Motivation Science

ISSN: 2333-8113

2022, Vol. 8, No. 2, 150–160
https://doi.org/10.1037/mot0000251

The Cerebellum in Aggression: Extending the Cortico-Limbic Dual-Route Model of Motivation and Emotion

Eline S. Kruithof, Jana Klaus, and Dennis J. L. G. Schutter
Department of Experimental Psychology, Helmholtz Institute, Utrecht University

According to the dual-route model of emotion, impulsive (affective) aggression involves fast acting limbic regions, whereas in instrumental (predatory) aggression the neural focus lies on top-down anterior cortical areas. However, increasing neuroscientific evidence now points toward differential involvement of the cerebellum in the aggression circuit. In particular, the medial cerebellum, the vermis, is suggested to be part of the limbic circuit involved in fast, preattentive processing during imminent threat and provocation, mediating impulsive forms of aggression. By contrast, the lateral cerebellar hemispheres with their connections to the motor and prefrontal cortex provide a substrate for the top-down regulatory control mechanisms that allow for premeditated and instrumental forms of aggression. This theoretical account can be reconciled with the involvement of the cerebellum in homeostatic functions and predictive coding. The available scientific evidence provides an empirical basis for the view that the cortico-limbic dual-route model of aggression should be extended to include the cerebellum.

Keywords: aggression, cerebellum, dual-route model, emotion

Aggression can be characterized as behavior directed toward harming or injuring another living being who is motivated to avoid such treatment (Blair, 2016). The neural circuitry underlying aggression consists of subcortical limbic and cerebral cortical areas, where the subcortical regions are conserved across mammalian species and subserve survival-related behaviors (LeDoux, 2012; Panksepp & Zellner, 2004; Siegel & Pott, 1988). The limbic circuit makes up a complex network that connects sensory thalamic nuclei to the amygdala, hypothalamus and periaqueductal gray (PAG) and allows an organism to survive and thrive by fast detection of and responding to environmental challenges and opportunities (LeDoux, 2012). In particular, the amygdala is involved in automatic, preattentive threat detection (LeDoux, 2000). Following threat detection, the dorsomedial hypothalamus and PAG receive input from the amygdala and are involved in the initiation of autonomic responses associated with fight–flight behavior (Fontes et al., 2011; Mobbs et al., 2007; Todd & Machado, 2019). Cortical association areas including the prefrontal cortex interact with the limbic circuit by exerting a top-down modulatory influence over these structures (Fontes et al., 2011; Mobbs et al., 2007; Todd & Machado, 2019). Specifically, the dorsolateral parts of the prefrontal cortex are involved in appraisal and expression of survival behaviors, whereas the ventromedial parts serve an integrating and regulatory function on emotion (Alia-Klein et al., 2020; Etkin et al., 2011; Ochsner et al., 2012).

Eline S. Kruithof https://orcid.org/0000-0001-5054-694X
Jana Klaus https://orcid.org/0000-0003-4398-8672
Dennis J. L. G. Schutter https://orcid.org/0000-0003-0738-1865

The authors have no competing interests to declare. This work was supported by the Dutch Research Foundation (NWO, VI.C.181.005).

Correspondence concerning this article should be addressed to Eline S. Kruithof, Department of Experimental Psychology, Helmholtz Institute, Utrecht University, Heidelberglaan 1, 3584 CS, Utrecht, the Netherlands. Email: e.s.kruithof@uu.nl

Impulsive and Instrumental Aggression and Their Neural Underpinnings

In humans and other mammals, roughly two forms of aggression can be distinguished: Impulsive (affective) and instrumental (predatory) aggression. Impulsive aggression typically occurs in response to an unescapable threat or provocation and is accompanied by a strong sympathetic physiological response (Meloy, 1988; Siegel et al., 1997; Weinshenker & Siegel, 2002). In cats, affective attack elicited by injecting a neurokinin 1 receptor agonist in the medial hypothalamus is characterized by growling, hissing, agitation, pupillary dilatation and rearing (Bhatt et al., 2003). By contrast, instrumental aggression often involves more premeditated and goal-directed behavior in the absence of sympathetic arousal (Blair, 2010; Meloy, 1988; Weinshenker & Siegel, 2002). Although instrumental aggression in humans may initially be less prey-centered as compared to predatory aggression in animals, both forms of aggression nonetheless do share behavioral characteristics (Siegel & Victoroff, 2009; Weinshenker & Siegel, 2002). In support of this assumption, comparative research has provided evidence for the idea that animals and humans share neural and physiological characteristics that link predatory aggression in animals to instrumental aggression in humans (LeDoux, 2012; Panksepp, 2011; Panksepp & Zellner, 2004).

In both humans (Blair, 2016) and animals (Panksepp & Zellner, 2004), the limbic system, which includes the amygdala, medial hypothalamus and PAG, mediates impulsive aggression. The activation of the medial hypothalamus and PAG, both involved in

initiating autonomic responses, is suggested to be critical for the sympathetic arousal observed during impulsive aggression (Panksepp & Zellner, 2004). The prefrontal cortex can exert a modulatory role over subcortical limbic regions underlying impulsive aggression (Blair, 2016; Panksepp & Zellner, 2004; Potegal, 2012). Instrumental aggression is argued to be another form of goal-directed behavior that is no different from any other motor response and as such is mediated by the motor cortex and the caudate (Blair, 2010). Whereas impulsive aggression is mediated by the medial hypothalamus, animal studies suggest that the lateral hypothalamus is involved in instrumental aggression (Gregg & Siegel, 2001; Siegel & Victoroff, 2009). Furthermore, prefrontal regions and the brain's reward circuit (e.g., ventral striatum) are suggested to be part of the brain regions that are recruited during instrumental aggression, both in human (Nelson & Trainor, 2007) and nonhuman mammals (Panksepp & Zellner, 2004). As mentioned earlier, the prefrontal cortex is involved in impulsive aggression as well. However, when threat is imminent and potentially life threatening, the brain's subcortical survival circuit will overrule the cortical control processes to allow for fast defensive responses (Mobbs et al., 2007). We suggest that the contribution of the prefrontal cortex differs between impulsive and instrumental aggression. For impulsive aggression, the role of prefrontal regions is to inhibit ongoing aggressive behavior (Blair, 2016; Potegal, 2012). This is relevant in the context of the violence inhibition mechanism, where ceasing of aggression is the result of the opponent's submissive cues (Blair, 1995). In instrumental aggression the role of prefrontal cortical regions lies more in governing cognitive control mechanisms that facilitate the premeditated and goal-directed nature of this type of aggressive behavior. Additionally, researchers suggest that reward can play a role in impulsive aggression as well (Chester & DeWall, 2016), in particular frustrative nonreward that activates the ventral striatum together with the insula and frontal brain areas (Bertsch et al., 2020). Yet, activation of reward-dedicated brain regions is generally more associated with instrumental aggression, which corresponds to the anticipation and outcome of reward serving as the primary motivation (Siegel & Victoroff, 2009). In contrast, the core motivation underlying impulsive aggression has more to do with getting rid of unescapable frustration or threat. Here, we aim to provide a theoretical framework that is based on the evolutionary lineage of the mammalian species in which the primordial circuits dedicated to motivation and emotion have been conserved in humans (Panksepp, 2011). The cerebral cortical system is proposed to be an expansion of these more ancient subcortical (limbic) circuits which allows for more complex forms of behavior (Giaccio, 2006). In this review we argue that the cerebellum followed a similar evolutionary trajectory which together with its intrinsic connections to the cortico-limbic regions should be considered in psychoneural theories of aggression.

The Cerebellum in Aggressive Behavior

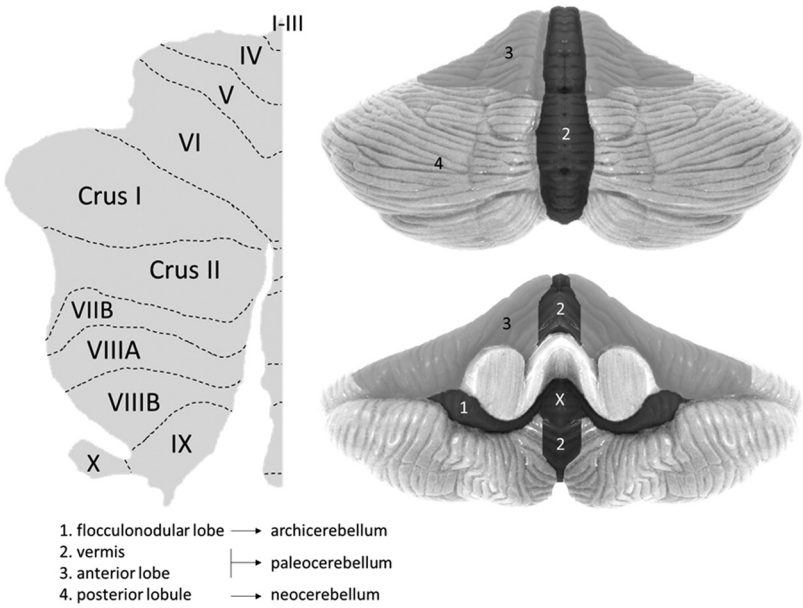
The cerebellum is a brain structure located in the posterior fossa of the skull beneath the tentorium and the occipital lobe of the cerebral hemisphere (O'Hearn & Molliver, 2001). Although it represents 10% of total brain weight, it accounts for more than 50% of total neurons present in the human brain (Cardinali, 2017). In addition, the surface of the cerebellar cortex makes up 80% of the total surface of the cerebral cortex (Sereno et al., 2020). During the course of evolution, the cerebellum expanded in concert with the cerebral cortex, particularly with prefrontal and association areas (Balsters et al., 2010; Weaver, 2005). The cerebellum consists of a three-layered cortex, deep cerebellar nuclei (DCN) and white matter (O'Hearn & Molliver, 2001). From a phylogenetic point of view, it can be divided into three parts: the archicerebellum (flocculonodular lobe), paleocerebellum (anterior lobe and vermis) and neocerebellum (posterolateral hemispheres; O'Hearn & Molliver, 2001). The archicerebellum, the phylogenetically oldest part of the cerebellum, is connected to the vestibular system and reticular formation in the brainstem and is implicated in the control of body posture and ocular movements (Cardinali, 2017; Schutter, 2013). The paleocerebellum is connected with the spinal cord and the brainstem as well as subcortical structures (Schutter, 2013). It controls proximal musculature, posture, muscle tone and reflexes (O'Hearn & Molliver, 2001). Moreover, its connections with subcortical structures underlie its role in motivation and emotion (Schutter, 2013). The neocerebellum is the phylogenetically youngest part of the cerebellum and is involved in motor planning as well as higher-order affective and cognitive functions (Adamaszek et al., 2017; O'Hearn & Molliver, 2001). Alternatively, the cerebellum can be divided into lobes and lobules. The anterior lobe, which is mainly involved in sensorimotor function (Stoodley & Schmahmann, 2009), consists of lobules I-V (O'Hearn & Molliver, 2001), whereas the posterior lobe is mainly involved in cognitive functions (Stoodley & Schmahmann, 2009) and consists of lobules VI-IX (O'Hearn & Molliver, 2001). The flocculonodular lobe is equivalent to lobule X (O'Hearn & Molliver, 2001). Figure 1 depicts the anatomy of the cerebellum.

While the cerebellum has received little attention in the neuroscientific study of emotion, the aim of this selective review is to discuss the available empirical evidence in support of cerebellar involvement in aggression. To address this assumption, lesion studies, structural and functional neuroimaging work and brain stimulation studies will be discussed. The evidence supports an extension of the existing cortico-limbic dual-route model of motivation and emotion to the cerebellum in the context of aggression.

Lesion Studies

Patients with congenital or acquired cerebellar abnormalities provide an important line of empirical work that contributes to insights on the role of the cerebellum in aggression. Acquired cerebellar damage can cause behavioral impairments known as the cerebellar cognitive affective syndrome or Schmahmann's syndrome, which is characterized by disturbed executive functioning, impaired spatial cognition, language deficits and emotion dysregulation (Greve et al., 1999; Hoche et al., 2018; Schmahmann & Sherman, 1998). Impairments in emotion regulation include increases in impulsivity, irritability, anger and aggression (Greve et al., 1999; Kronemer et al., 2021; Schmahmann et al., 2007). Lesions of the vermis in particular are associated with emotional problems and behavioral disturbances (Schmahmann & Sherman, 1998). Interestingly, most cerebellar patients displaying anger or aggression show lesions that include the vermis (Schmahmann et al., 2007). Although these findings are in contrast with observations in cats and monkeys, where a taming effect has been reported after vermal lesions (Berman et al., 1974; Peters & Monjan,

Figure 1
Basic Neuroanatomy of the Cerebellum



Note. Flatmap showing the lobular organization of the cerebellum (A) and main cerebellar structures according to evolutionary developmental biology (B).

1971), the link between the vermis and aggression is nonetheless notable.

Studies in pediatric populations further add to our understanding of the involvement of the cerebellum in anger and aggression. Neuropsychological evaluations in children with cerebellar lesions and malformations indicate that the cerebellar cognitive affective syndrome is evident in children as well (Levisohn et al., 2000; Tavano et al., 2007). In several studies, vermal lesions were associated with impaired regulation of affect and behavioral disturbances (Levisohn et al., 2000; Richter et al., 2005; Riva & Giorgi, 2000; Steinlin et al., 2003; Tavano et al., 2007). Based on self-ratings and parental ratings of changes in behavior and affect after cerebellar tumor resection, Richter et al. (2005) reported increased aggression in two out of nine children with lesions that included the vermis. Notably, the lesion was confined exclusively to the vermis in one of these patients. Conversely, another patient showed reduced aggression, which is an interesting finding that does not concur with the theory that the vermis is involved in affect dysregulation. However, as this patient had an extensive lesion from lobule III extending to lobule X, which was not limited to the vermis, lesions in more lateral regions may account for the observed reduction in aggression. A recent case study of a boy who exhibited psychiatric symptoms including aggression as a consequence of a congenital cerebellar lesion characterized by agenesis of the vermis and fusion of cerebellar hemispheres supports the notion that vermal abnormalities can be accompanied by aggression (Schutter et al., 2021).

In sum, lesion studies provide evidence for the role of the cerebellum in aggression. Lesions and malformations of the vermis particularly are associated with emotional dysregulation and behavioral disturbances, including anger and aggression.

Structural MRI Studies

Structural brain alterations have been observed in psychopathic, antisocial and violent individuals and can give insights in brain regions that are involved in aggression. Whereas reductions in gray matter volume are predominantly found in prefrontal, temporal and limbic regions (Aoki et al., 2014; Gregory et al., 2012; Rogers & De Brito, 2016; Tiihonen et al., 2008; Yang et al., 2009; Yang & Raine, 2009), findings for the cerebellum are less consistent, as both reductions and increases in gray matter volume have been reported in these individuals.

Lower gray matter volumes in the left cerebellum, specifically lobules I–IV, V and VIIB, and in right lobule VIIB have been observed in antisocial offenders compared to controls (Bertsch et al., 2013). Additionally, Puri et al. (2008) reported total cerebellar gray matter volume reductions in schizophrenic patients with a history of violent offenses as compared to nonviolent patients with schizophrenia. A study in healthy adolescents showed that higher aggression scores were associated with lower gray matter volumes of the left anterior lobe and lower gray matter volumes of right posterior lobules VIIB and VIIIA (Wolfs et al., in press). In boys with conduct disorder, smaller gray matter volumes have been found in bilateral Crus I (Dalwani et al., 2011) and right lobule VIIIB and X (Zhang et al., 2018). Furthermore, lower gray matter volume and gray matter concentration of the vermis have been demonstrated in this patient population (De Brito et al., 2009; Huebner et al., 2008). In contrast, Huebner et al. (2008) reported enhanced bilateral gray matter volume in lobule IX in boys with conduct disorder. This finding is in line with results from Leutgeb et al. (2015), who reported increased gray matter volumes in lobule IX as well as in vermal lobule I–IV in male high-risk offenders relative to controls. Additionally, increased gray matter

volumes have been found in left Crus I in violent offenders (Leutgeb et al., 2016). Another study in violent offenders with antisocial personality disorders and substance dependence reported larger white matter volumes in the left cerebellum and larger gray matter volumes in the right cerebellum (Tiihonen et al., 2008). Gray matter volumes in both right and left vermal and lateral cerebellar regions correlated positively with interpersonal and affective psychopathic problems, risk of recidivism, temperament and anger in violent offenders (Leutgeb et al., 2015). Similarly, impulsivity was correlated positively with gray matter volumes of the posterior vermis in healthy adolescents (Wolfs et al., in press).

Volumetric reductions are typically found in brain regions involved in emotional processing, morality, decision-making, learning and behavioral control (Santana, 2016; Tiihonen et al., 2008; Yang & Raine, 2009) and provide insights into the functional neuroanatomic substrate of antisocial and violent behaviors. The observation of a positive relationship between vermal gray matter volumes and impulsivity supports the idea that structural alterations reflect abnormalities in behavioral control (Wolfs et al., in press), facilitating aggressive behavior arguably as a result of diminished inhibitory cerebellar output to the forebrain. In psychopaths, smaller posterior cerebellar volumes were associated with worse recognition of emotional faces (Pera-Guardiola et al., 2016), suggesting that the relationship between the cerebellum and aggression may involve abnormalities in emotion perception. It should be noted that larger volumes do not necessarily imply better functionality, as larger brain volumes could also be indicative of atypical neural development that promotes early-onset aggressive behavior (Tiihonen et al., 2008).

In sum, both differences in gray matter volume observed in cerebellar regions of violent individuals and associations between cerebellar volume differences and indices of aggression and impulsivity support the idea of cerebellar involvement in aggression.

Functional MRI Studies

Because anger is an emotional state that drives aggression (Panksepp & Zellner, 2004), fMRI studies on the involvement of the cerebellum in anger are relevant for understanding the relationship between the cerebellum and aggression. During anger processing, hemodynamic activity has been reported in left Crus I, left Crus II, left lobule VIIB, right and vermal lobule V and vermal lobule VI (Grosbras & Paus, 2006; Lin et al., 2016; Park et al., 2010; Spoont et al., 2010). Cerebellar activity patterns associated with anger processing have been confirmed in a recent meta-analysis in which anger and threat processing were shown to evoke activity in bilateral Crus I and Crus II, right lobule VI and left lobules VIIIA, VIIIB and X (Klaus & Schutter, 2021). In a previous study that investigated the functional cerebellar topography of primary emotions, anger evoked activity in vermal, paravermal and right lobule VI, vermal lobule IX and right Crus I (Baumann & Mattingley, 2012). However, activity in lobule VI and Crus I was not specific for anger processing as the activity overlapped with cerebellar activity during fear processing. Importantly, both anger and fear are emotions that are elicited in response to threat (Blair, 2012; LeDoux, 2000), suggesting that these emotions share a common neural pathway that is involved in the processing of threat-related stimuli and that mediates autonomic fight-flight responses (Baumann & Mattingley, 2012). The subcortical circuit is likely to be implicated in this shared neural network, given its involvement in survival behaviors and association with affective attack (LeDoux, 2012; Panksepp & Zellner, 2004; Siegel & Pott, 1988).

Brain activity associated with aggression is typically investigated in laboratory paradigms that evoke aggression through provocation and frustration. The studies that will be discussed here focused on healthy volunteers. The Taylor Aggression Paradigm (TAP; Taylor, 1967) is among the most frequently used laboratory aggression tasks and starts with a decision phase, during which the severity of the prospective punishment (i.e., a noise blast) of the opponent is set by the participant. This phase is then followed by a competitive reaction time (RT) task and an outcome phase, during which the actual punishment is administered to the player who lost the game. Buades-Rotger et al. (2017) reported activation in right lobule VI when participants decided to face the opponent, implying that they would compete in another RT trial of the TAP. Neural activity specific to retaliation (i.e., selecting a high punishment under provocation) has been found in right lobules I-IV, V and VI (Chester & DeWall, 2016; Dambacher, Sack, et al., 2015; Krämer et al., 2007). Krämer et al. (2007) reported activity in right Crus I when participants won the RT task, as well as activity in left Crus I when participants won after high provocation compared to low provocation. Confrontation with high compared to low provocation in the feedback phase was associated with activity in left Crus I and left lobule VI (Wagels et al., 2019).

Violent video games, social exchange paradigms and the Point Subtraction Aggression Paradigm (PSAP; Cherek et al., 1997) are other tasks used to elicit aggression through provocation. Activity in right Crus I has been observed when participants engaged in a violent video game and was postulated to reflect higher sensorimotor integration needed to control the violent video game with the right hand (Mathiak & Weber, 2006). In a social fairness game, participants could accept a fair or unfair monetary offer of a partner in exchange for $3 or they could spend some of their $3 to punish the partner for his or her offer (White et al., 2014). Increased right-sided activity in lobules V, VI and Crus II accompanied by decreased activity in left lobule V was observed as participants' punishment of the partner increased. According to the authors, cerebellar activity is consistent with an affective aggressive response to provocation, instead of a reward-related response to being treated unfairly. Based on increased activity in both impulsive aggressive individuals and controls, left lobule VI has been identified as a region specifically implicated in choosing retaliation over monetary reward on the PSAP (Gan et al., 2016).

A region consistently linked to aggression in fMRI studies is the cerebellar anterior lobe. A meta-analysis on the functional topography of the cerebellum demonstrated that lobule V and adjacent lobule VI are activated across sensorimotor tasks (Stoodley & Schmahmann, 2009), suggesting that activity in these areas observed during aggressive behavior reflects a motor component of the aggressive response. Activity related to motor functioning would be plausible, given the motor response that usually has to be executed in laboratory aggression paradigms. A meta-analysis on the functional topography of aggression in the cerebellum showed that aggression evoked activity in lobules V and VI, thus overlapping with the regions involved in sensorimotor functioning (Klaus & Schutter, 2021). Clusters of activity in the anterior lobe displayed connectivity with the somatomotor and default mode network, providing additional support for the notion that activity in the anterior lobe is associated with motor execution during

aggression. Another meta-analysis on neural networks of aggression showed that the right cerebellum, the peak of the cluster being located in lobule V, is connected with cerebral somatosensory regions during elicited aggression (Wong et al., 2019). This network was found to be involved in the execution, preparation and mental imagery of actions.

Whereas the anterior lobe of the cerebellum is specialized in sensorimotor functioning, the posterior lobe is known to be involved in cognitive and emotional functioning (Stoodley & Schmahmann, 2009). As such, activity observed in the posterior lobe of the cerebellum during aggression, which is located particularly in Crus I and Crus II, is likely to reflect the recruitment of those functions. Crus I and Crus II are involved in a variety of cognitive functions that could underlie anger experience and expression of aggressive behavior (E et al., 2014; Stoodley & Schmahmann, 2009). Arguably, activity in these regions could reflect efforts to maintain self-regulation when being provoked, as well as improvements in focus and self-monitoring abilities that enable optimal performance in a competitive provocation task. Furthermore, the role of these regions in social cognition indicates that activity could reflect social–cognitive processes during aggression (Van Overwalle et al., 2014, 2020). This is supported by overlap in posterior lobe activity between retaliation and cognitive processes, particularly hostile attribution bias and negative emotional response (Coccaro et al., 2021), which are associated with aggression (Coccaro et al., 2017; Tuente et al., 2019). Because anger facilitates aggression, the roles of Crus I in anger processing (Baumann & Mattingley, 2012) and Crus II in emotional self-experiences (Van Overwalle et al., 2020) suggest that these emotional functions may underlie activity related to aggression as well. The preference for processing negative emotional stimuli that is observed in several cerebellar regions, including Crus I and Crus II, implies that the cerebellum is involved particularly in goal-directed behavior in reaction to negative emotional stimuli (Schraa-Tam et al., 2012). It is therefore conceivable that activity in Crus I and Crus II reflects emotional processes that guide goal-directed behavior during aggression.

Finally, it should be noted that thus far, only a limited number of fMRI studies investigating neural correlates of anger and aggression reported cerebellar activation. This underrepresentation may partly be explained by a selective preference for frontal brain regions in scanning parameters and analysis pipelines (Schlerf et al., 2014), making it difficult to actually detect responses in the cerebellum. Consequently, future studies are strongly encouraged to include the cerebellum in scanning protocols, which would allow for a more accurate picture on neural regions involved in anger and aggression.

In sum, activity that is observed in the anterior lobe, specifically lobule V and adjacent lobule VI, during aggression likely represents motor execution. By contrast, activity in the posterior lobe associated with aggression may reflect the recruitment of processes related to emotion and cognition.

Brain Stimulation Studies

Direct evidence for the involvement of the cerebellum in aggression stems from early intracranial brain stimulation studies in animals and humans. In animals, electrical stimulation of the DCN (i.e., fastigial nucleus) in cats elicited sham rage (Zanchetti & Zoccolini, 1954) and affective attack (Reis et al., 1973). Recently, increasing Purkinje cell activity in the cerebellar cortex of the vermis via optogenetic stimulation in mice was shown to significantly reduce the frequency of attacks toward an intruder (Jackman et al., 2020). Conversely, inhibiting Purkinje cell activity in the vermis had the opposite effect. This finding concurs with the inhibitory projections of the Purkinje cells to the DCN (Telgkamp & Raman, 2002) which, in turn, reduce the DCN excitatory drive to extracerebellar regions including the hypothalamus. In psychiatric patients, electrical stimulation of electrodes implanted in the vermis led to substantial improvements of aggressive behavior (Heath, 1977; Heath et al., 1980).

In line with electrical stimulation studies in animals (Reis et al., 1973; Zanchetti & Zoccolini, 1954), results from a noninvasive transcranial magnetic stimulation (TMS) study in humans support the hypothesis that the cerebellum is involved in autonomic activity underlying aggression. Increasing excitability of the vermis using intermittent theta burst stimulation caused a significant decrease in heart rate (Demirtas-Tatlidede et al., 2011). Reciprocal projections from the cerebellum to the hypothalamus, a critical region involved in regulating autonomic responses (Fontes et al., 2011; Todd & Machado, 2019), are proposed to underlie this modulatory effect of the cerebellum on autonomic functions (Wen et al., 2004; Zhu et al., 2006). Furthermore, inhibitory low-frequency TMS over vermis was shown to impair emotion regulation (Schutter & Van Honk, 2009). The link between lower emotion regulation and increased anger after provocation (Mauss et al., 2006) and aggression (Holley et al., 2017) suggests that cerebellar-related impairments in emotion regulation may underlie aggression. In another study, the administration of transcranial direct current stimulation (tDCS) to the medial cerebellum provided evidence for cerebellar involvement in response inhibition (Wynn et al., 2019), adding further support to the proposed links between the cerebellum, behavioral control and aggression (Denny & Siemer, 2012; Madole et al., 2020; Pawliczek et al., 2013). Moreover, noninvasive brain stimulation studies have demonstrated that the cerebellum is implicated in anger processing. Anodal and cathodal cerebellar tDCS enhanced the recognition of facial anger (Ferrucci et al., 2012). TMS over the left posterior medial cerebellum interfered with participants' ability to discriminate between an angry and either another negative or positive body posture, but not with the ability to discriminate between body postures displaying positive emotions (Ferrari et al., 2019).

In sum, electrical and optogenetic stimulation in animals as well as intracranial brain stimulation in humans provides direct evidence for the role of the cerebellum in aggression. Noninvasive brain stimulation studies have provided additional support for cerebellar contributions to physiologic, cognitive and emotional processes of aggression.

Discussion

In the previous sections, evidence from lesion, structural and functional neuroimaging and brain stimulation studies was presented in support of the involvement of the cerebellum in aggression. It seems reasonable to assume that different regions of the cerebellum will be involved in implementing goal-directed behavior versus the more automatic responses associated with impulsive aggression. In support, the vermis with its connections to the PAG and limbic system has been linked to physiological arousal and impulse regulation. The posterolateral cerebellum as part of the

cerebello-cortical system is proposed to play a more pronounced role in the cognitive control mechanisms associated with the regulation of premeditated and goal-directed forms of aggression. As such, the findings warrant an extension of the cortico-limbic dual-route model of motivation and emotion to the cerebellum in the context of aggression. In this extended model, the fast route involves the vermis and the slow route involves the lateral cerebellar hemispheres, which are particularly relevant for impulsive (affective) and instrumental (predatory) aggression, respectively.

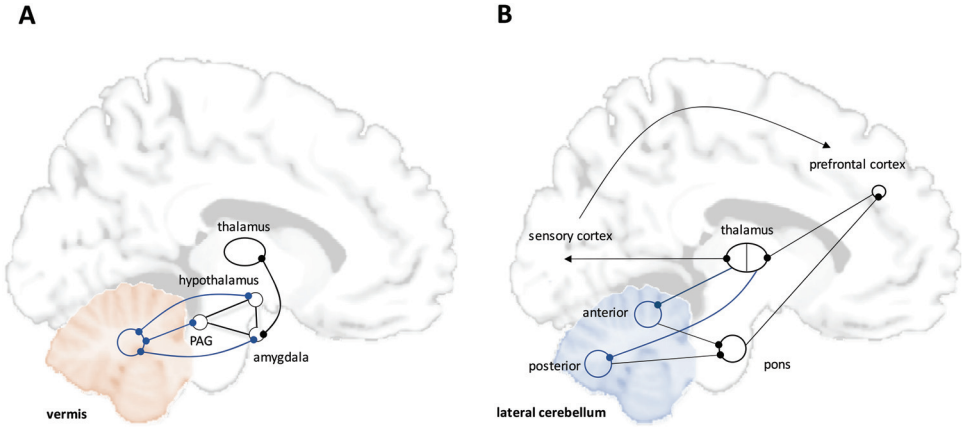
It should be noted that impulsive aggression seems to be an overly broad concept that covers at least offensive and defensive aggression, which are considered to be quite distinct forms of behavior by many researchers who study aggression in animals. Offensive aggression is likely anger-related and often occurs in response to loss of resources, whereas defensive aggression is likely fear-related and often occurs in response to threats when the animal cannot escape (Blanchard & Blanchard, 2003). As noted earlier, impulsive aggression is mediated by the amygdala, medial hypothalamus and PAG (Panksepp & Zellner, 2004). These regions are important in the detection of and response to threat (Blair, 2016; Méndez-Bértolo et al., 2016). Animal research shows that the vermis has connections to the limbic system including the hypothalamus (Schmahmann, 2000; Wen et al., 2004; Zhang et al., 2016). Based on these connections, the vermis has been coined the "limbic cerebellum" (Schmahmann et al., 2007) and arguably participates in impulsive forms of aggression. This assumption is supported by several lines of evidence reviewed above that show specific involvement of the vermis in functions particularly important in impulsive aggression. First, insights on the role of the vermis in the regulation of cardiovascular responses during aggression, as demonstrated in animal (Reis et al., 1973; Zanchetti & Zoccolini, 1954) and human (Demirtas-Tatlidede et al., 2011) brain stimulation studies, add to the idea that the vermis is involved in impulsive aggression. Contrary to instrumental aggression, which is characterized by low autonomic arousal, impulsive aggression is marked by heightened autonomic arousal (Conner et al., 2009; Vitiello & Stoff, 1997; Weinshenker & Siegel, 2002). Connections of the vermis with the hypothalamus provide a neuroanatomical pathway for autonomic arousal associated with impulsive aggression (Wen et al., 2004; Zhu et al., 2006). Additionally, anger, one of the main emotions driving impulsive aggression (Panksepp & Zellner, 2004), evokes activity in the vermis (Baumann & Mattingley, 2012; Ferrari et al., 2019; Spoont et al., 2010). It should furthermore be noted that other emotions that signal threat, for example fear and disgust, evoke activity in the vermis as well (Baumann & Mattingley, 2012). These findings indicate that the vermis is part of the subcortical survival circuit involved in fast threat detection and the automatic initiation of fight-flight behaviors. Indeed, the rapid detection of and response to salient information is subserved by the subcortical thalamo-amygdala circuit (LeDoux, 1995, 1996, 2012). Furthermore, the involvement of the medial cerebellum in emotion regulation (Schutter & Van Honk, 2009) and response inhibition (Wynn et al., 2019), as indicated by noninvasive brain stimulation studies in humans, demonstrates that the vermis is an integral part of the brain's subcortical survival circuit. Finally, the role of the vermis in impulsive aggression is supported by human lesion studies, showing that lesions or malformations of the vermis are consistently associated with emotion dysregulation, anger and aggressive behavior (Levisohn et al., 2000; Richter et al., 2005; Riva & Giorgi, 2000; Schmahmann et al., 2007; Schmahmann & Sherman, 1998; Schutter et al., 2021; Steinlin et al., 2003; Tavano et al., 2007).

Based on this evidence, a circuit comprising the vermis, thalamus, amygdala, hypothalamus and PAG is suggested to provide a fast route in the context of aggression that is particularly relevant for impulsive aggression. This pathway extends the fast route proposed by LeDoux (1995, 1996), which runs from the thalamus to the amygdala and enables rapid processing of salient stimuli. The fast subcortical route applies to impulsive aggression, as this form of aggression is driven by anger, is characterized by autonomic arousal and requires fast responding to imminent threat and provocation.

Instrumental aggression is suggested to be mediated by the lateral hypothalamus, motor and reward regions and higher cortical systems (Blair, 2010; Gregg & Siegel, 2001; Nelson & Trainor, 2007; Panksepp & Zellner, 2004; Siegel & Victoroff, 2009). The evolution of cerebellar lateral lobules mirrored the development of neocortical areas to which they are connected (Balsters et al., 2010). This simultaneous development indicates that these regions are functionally coupled and subserve higher cognitive functions in humans (Balsters et al., 2010). Posterior lateral regions, specifically Crus I and Crus II, are selectively connected to prefrontal cortices (Buckner et al., 2011; Sang et al., 2012) and thus offer a neural gateway for top-down modulation of the experience and expression of anger and aggression that is more cognitively oriented (Ochsner & Gross, 2005). Given the coevolution of and connections between these regions, the recruitment of posterolateral cerebellar regions during aggression is suggested to reflect cognitive control mechanisms that are particularly relevant for instrumental aggression, as these mechanisms enable deliberate and goal-directed behavior.

Lobules IV and V in the anterior lobe and lobule VI in the posterior lobe are connected to cerebral somatomotor cortices (Buckner et al., 2011; Sang et al., 2012). As such, these regions are suggested to be involved in motor functioning during aggression. Motor regions that are recruited during aggression might also reflect approach-related motivational tendencies that guide the transition from motivation to action. Indeed, the previously discussed meta-analysis on cerebellar functional activity patterns associated with aggression suggests that the right-sided activity observed in lobules V and VI during aggression reflects sensorimotor processes related to approach motivation caused by frustration and/or provocation (Klaus & Schutter, 2021). The crossed cerebello-thalamo-cortical and cortico-pontine-cerebellar loops (Kelly & Strick, 2003; Palesi et al., 2015) provide a neuroanatomical basis for approach- and avoidance-related aggressive behaviors. Functional asymmetries underlying nonmotor functions in the cerebral cortex show parallel but reversed asymmetries in the cerebellum (Wang et al., 2013). Accordingly, the lateralization of approach-avoidance motivations in the frontal cortex, where approach motivation is relatively left-lateralized and avoidance motivation is relatively right-lateralized (Kelley et al., 2017; Schutter & Harmon-Jones, 2013), would hypothetically be mirrored in the cerebellar hemispheres (Schutter, 2020). Instrumental aggression is driven by a strong reward-related motivation to achieve a certain state of affairs (Panksepp & Zellner, 2004), suggesting that the motivation to approach is central for this form of aggression. This is supported by human studies that demonstrate a link between instrumental forms of aggression and reduced

Figure 2
The Cerebello-Cortico-Limbic Dual-Route Model of Aggression



Note. The fast, reactive route comprising the vermis, periaqueductal gray, thalamus, amygdala, hypothalamus and prefrontal cortex is particularly involved during impulsive forms of (affective) aggression (A). The slow control route comprising lateral cerebellar, motor and prefrontal cortices is particularly involved in goal-directed and instrumental forms of (predatory) aggression (B). PAG = periaqueductal gray. See the online article for the color version of this figure.

avoidance tendencies (Dambacher, Schuhmann, et al., 2015; Von Borries et al., 2012). Based on this evidence, an overlap between cerebellar regions implicated in instrumental aggression and approach motivation is anticipated.

Taken together, the lateral cerebellar hemispheres are proposed to be part of a slow control route in the context of aggression that is particularly relevant for instrumental aggression. This route is an extension of the slow route proposed by LeDoux (1995, 1996), which runs from the thalamus to the amygdala via the frontal cortex and provides slower, but more complex and precise processing of salient stimuli. Specifically, the circuit that connects the anterior cerebellar lobe with the motor cortices subserves the action component of aggression. The circuit comprising the cerebellar posterior lobe and prefrontal regions subserves cognitive control functions in the context of aggression. Cognitive control is required specifically for instrumental aggression, because it enables deliberate, premeditated and goal-directed behavior.

Summary and Conclusion

Several independent lines of evidence support the involvement of the cerebellum in aggression. According to the dual-route model of motivation and emotion, impulsive (affective) aggression involves fast acting limbic regions, whereas in instrumental (predatory) aggression the neural focus lies on top-down anterior cortical areas. As illustrated in Figure 2, we propose an extension of this cortico-limbic dual-route model that also incorporates the cerebellum in the context of aggression. A circuit comprising the vermis, PAG, thalamus, amygdala, hypothalamus and prefrontal cortex is suggested to provide a fast route, which is particularly relevant for impulsive aggression because it enables emotion-driven, rapid responses to threatening or provocative situations. Additionally, a circuit comprising lateral cerebellar, motor and prefrontal cortices provides a slow control route of aggression that is involved predominantly during instrumental aggression, as these regions subserve functions that enable deliberate, premeditated, and goal-directed behavior.

References

Adamaszek, M., D'Agata, F., Ferrucci, R., Habas, C., Keulen, S., Kirkby, K. C., & Verhoeven, J. (2017). Consensus paper: Cerebellum and emotion. *Cerebellum*, *16*, 552–576. https://doi.org/10.1007/s12311-016-0815-8

Alia-Klein, N., Gan, G., Gilam, G., Bezek, J., Bruno, A., Denson, T. F., Hendler, T., Lowe, L., Mariotti, V., Muscatello, M. R., Palumbo, S., Pellegrini, S., Pietrini, P., Rizzo, A., & Verona, E. (2020). The feeling of anger: From brain networks to linguistic expressions. *Neuroscience and Biobehavioral Reviews*, *108*, 480–497. https://doi.org/10.1016/j.neubiorev.2019.12.002

Aoki, Y., Inokuchi, R., Nakao, T., & Yamasue, H. (2014). Neural bases of antisocial behavior: A voxel-based meta-analysis. *Social Cognitive and Affective Neuroscience*, *9*(8), 1223–1231. https://doi.org/10.1093/scan/nst104

Balsters, J. H., Cussans, E., Diedrichsen, J., Phillips, K. A., Preuss, T. M., Rilling, J. K., & Ramnani, N. (2010). Evolution of the cerebellar cortex: The selective expansion of prefrontal-projecting cerebellar lobules. *NeuroImage*, *49*(3), 2045–2052. https://doi.org/10.1016/j.neuroimage.2009.10.045

Baumann, O., & Mattingley, J. B. (2012). Functional topography of primary emotion processing in the human cerebellum. *NeuroImage*, *61*(4), 805–811. https://doi.org/10.1016/j.neuroimage.2012.03.044

Berman, A. J., Berman, D., & Prescott, J. W. (1974). The effect of cerebellar lesions on emotional behavior in the rhesus monkey. In I. S. Cooper, M. Riklan, & R. S. Snider (Eds.), *The cerebellum, epilepsy, and behavior* (pp. 277–284). Springer. https://doi.org/10.1007/978-1-4613-4508-4_12

Bertsch, K., Florange, J., & Herpertz, S. C. (2020). Understanding brain mechanisms of reactive aggression. *Current Psychiatry Reports*, *22*(12), 81. https://doi.org/10.1007/s11920-020-01208-6

Bertsch, K., Grothe, M., Prehn, K., Vohs, K., Berger, C., Hauenstein, K., Keiper, P., Domes, G., Teipel, S., & Herpertz, S. C. (2013). Brain volumes differ between diagnostic groups of violent criminal offenders.

European Archives of Psychiatry and Clinical Neuroscience, *263*(7), 593–606. https://doi.org/10.1007/s00406-013-0391-6

Bhatt, S., Gregg, T. R., & Siegel, A. (2003). NK1 receptors in the medial hypothalamus potentiate defensive rage behavior elicited from the midbrain periaqueductal gray of the cat. *Brain Research*, *966*(1), 54–64. https://doi.org/10.1016/S0006-8993(02)04189-6

Blair, R. J. R. (1995). A cognitive developmental approach to mortality: Investigating the psychopath. *Cognition*, *57*(1), 1–29. https://doi.org/10.1016/0010-0277(95)00676-P

Blair, R. J. R. (2010). Neuroimaging of psychopathy and antisocial behavior: A targeted review. *Current Psychiatry Reports*, *12*(1), 76–82. https://doi.org/10.1007/s11920-009-0086-x

Blair, R. J. R. (2012). Considering anger from a cognitive neuroscience perspective. *Wiley Interdisciplinary Reviews: Cognitive Science*, *3*(1), 65–74. https://doi.org/10.1002/wcs.154

Blair, R. J. R. (2016). The neurobiology of impulsive aggression. *Journal of Child and Adolescent Psychopharmacology*, *26*(1), 4–9. https://doi.org/10.1089/cap.2015.0088

Blanchard, D. C., & Blanchard, R. J. (2003). What can animal aggression research tell us about human aggression? *Hormones and Behavior*, *44*(3), 171–177. https://doi.org/10.1016/S0018-506X(03)00133-8

Buades-Rotger, M., Beyer, F., & Krämer, U. M. (2017). Avoidant responses to interpersonal provocation are associated with increased amygdala and decreased mentalizing network activity. *eNeuro*, *4*(3), e0337. https://doi.org/10.1523/ENEURO.0337-16.2017

Buckner, R. L., Krienen, F. M., Castellanos, A., Diaz, J. C., & Yeo, B. T. (2011). The organization of the human cerebellum estimated by intrinsic functional connectivity. *Journal of Neurophysiology*, *106*(5), 2322–2345. https://doi.org/10.1152/jn.00339.2011

Cardinali, D. P. (2017). *Autonomic nervous system: Basic and clinical aspects*. Springer International Publishing AG. https://doi.org/10.1007/978-3-319-57571-1

Cherek, D. R., Moeller, F. G., Schnapp, W., & Dougherty, D. M. (1997). Studies of violent and nonviolent male parolees: I. Laboratory and psychometric measurements of aggression. *Biological Psychiatry*, *41*(5), 514–522. https://doi.org/10.1016/S0006-3223(96)00059-5

Chester, D. S., & DeWall, C. N. (2016). The pleasure of revenge: Retaliatory aggression arises from a neural imbalance toward reward. *Social Cognitive and Affective Neuroscience*, *11*(7), 1173–1182. https://doi.org/10.1093/scan/nsv082

Coccaro, E. F., Fanning, J. R., Fisher, E., Couture, L., & Lee, R. J. (2017). Social emotional information processing in adults: Development and psychometrics of a computerized video assessment in healthy controls and aggressive individuals. *Psychiatry Research*, *248*, 40–47. https://doi.org/10.1016/j.psychres.2016.11.004

Coccaro, E. F., Keedy, S., Lee, R., & Phan, K. L. (2021). Neuronal responses to adverse social threat in healthy human subjects. *Journal of Psychiatric Research*, *136*, 47–53. https://doi.org/10.1016/j.jpsychires.2021.01.015

Conner, K. R., Swogger, M. T., & Houston, R. J. (2009). A test of the reactive aggression-suicidal behavior hypothesis: Is there a case for proactive aggression? *Journal of Abnormal Psychology*, *118*(1), 235–240. https://doi.org/10.1037/a0014659

Dalwani, M., Sakai, J. T., Mikulich-Gilbertson, S. K., Tanabe, J., Raymond, K., McWilliams, S. K., & Crowley, T. J. (2011). Reduced cortical gray matter volume in male adolescents with substance and conduct problems. *Drug and Alcohol Dependence*, *118*(2–3), 295–305. https://doi.org/10.1016/j.drugalcdep.2011.04.006

Dambacher, F., Sack, A. T., Lobbestael, J., Arntz, A., Brugman, S., & Schuhmann, T. (2015). Out of control: Evidence for anterior insula involvement in motor impulsivity and reactive aggression. *Social Cognitive and Affective Neuroscience*, *10*(4), 508–516. https://doi.org/10.1093/scan/nsu077

Dambacher, F., Schuhmann, T., Lobbestael, J., Arntz, A., Brugman, S., & Sack, A. T. (2015). Reducing proactive aggression through non-invasive brain stimulation. *Social Cognitive and Affective Neuroscience*, *10*(10), 1303–1309. https://doi.org/10.1093/scan/nsv018

De Brito, S. A., Mechelli, A., Wilke, M., Laurens, K. R., Jones, A. P., Barker, G. J., Hodgins, S., & Viding, E. (2009). Size matters: Increased grey matter in boys with conduct problems and callous-unemotional traits. *Brain: A Journal of Neurology*, *132*(Part 4), 843–852. https://doi.org/10.1093/brain/awp011

Demirtas-Tatlidede, A., Freitas, C., Pascual-Leone, A., & Schmahmann, J. D. (2011). Modulatory effects of theta burst stimulation on cerebellar nonsomatic functions. *Cerebellum*, *10*(3), 495–503. https://doi.org/10.1007/s12311-010-0230-5

Denny, K. G., & Siemer, M. (2012). Trait aggression is related to anger-modulated deficits in response inhibition. *Journal of Research in Personality*, *46*(4), 450–454. https://doi.org/10.1016/j.jrp.2012.04.001

E, K.-H., Chen, S.-H. A., Ho, M.-H. R., & Desmond, J. E. (2014). A meta-analysis of cerebellar contributions to higher cognition from PET and fMRI studies. *Human Brain Mapping*, *35*(2), 593–615. https://doi.org/10.1002/hbm.22194

Etkin, A., Egner, T., & Kalisch, R. (2011). Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends in Cognitive Sciences*, *15*(2), 85–93. https://doi.org/10.1016/j.tics.2010.11.004

Ferrari, C., Ciricugno, A., Urgesi, C., & Cattaneo, Z. (2019). Cerebellar contribution to emotional body language perception: A TMS study. *Social Cognitive and Affective Neuroscience*. Advance online publication. https://doi.org/10.1093/scan/nsz074

Ferrucci, R., Giannicola, G., Rosa, M., Fumagalli, M., Boggio, P. S., Hallett, M., Zago, S., & Priori, A. (2012). Cerebellum and processing of negative facial emotions: Cerebellar transcranial DC stimulation specifically enhances the emotional recognition of facial anger and sadness. *Cognition and Emotion*, *26*(5), 786–799. https://doi.org/10.1080/02699931.2011.619520

Fontes, M. A. P., Xavier, C. H., de Menezes, R. C. A., & Dimicco, J. A. (2011). The dorsomedial hypothalamus and the central pathways involved in the cardiovascular response to emotional stress. *Neuroscience*, *184*, 64–74. https://doi.org/10.1016/j.neuroscience.2011.03.018

Gan, G., Preston-Campbell, R. N., Moeller, S. J., Steinberg, J. L., Lane, S. D., Maloney, T., Parvaz, M. A., Goldstein, R. Z., & Alia-Klein, N. (2016). Reward vs. retaliation—the role of the mesocorticolimbic salience network in human reactive aggression. *Frontiers in Behavioral Neuroscience*, *10*, 179. https://doi.org/10.3389/fnbeh.2016.00179

Giaccio, R. G. (2006). The dual origin hypothesis: An evolutionary brain-behavior framework for analyzing psychiatric disorders. *Neuroscience and Biobehavioral Reviews*, *30*(4), 526–550. https://doi.org/10.1016/j.neubiorev.2005.04.021

Gregg, T. R., & Siegel, A. (2001). Brain structures and neurotransmitters regulating aggression in cats: Implications for human aggression. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *25*(1), 91–140. https://doi.org/10.1016/S0278-5846(00)00150-0

Gregory, S., ffytche, D., Simmons, A., Kumari, V., Howard, M., Hodgins, S., & Blackwood, N. (2012). The antisocial brain: Psychopathy matters. *Archives of General Psychiatry*, *69*(9), 962–972. https://doi.org/10.1001/archgenpsychiatry.2012.222

Greve, K. W., Stanford, M. S., Sutton, C., & Foundas, A. L. (1999). Cognitive and emotional sequelae of cerebellar infarct: A case report. *Archives of Clinical Neuropsychology*, *14*(5), 455–469. https://doi.org/10.1016/S0887-6177(99)00010-4

Grosbras, M. H., & Paus, T. (2006). Brain networks involved in viewing angry hands or faces. *Cerebral Cortex*, *16*(8), 1087–1096. https://doi.org/10.1093/cercor/bhj050

Heath, R. G. (1977). Modulation of emotion with a brain pacemaker. *Journal of Nervous and Mental Disease*, *165*(5), 300–317. https://doi.org/10.1097/00005053-197711000-00002

Heath, R. G., Llewellyn, R. C., & Rouchell, A. M. (1980). The cerebellar pacemaker for intractable behavioral disorders and epilepsy: Follow-up report. *Biological Psychiatry*, *15*(2), 243–256.

Hoche, F., Guell, X., Vangel, M. G., Sherman, J. C., & Schmahmann, J. D. (2018). The cerebellar cognitive affective/Schmahmann Syndrome Scale. *Brain: A Journal of Neurology*, *141*(1), 248–270. https://doi.org/10.1093/brain/awx317

Holley, S. R., Ewing, S. T., Stiver, J. T., & Bloch, L. (2017). The relationship between emotion regulation, executive functioning, and aggressive behaviors. *Journal of Interpersonal Violence*, *32*(11), 1692–1707. https://doi.org/10.1177/0886260515592619

Huebner, T., Vloet, T. D., Marx, I., Konrad, K., Fink, G. R., Herpertz, S. C., & Herpertz-Dahlmann, B. (2008). Morphometric brain abnormalities in boys with conduct disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, *47*(5), 540–547. https://doi.org/10.1097/CHI.0b013e3181676545

Jackman, S. L., Chen, C. H., Offermann, H. L., Drew, I. R., Harrison, B. M., Bowman, A. M., & Regehr, W. G. (2020). Cerebellar Purkinje cell activity modulates aggressive behavior. *eLife*, *9*, e53229 https://doi.org/10.7554/eLife.53229

Kelley, N. J., Hortensius, R., Schutter, D. J. L. G., & Harmon-Jones, E. (2017). The relationship of approach/avoidance motivation and asymmetric frontal cortical activity: A review of studies manipulating frontal asymmetry. *International Journal of Psychophysiology*, *119*, 19–30. https://doi.org/10.1016/j.ijpsycho.2017.03.001

Kelly, R. M., & Strick, P. L. (2003). Cerebellar loops with motor cortex and prefrontal cortex of a nonhuman primate. *The Journal of Neuroscience*, *23*(23), 8432–8444. https://doi.org/10.1523/JNEUROSCI.23-23-08432.2003

Klaus, J., & Schutter, D. J. L. G. (2021). Functional topography of anger and aggression in the human cerebellum. *NeuroImage*, *226*, 117582. https://doi.org/10.1016/j.neuroimage.2020.117582

Krämer, U. M., Jansma, H., Tempelmann, C., & Münte, T. F. (2007). Tit-for-tat: The neural basis of reactive aggression. *NeuroImage*, *38*(1), 203–211. https://doi.org/10.1016/j.neuroimage.2007.07.029

Kronemer, S. I., Slapik, M. B., Pietrowski, J. R., Margron, M. J., Morgan, O. P., Bakker, C. C., & Marvel, C. L. (2021). Neuropsychiatric symptoms as a reliable phenomenology of cerebellar ataxia. *Cerebellum*, *20*, 141–150. https://doi.org/10.1007/s12311-020-01195-7

LeDoux, J. (1996). *The emotional brain: the mysterious underpinnings of emotional life*. Simon & Schuster.

LeDoux, J. (2012). Rethinking the emotional brain. *Neuron*, *73*(4), 653–676. https://doi.org/10.1016/j.neuron.2012.02.004

LeDoux, J. E. (2000). Emotion circuits in the brain. *Annual Review of Neuroscience*, *23*, 155–184. https://doi.org/10.1146/annurev.neuro.23.1.155

LeDoux, J. E. (1995). Emotion: Clues from the brain. *Annual Review of Psychology*, *46*, 209–235. https://doi.org/10.1146/annurev.ps.46.020195.001233

Leutgeb, V., Leitner, M., Wabnegger, A., Klug, D., Scharmüller, W., Zussner, T., & Schienle, A. (2015). Brain abnormalities in high-risk violent offenders and their association with psychopathic traits and criminal recidivism. *Neuroscience*, *308*, 194–201. https://doi.org/10.1016/j.neuroscience.2015.09.011

Leutgeb, V., Wabnegger, A., Leitner, M., Zussner, T., Scharmüller, W., Klug, D., & Schienle, A. (2016). Altered cerebellar-amygdala connectivity in violent offenders: A resting-state fMRI study. *Neuroscience Letters*, *610*, 160–164. https://doi.org/10.1016/j.neulet.2015.10.063

Levisohn, L., Cronin-Golomb, A., & Schmahmann, J. D. (2000). Neuropsychological consequences of cerebellar tumour resection in children: Cerebellar cognitive affective syndrome in a paediatric population. *Brain: A Journal of Neurology*, *123*, 1041–1050. https://doi.org/10.1093/brain/123.5.1041

Lin, H., Mueller-Bardorff, M., Mothes-Lasch, M., Buff, C., Brinkmann, L., Miltner, W. H., & Straube, T. (2016). Effects of intensity of facial expressions on amygdalar activation independently of valence. *Frontiers in Human Neuroscience*, *10*, 646. https://doi.org/10.3389/fnhum.2016.00646

Madole, J. W., Johnson, S. L., & Carver, C. S. (2020). A model of aggressive behavior: Early adversity, impulsivity, and response inhibition. *Journal of Aggression, Maltreatment & Trauma*, *29*(5), 594–610. https://doi.org/10.1080/10926771.2019.1591561

Mathiak, K., & Weber, R. (2006). Toward brain correlates of natural behavior: fMRI during violent video games. *Human Brain Mapping*, *27*(12), 948–956. https://doi.org/10.1002/hbm.20234

Mauss, I. B., Evers, C., Wilhelm, F. H., & Gross, J. J. (2006). How to bite your tongue without blowing your top: Implicit evaluation of emotion regulation predicts affective responding to anger provocation. *Personality and Social Psychology Bulletin*, *32*(5), 589–602. https://doi.org/10.1177/0146167205283841

Meloy, J. R. (1988). *The psychopathic mind: Origins, dynamics, and treatment*. Rowman & Littlefield.

Méndez-Bértolo, C., Moratti, S., Toledano, R., Lopez-Sosa, F., Martínez-Alvarez, R., Mah, Y. H., Vuilleumier, P., Gil-Nagel, A., & Strange, B. A. (2016). A fast pathway for fear in human amygdala. *Nature Neuroscience*, *19*(8), 1041–1049. https://doi.org/10.1038/nn.4324

Mobbs, D., Petrovic, P., Marchant, J. L., Hassabis, D., Weiskopf, N., Seymour, B., Dolan, R. J., & Frith, C. D. (2007). When fear is near: Threat imminence elicits prefrontal-periaqueductal gray shifts in humans. *Science*, *317*(5841), 1079–1083. https://doi.org/10.1126/science.1144298

Nelson, R. J., & Trainor, B. C. (2007). Neural mechanisms of aggression. *Nature Reviews Neuroscience*, *8*(7), 536–546. https://doi.org/10.1038/nrn2174

O'Hearn, E., & Molliver, M. E. (2001). Organizational principles and microcircuitry of the cerebellum. *International Review of Psychiatry*, *13*, 232–246. https://doi.org/10.1080/09540260120082083

Ochsner, K. N., & Gross, J. J. (2005). The cognitive control of emotion. *Trends in Cognitive Sciences*, *9*(5), 242–249. https://doi.org/10.1016/j.tics.2005.03.010

Ochsner, K. N., Silvers, J. A., & Buhle, J. T. (2012). Functional imaging studies of emotion regulation: A synthetic review and evolving model of the cognitive control of emotion. *Annals of the New York Academy of Sciences*, *1251*, E1–E24. https://doi.org/10.1111/j.1749-6632.2012.06751.x

Palesi, F., Tournier, J.-D., Calamante, F., Muhlert, N., Castellazzi, G., Chard, D., D'Angelo, E., & Wheeler-Kingshott, C. A. M. (2015). Contralateral cerebello-thalamo-cortical pathways with prominent involvement of associative areas in humans in vivo. *Brain Structure & Function*, *220*(6), 3369–3384. https://doi.org/10.1007/s00429-014-0861-2

Panksepp, J. (2011). The basic emotional circuits of mammalian brains: Do animals have affective lives? *Neuroscience and Biobehavioral Reviews*, *35*(9), 1791–1804. https://doi.org/10.1016/j.neubiorev.2011.08.003

Panksepp, J., & Zellner, M. (2004). Towards a neurobiologically based unified theory of aggression. *Revue Internationale de Psychologie Sociale*, *17*(2), 37–61.

Park, J. Y., Gu, B. M., Kang, D. H., Shin, Y. W., Choi, C. H., Lee, J. M., & Kwon, J. S. (2010). Integration of cross-modal emotional information in the human brain: An fMRI study. *Cortex*, *46*(2), 161–169. https://doi.org/10.1016/j.cortex.2008.06.008

Pawliczek, C. M., Derntl, B., Kellermann, T., Kohn, N., Gur, R. C., & Habel, U. (2013). Inhibitory control and trait aggression: Neural and behavioral insights using the emotional stop signal task. *NeuroImage*, *79*, 264–274. https://doi.org/10.1016/j.neuroimage.2013.04.104

Pera-Guardiola, V., Contreras-Rodríguez, O., Batalla, I., Kosson, D., Menchón, J. M., Pifarré, J., & Soriano-Mas, C. (2016). Brain structural correlates of emotion recognition in psychopaths. *PLoS ONE*, *11*(5), e0149807. https://doi.org/10.1371/journal.pone.0149807

Peters, M., & Monjan, A. A. (1971). Behavior after cerebellar lesions in cats and monkeys. *Physiology & Behavior*, *6*(2), 205–206. https://doi.org/10.1016/0031-9384(71)90091-6

Potegal, M. (2012). Temporal and frontal lobe initiation and regulation of the top-down escalation of anger and aggression. *Behavioural Brain Research*, *231*(2), 386–395. https://doi.org/10.1016/j.bbr.2011.10.049

Puri, B. K., Counsell, S. J., Saeed, N., Bustos, M. G., Treasaden, I. H., & Bydder, G. M. (2008). Regional grey matter volumetric changes in forensic schizophrenia patients: An MRI study comparing the brain structure of patients who have seriously and violently offended with that of patients who have not. *BMC Psychiatry*, *8*(S1), S6. https://doi.org/10.1186/1471-244X-8-S1-S6

Reis, D. J., Doba, N., & Nathan, M. A. (1973). Predatory attack, grooming, and consummatory behaviors evoked by electrical stimulation of cat cerebellar nuclei. *Science*, *182*(4114), 845–847. https://doi.org/10.1126/science.182.4114.845

Richter, S., Schoch, B., Kaiser, O., Groetschel, H., Dimitrova, A., Hein-Kropp, C., Maschke, M., Gizewski, E. R., & Timmann, D. (2005). Behavioral and affective changes in children and adolescents with chronic cerebellar lesions. *Neuroscience Letters*, *381*(1-2), 102–107. https://doi.org/10.1016/j.neulet.2005.02.011

Riva, D., & Giorgi, C. (2000). The cerebellum contributes to higher functions during development: Evidence from a series of children surgically treated for posterior fossa tumours. *Brain: A Journal of Neurology*, *123*(Pt 5), 1051–1061. https://doi.org/10.1093/brain/123.5.1051

Rogers, J. C., & De Brito, S. A. (2016). Cortical and subcortical gray matter volume in youths with conduct problems: A meta-analysis. *JAMA Psychiatry*, *73*(1), 64–72. https://doi.org/10.1001/jamapsychiatry.2015.2423

Sang, L., Qin, W., Liu, Y., Han, W., Zhang, Y., Jiang, T., & Yu, C. (2012). Resting-state functional connectivity of the vermal and hemispheric subregions of the cerebellum with both the cerebral cortical networks and subcortical structures. *NeuroImage*, *61*(4), 1213–1225. https://doi.org/10.1016/j.neuroimage.2012.04.011

Santana, E. J. (2016). The brain of the psychopath: A systematic review of structural neuroimaging studies. *Psychology & Neuroscience*, *9*(4), 420–443. https://doi.org/10.1037/pne0000069

Schlerf, J., Wiestler, T., Verstynen, T., & Diedrichsen, J. (2014). Big challenges from the little brain - imaging the cerebellum. In T. D. Papageorgiou, G. I. Christopoulos, & S. M. Smirnakis (Eds.), *Advanced brain neuroimaging topics in health and disease - methods and applications*. IntechOpen. https://doi.org/10.5772/58266

Schmahmann, J. D. (2000). The role of the cerebellum in affect and psychosis. *Journal of Neurolinguistics*, *13*(2-3), 189–214. https://doi.org/10.1016/S0911-6044(00)00011-7

Schmahmann, J. D., & Sherman, J. C. (1998). The cerebellar cognitive affective syndrome. *Brain: A Journal of Neurology*, *121*(Pt 4), 561–579. https://doi.org/10.1093/brain/121.4.561

Schmahmann, J. D., Weilburg, J. B., & Sherman, J. C. (2007). The neuropsychiatry of the cerebellum - insights from the clinic. *Cerebellum (London, England)*, *6*(3), 254–267. https://doi.org/10.1080/14734220701490995

Schraa-Tam, C. K. L., Rietdijk, W. J. R., Verbeke, W. J. M. I., Dietvorst, R. C., van den Berg, W. E., Bagozzi, R. P., & De Zeeuw, C. I. (2012). fMRI activities in the emotional cerebellum: A preference for negative stimuli and goal-directed behavior. *Cerebellum*, *11*(1), 233–245. https://doi.org/10.1007/s12311-011-0301-2

Schutter, D. J. L. G. (2013). Human cerebellum in motivation and emotion. In M. Manto, D. L. Gruol, J. D. Schmahmann, N. Koibuchi, & F. Rossi (Eds.), *Handbook of the cerebellum and cerebellar disorders* (pp. 1771–1782). Springer. https://doi.org/10.1007/978-94-007-1333-8_79

Schutter, D. J. L. G. (2020). *The cerebellum in emotions and psychopathology*. Routledge. https://doi.org/10.4324/9781315145082

Schutter, D. J. L. G., & Harmon-Jones, E. (2013). The corpus callosum: A commissural road to anger and aggression. *Neuroscience and Biobehavioral Reviews*, *37*(10 Part 2), 2481–2488. https://doi.org/10.1016/j.neubiorev.2013.07.013

Schutter, D. J. L. G., Paalman, M., Henssen, D., & Deschamps, P. K. H. (2021). A case of attention deficit hyperactivity disorder in rhombencephalosynapsis. *Cerebellum*, *20*(4), 659–661. https://doi.org/10.1007/s12311-021-01234-x

Schutter, D. J. L. G., & van Honk, J. (2009). The cerebellum in emotion regulation: A repetitive transcranial magnetic stimulation study. *Cerebellum*, *8*(1), 28–34. https://doi.org/10.1007/s12311-008-0056-6

Sereno, M. I., Diedrichsen, J., Tachrount, M., Testa-Silva, G. D., Arceuil, H., & De Zeeuw, C. (2020). The human cerebellum has almost 80% of the surface area of the neocortex. *Proceedings of the National Academy of Sciences of the United States of America*, *117*(32), 19538–19543. https://doi.org/10.1073/pnas.2002896117

Siegel, A., & Pott, C. B. (1988). Neural substrates of aggression and flight in the cat. *Progress in Neurobiology*, *31*(4), 261–283. https://doi.org/10.1016/0301-0082(88)90015-9

Siegel, A., Schubert, K. L., & Shaikh, M. B. (1997). Neurotransmitters regulating defensive rage behavior in the cat. *Neuroscience and Biobehavioral Reviews*, *21*(6), 733–742. https://doi.org/10.1016/S0149-7634(96)00056-5

Siegel, A., & Victoroff, J. (2009). Understanding human aggression: New insights from neuroscience. *International Journal of Law and Psychiatry*, *32*(4), 209–215. https://doi.org/10.1016/j.ijlp.2009.06.001

Spoont, M. R., Kuskowski, M., & Pardo, J. V. (2010). Autobiographical memories of anger in violent and non-violent individuals: A script-driven imagery study. *Psychiatry Research: Neuroimaging*, *183*(3), 225–229. https://doi.org/10.1016/j.pscychresns.2010.06.004

Steinlin, M., Imfeld, S., Zulauf, P., Boltshauser, E., Lövblad, K.-O., Ridolfi Lüthy, A., Perrig, W., & Kaufmann, F. (2003). Neuropsychological long-term sequelae after posterior fossa tumour resection during childhood. *Brain: A Journal of Neurology*, *126*(Pt 9), 1998–2008. https://doi.org/10.1093/brain/awg195

Stoodley, C. J., & Schmahmann, J. D. (2009). Functional topography in the human cerebellum: A meta-analysis of neuroimaging studies. *NeuroImage*, *44*(2), 489–501. https://doi.org/10.1016/j.neuroimage.2008.08.039

Tavano, A., Grasso, R., Gagliardi, C., Triulzi, F., Bresolin, N., Fabbro, F., & Borgatti, R. (2007). Disorders of cognitive and affective development in cerebellar malformations. *Brain: A Journal of Neurology*, *130*(Part 10), 2646–2660. https://doi.org/10.1093/brain/awm201

Taylor, S. P. (1967). Aggressive behavior and physiological arousal as a function of provocation and the tendency to inhibit aggression. *Journal of Personality*, *35*(2), 297–310. https://doi.org/10.1111/j.1467-6494.1967.tb01430.x

Telgkamp, P., & Raman, I. M. (2002). Depression of inhibitory synaptic transmission between Purkinje cells and neurons of the cerebellar nuclei. *The Journal of Neuroscience*, *22*(19), 8447–8457. https://doi.org/10.1523/JNEUROSCI.22-19-08447.2002

Tiihonen, J., Rossi, R., Laakso, M. P., Hodgins, S., Testa, C., Perez, J., Repo-Tiihonen, E., Vaurio, O., Soininen, H., Aronen, H. J., Könönen, M., Thompson, P. M., & Frisoni, G. B. (2008). Brain anatomy of persistent violent offenders: More rather than less. *Psychiatry Research: Neuroimaging*, *163*(3), 201–212. https://doi.org/10.1016/j.pscychresns.2007.08.012

Todd, W. D., & Machado, N. L. (2019). A time to fight: Circadian control of aggression and associated autonomic support. *Autonomic Neuroscience*, *217*, 35–40. https://doi.org/10.1016/j.autneu.2018.12.008

Tuente, S. K., Bogaerts, S., & Veling, W. (2019). Hostile attribution bias and aggression in adults - a systematic review. *Aggression and Violent Behavior*, *46*, 66–81. https://doi.org/10.1016/j.avb.2019.01.009

Van Overwalle, F., Baetens, K., Mariën, P., & Vandekerckhove, M. (2014). Social cognition and the cerebellum: A meta-analysis of over 350 fMRI studies. *NeuroImage*, *86*, 554–572. https://doi.org/10.1016/j.neuroimage.2013.09.033

Van Overwalle, F., Ma, Q., & Heleven, E. (2020). The posterior crus II cerebellum is specialized for social mentalizing and emotional self-experiences: A meta-analysis. *Social Cognitive and Affective Neuroscience*, *15*(9), 905–928. https://doi.org/10.1093/scan/nsaa124

Vitiello, B., & Stoff, D. M. (1997). Subtypes of aggression and their relevance to child psychiatry. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36*(3), 307–315. https://doi.org/10.1097/00004583-199703000-00008

von Borries, A. K. L., Volman, I., de Bruijn, E. R. A., Bulten, B. H., Verkes, R. J., & Roelofs, K. (2012). Psychopaths lack the automatic avoidance of social threat: Relation to instrumental aggression. *Psychiatry Research*, *200*(2–3), 761–766. https://doi.org/10.1016/j.psychres.2012.06.026

Wagels, L., Votinov, M., Kellermann, T., Konzok, J., Jung, S., Montag, C., Schneider, F., Eisert, A., Beyer, C., & Habel, U. (2019). Exogenous testosterone and the monoamine-oxidase A polymorphism influence anger, aggression and neural responses to provocation in males. *Neuropharmacology*, *156*, 107491. https://doi.org/10.1016/j.neuropharm.2019.01.006

Wang, D., Buckner, R. L., & Liu, H. (2013). Cerebellar asymmetry and its relation to cerebral asymmetry estimated by intrinsic functional connectivity. *Journal of Neurophysiology*, *109*(1), 46–57. https://doi.org/10.1152/jn.00598.2012

Weaver, A. H. (2005). Reciprocal evolution of the cerebellum and neocortex in fossil humans. *Proceedings of the National Academy of Sciences of the United States of America*, *102*(10), 3576–3580. https://doi.org/10.1073/pnas.0500692102

Weinshenker, N. J., & Siegel, A. (2002). Bimodal classification of aggression: Affective defense and predatory attack. *Aggression and Violent Behavior*, *7*(3), 237–250. https://doi.org/10.1016/S1359-1789(01)00042-8

Wen, Y. Q., Zhu, J. N., Zhang, Y. P., & Wang, J. J. (2004). Cerebellar interpositus nuclear inputs impinge on paraventricular neurons of the hypothalamus in rats. *Neuroscience Letters*, *370*(1), 25–29. https://doi.org/10.1016/j.neulet.2004.07.072

White, S. F., Brislin, S. J., Sinclair, S., & Blair, J. R. (2014). Punishing unfairness: Rewarding or the organization of a reactively aggressive response? *Human Brain Mapping*, *35*(5), 2137–2147. https://doi.org/10.1002/hbm.22316

Wolfs, E. M. L., Klaus, J., & Schutter, D. J. L. G. (in press). Cerebellar grey matter volumes in reactive aggression and impulsivity in healthy volunteers. *Cerebellum*.

Wong, T. Y., Sid, A., Wensing, T., Eickhoff, S. B., Habel, U., Gur, R. C., & Nickl-Jockschat, T. (2019). Neural networks of aggression: ALE meta-analyses on trait and elicited aggression. *Brain Structure & Function*, *224*(1), 133–148. https://doi.org/10.1007/s00429-018-1765-3

Wynn, S. C., Driessen, J. M. A., Glennon, J. C., Brazil, I. A., & Schutter, D. J. L. G. (2019). Cerebellar transcranial direct current stimulation improves reactive response inhibition in healthy volunteers. *Cerebellum*, *18*(6), 983–988. https://doi.org/10.1007/s12311-019-01047-z

Yang, Y., & Raine, A. (2009). Prefrontal structural and functional brain imaging findings in antisocial, violent, and psychopathic individuals: A meta-analysis. *Psychiatry Research: Neuroimaging*, *174*(2), 81–88. https://doi.org/10.1016/j.pscychresns.2009.03.012

Yang, Y., Raine, A., Narr, K. L., Colletti, P., & Toga, A. W. (2009). Localization of deformations within the amygdala in individuals with psychopathy. *Archives of General Psychiatry*, *66*(9), 986–994. https://doi.org/10.1001/archgenpsychiatry.2009.110

Zanchetti, A., & Zoccolini, A. (1954). Autonomic hypothalamic outbursts elicited by cerebellar stimulation. *Journal of Neurophysiology*, *17*(5), 475–483. https://doi.org/10.1152/jn.1954.17.5.475

Zhang, J., Liu, W., Zhang, J., Wu, Q., Gao, Y., Jiang, Y., Gao, J., Yao, S., & Huang, B. (2018). Distinguishing adolescents with conduct disorder from typically developing youngsters based on pattern classification of brain structural MRI. *Frontiers in Human Neuroscience*, *12*, 152. https://doi.org/10.3389/fnhum.2018.00152

Zhang, X. Y., Wang, J. J., & Zhu, J. N. (2016). Cerebellar fastigial nucleus: From anatomic construction to physiological functions. *Cerebellum & Ataxias*, *3*(9), 9. https://doi.org/10.1186/s40673-016-0047-1

Zhu, J. N., Yung, W. H., Kwok-Chong Chow, B., Chan, Y. S., & Wang, J. J. (2006). The cerebellar-hypothalamic circuits: Potential pathways underlying cerebellar involvement in somatic-visceral integration. *Brain Research. Brain Research Reviews*, *52*, 93–106. https://doi.org/10.1016/j.brainresrev.2006.01.003

Received April 14, 2021
Revision received September 3, 2021
Accepted September 5, 2021 ■