolar disorder (in a euthymic state) showed specific mentalizing problems characterized by difficulties understanding another person's mental state and considering their beliefs and intentions (personal observations). In a recent single case study, Lupo and colleagues (Lupo et al. 2018) added new insight into the role of the cerebellum in socio-affective processing in the context of specific psychiatric conditions and demonstrated not only that there was an association between the onset of a manic state and the presence of a focal cerebellar lesion but also that the pattern of impaired functional connectivity in the patient overlapped with cerebello-cerebral mentalizing networks.

Finally, the cerebellum seems to be implicated in ASD (Fatemi et al. 2012), a neurodevelopmental condition mainly characterized by difficulties in ToM abilities (Baron-Cohen et al. 2001). Cerebellar dysfunction has recently gained attention as a potential biomarker of this condition (Fatemi et al. 2012). Indeed, early developmental damage in the cerebellum is considered one of the major risk factors for ASD (Wang et al.

2014) and has been associated with deficits in affective and internalizing behaviors and with social withdrawal (Limperopoulos et al. 2007), thus suggesting that atypical cerebellar development as well as dysfunctional cerebello-cerebellar networks could contribute to ASD-related behaviors (Stoodley and Limperopoulos 2016).

Further support for this idea has been derived from resting-state functional connectivity studies in individuals with ASD that reported reduced functional connectivity between specific regions in the posterior cerebellum and regions in the “social brain” relevant for social interaction. Indeed, low resting-state functional connectivity between the Crus II and the TPJ adjacent to the STS (Igelström et al. 2017) and altered functional connectivity between the dentate nucleus and the cortical regions involved in social cognition were reported in adults with ASD (Olivito et al. 2017a, 2018). Accordingly, a recent study in ASD showed that more severe scores on the Autism Diagnostic Observation Schedule were associated with the degree of hypo-connectivity between Crus I/II and lobule IX and brain areas involved in language, emotional and social domains, including the bilateral STS, inferior frontal gyrus, amygdala and specific nodes in the default mode network (Arnold Anteraper et al. 2019).

Taken together, these observations suggest that the study of cerebellar functioning in these pathologies could be crucial for a better comprehension of the neurobiological bases of social behavior impairments in neurodegenerative and psychiatric disorders, holding great promise for a better understanding and treatment of a variety of social impairments.

15.5 Conclusions and Future Directions

In the present chapter, we have described converging evidence from clinical studies in patients with cerebellar alterations and fMRI and neurostimulation studies in healthy individuals that point to recognizing the involvement of the cerebellum in specific aspects in the social-affective domain. The emotional and affective components

of social skills are crucial for adaptation to the surrounding environment, especially in the presence of pathological conditions. A better comprehension of the mechanisms by which the cerebellum influences the neural substrates of social-affective behavior could have important clinical implications not only in the presence of a cerebellar pathology but also in specific psychiatric and neurodevelopmental disorders.

Knowledge of these aspects is essential in clinical practice because, on the one hand, behavioral alterations can have an impact on quality of life and compliance with pharmacological and rehabilitative treatments of individuals; on the other hand, knowing the neural basis of these alterations can facilitate the development of rehabilitation protocols to modulate cerebellar excitability, allowing clinicians to influence/improve symptomatology in individuals suffering from social-affective alterations. Among these innovative treatments, non-invasive neuro-stimulation techniques should be mentioned as a useful method for investigating the causal and potential clinical role of the cerebellum in social functioning (van Dun et al. 2017).

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