# Cerebellum and Apraxia

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**Conflict of interest**

The authors declare that they have no conflicts of interest.

**Abstract**

As early as the beginning of the 19th century a variety of nonmotor cognitive and affective impairments associated with cerebellar pathology were occasionally documented. A causal link between cerebellar disease and nonmotor cognitive and affective disorders has, however, been dismissed for almost two centuries.

During the past decades the prevailing view of the cerebellum as a mere coordinator of autonomic and somatic motor function has changed fundamentally. Substantial progress has been made in elucidating the neuroanatomical connections of the cerebellum with the supratentorial association cortices that subserve non-motor cognition and affect. Furthermore, functional neuroimaging studies and neurophysiological and neuropsychological research have shown that the cerebellum is crucially involved in modulating cognitive and affective processes.

This paper presents an overview of the clinical and neuroradiological evidence supporting the view that the cerebellum plays an intrinsic part in purposeful, skilled motor actions. Despite the increasing number of studies devoted to a further refinement of the typology and anatomoclinical configurations of apraxia related to cerebellar pathology, the exact underlying pathophysiological mechanisms of cerebellar involvement remain to be elucidated. As genuine planning, organisation and execution disorders of skilled motor actions not due to motor, sensory or general intellectual failure, the apraxias following disruption of the cerebrocerebellar network may be hypothetically considered to form part of the executive cluster of the cerebellar cognitive affective syndrome (CCAS), a highly influential concept defined by Schmahmann and Sherman (1998) on the basis of four symptom clusters grouping related neurocognitive and affective deficits (executive, visuo-spatial, affective and linguistic impairments). However, since only a handful of studies have explored the possible role of the cerebellum in apraxic disorders the pathophysiological mechanisms subserving cerebellar induced apraxia remain to be elucidated.

## 1. Introduction

In 1866, John Hughlings Jackson (1835-1911) provided the first clear clinical description of ‘apraxia’ in a number of aphasic patients suffering from a condition which is currently known as bucco-labio-lingual or oro-facial apraxia. Hughlings Jackson noted that these patients were not able to voluntarily move sections of their face and their tongue on command, although there was no paralysis of the facial muscles or the tongue. Nevertheless, they did carry out these movements spontaneously (automatico-voluntary dissociation) [5].

A few years later, Heymann Steinthal, a German linguist, coined the term ‘apraxia’ to refer to the defective use of everyday objects (as cited in [13]). Early alternative terms for apraxic phenomena included ‘motor asymbolia’ (Pick, 1905) or ‘psychic paralysis’ (Nothnagel, 1187) [13]. In a series of hallmark papers written between 1900 and 1920, Karl Hugo Liepmann refined the definition of apraxia, acknowledging the conceptual similarity between ‘apraxia’ and ‘motor asymbolia’ and ‘psychic paralysis’. Modern definitions of apraxia characterize the condition in line with Liepmann's view as a disorder of skilled motor actions not caused by motor weakness, akinesia, deafferentiation, abnormal tone or posture, movement disorders (e.g. tremor, ataxia, chorea, ballismus, myoclonus), sensory-perceptual deficits, language comprehension deficits, general cognitive impairment or uncooperativeness [3, 6].

From a theoretical perspective Hugo Liepmann developed a connectionist model to explain apraxia. In this model, a neural network predominantly subserved by the left hemisphere is held responsible for the planning and execution of skilled motor actions. Liepmann assumes that gestures involve the whole cerebral cortex of the brain to create a ‘movement formula’ consisting of visual or acoustic images of actions stored in the parietal lobe. To perform skilled motor actions these ‘movement formulae’ have to be correctly retrieved and transferred via the connections associated with the stored innervatory patterns in the sensorimotor areas of the left hemisphere (precentral and postcentral gyri, foot of the superior, middle and inferior frontal convolutions). The final step before motor execution is the transfer of formula information via the associated innervatory patterns to the left primary motor areas. The corpus callosum conveys this information to the right motor cortex if the movement is to be executed by the left side of the body [13]. Disruptions in the creation of movement formulae, their retrieval, activation or transfer of information induce semiologically distinct forms of apraxia such as ideomotor apraxia, innervatory or ideational apraxia. [13]

Hypothetically, the apraxias resulting from cerebellar damage may be considered to relate to

the executive cluster of the cerebellar cognitive affective syndrome (CCAS), a concept introduced by Schmahmann and Sherman (1998) [15]. Schmahmann and Sherman (1998) [15] defined this syndrome as a constellation of deficits affecting executive, linguistic, spatial and affective function in a group of 20 patients with disorders confined to the cerebellum. Not all deficits occurred in each patient but decreased verbal fluency and visuo-spatial "disintegration" were particularly prominent [15]. Executive dysfunctions are defined as disturbances in planning, set-shifting, abstract reasoning, and working memory. As a genuine planning, organisation, and execution disorder of skilled motor actions, apraxia might be hypothetically considered to form part of the executive cluster of the CCAS, suggesting a role for the cerebellum in a variety of apraxic disorders.

## 2. Apraxia and the Cerebellum

Most forms of apraxia typically occur after lesions affecting distinct supratentorial areas including the inferior parietal lobe, the prefrontal lobe of the left hemisphere and the corpus callosum. However, an increasing number of recent clinical studies report apraxic phenomena following cerebellar damage and this seems to suggest that the cerebellum is an intrinsic part of the neural network which subserves skilled motor actions.

### 2.1. Apraxia of Speech (AoS)

AoS is a motor speech planning and programming disorder, which selectively disrupts speech movements. Patients with AoS are no longer capable to convert phonological knowledge into the correct verbal-motor commands and this results in inconsistent misarticulations, phonetic alterations of vowel and consonant production, articulatory groping, sequencing errors, flattened voice volume, prosodic abnormalities, slow articulation, and scanning of speech. AoS typically follows from injury to the language dominant motor speech region (anterior insula, inferior premotor and motor cortex, BA 44 of Broca's area) but its striking semiological similarities with ataxic dysarthria, a cerebellar induced motor speech disorder, suggests that both conditions may be related phenomena, resulting from a distortion of the motor speech planning and the coordinating network subserved by a close functional interplay between the anterior motor speech region of the language dominant hemisphere and the contralateral right cerebellum.

Mariën et al. (2006) [10] and Mariën and Verhoeven (2007) [8] reported two right-handed

patients who developed Foreign Accent Syndrome (FAS) after a left hemisphere stroke. FAS is generally considered as a subtype of AoS. In these patients, Tc-99m-ECD SPECT perfusion scans of the brain did not only show a hypoperfusion in the left language dominant hemisphere (the lesion site), but also a secondary, significant hypoperfusion affecting the contralateral right cerebellum (crossed cerebrocerebellar diaschisis). During longitudinal follow-up, remission of FAS was accompanied by a resolution of the crossed cerebrocerebellar diaschisis. This parallellism between remission of the right cerebellar hypoperfusion and the clinical recovery of FAS seems to indicate that: 1) FAS, as a subtype of AoS, may follow from a dysfunctional interaction between the supra- and infratentorial motor speech centers and 2) the cerebellum plays a crucial role in motor speech planning. Cohen et al. (2009) [1] provided additional evidence for the causative role of the cerebellum in FAS. Their patient developed FAS after a left parietal stroke, while a second right cerebellar stroke paradoxically resolved FAS rather than further impairing speech. The authors speculated that the cerebellum is involved in controlling the rhythmic and prosodic patterns of speech by competitive interactions between both cerebellar hemispheres. The authors argued that after right cerebellar damage, the desinhibited left cerebellar hemisphere took over the functional role in motor speech production resulting in the resolution of FAS [1]. The idea of activation of an alternative (contralateral) functional network after unilateral cerebral damage has been described by Riecker et al. (2002) [14]. By means of an fMRI study the authors demonstrated that remission of dysarthria due to a left internal capsule stroke was reflected by a functional transposition of motor speech control to the homologue right hemisphere rolandic cortex and contralateral left cerebellum.

### 2.2. Apraxic Agraphia (AA)

AA is a peripheral neurogenic writing disorder caused by a loss or lack of access to the motor engrams that plan and program the movements necessary to produce letters. AA is characterized by hesitant, awkward, and imprecise handwriting and in severe cases illegible scrawls. Clinical and functional neuroimaging studies have demonstrated that the neural network responsible for writing includes the superior parietal region and the dorsolateral and medial premotor cortex (Exner's area) of the language dominant hemisphere [2]. Mariën et al. (2007) [9], however, reported a right-handed patient who presented with AA after a right cerebellar hemorrhage (Figure 1A). A quantified Tc-99m-ECD SPECT scan of the brain

revealed a significant hypoperfusion in the right cerebellar hemisphere (lesion site) and the anatomoclinically suspected medial and lateral regions of the prefrontal left cerebral hemisphere (Figure 1B).

Insert Figure 1A-B near here

In a review paper, De Smet et al. (2011) [2] discussed three additional cases of AA due to focal damage of the cerebellum. In addition, Mariën et al. (2013) [7] identified "apraxic agraphia" on a neurodevelopmental basis in a 15-year-old left-handed patient. These observations seem to indicate that disruption of the cerebrocerebellar network due to focal damage to the cerebellum or incomplete maturation due to a neurodevelopmental cause may induce AA.

### 2.3. Developmental Coordination Disorder (DCD)

DCD is a neurodevelopmental disorder that affects approximately 5% of school-aged children. DCD is characterized by difficulties in acquiring motor skills, sensorimotor coordination disturbances, impaired postural control, strategic planning problems, disrupted visuo-spatial information processing, executive dysfunction, and usually a much lower PIQ than VIQ [12]. Since DCD is also frequently associated with affective, behavioural and social disturbances [4], the condition resembles CCAS [15].

Mariën et al. (2010) [12] described a 19-year-old left-handed patient with typical DCD features, including constructional and drawing apraxia. Structural MRI of the brain only revealed a slight anterior/superior asymmetry of vermal fissures consistent with rostral vermisdysplasia. In addition to a generally decreased perfusion of the cerebellum, quantified Tc-99m-ECD SPECT showed functional suppression of the anatomoclinically suspected supratentorial regions involved in the execution of planned actions, visuo-spatial processing and affective regulation. Based on these findings it was hypothesized that the cerebellum is crucially involved in the pathophysiological mechanisms of DCD, reflecting disruption of the cerebrocerebellar network involved in the execution of planned actions, visuo-spatial cognition and the regulation of affect.

#### Mastication Dyspraxia (MD)

In addition to prototypical DCD, Mariën et al. (2013) [11] reported a 19-year-old patient in

whom the development of mastication was severely impaired while no evidence of swallowing apraxia, dysphagia, sensorimotor disturbances, abnormal tone or impaired general cognition was found. Repeat MRI during follow-up disclosed mild structural abnormalities as the sequellae of a perinatal intraventricular bleeding but this could not explain impaired mastication behaviour. Quantified Tc-99m-ECD SPECT, however, revealed decreased perfusion in the left cerebellar hemisphere, as well as in both inferior lateral frontal regions, both motor cortices and the right anterior and lateral temporal areas. Diffuse Tensor Imaging tractography demonstrated that several tracts from the dentate nucleus to the motor cortex were absent. Anatomoclinical findings in this patient with DCD not only indicated that the functional integrity of the cerebrocerebellar network is crucially important in the planning and execution of skilled actions, but also seemed to show that mastication deficits may be of true apraxic origin. As a result it was hypothesized that "mastication dyspraxia" may have to be considered as a distinct nosological entity within the group of the developmental dyspraxias following a disruption of the cerebrocerebellar network involved in planned actions.

## 3. Conclusion

Accumulating evidence from recent anatomoclinical studies of patients with neurodevelopmental and acquired neurological disorders affecting the cerebellum seem to indicate that the cerebrocerebellar network is directly implicated in the pathophysiology of different forms of apraxia such as apraxia of speech, apraxic agraphia, constructional apraxia, drawing apraxia, and mastication dyspraxia. As such, it might be hypothesized that the cerebellum constitutes an intrinsic part of Liepmann's connectionist neural network subserving the planning, organisation and execution of skilled motor actions. The left parietal lobe stores the movement formulae for skilled motor actions, the left prefrontal lobe subserves the execution of the formulae and the corpus callosum conveys this information to the right motor cortex. Within this model, the cerebellum may be held responsible for the planning, timing and coordination of the execution process of the skilled movement formulae. As such apraxic disorders following cerebellar pathology may form part of the cluster of executive symptoms of the CCAS but future research is needed to ground this hypothesis.

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**Legend to Figure 1**

CT scan of the brain (A) showing a haemorrhagic lesion in the right cerebellar hemisphere involving cortex and medullary core. Quantified Tc-99m-ECD SPECT (B) demonstrating a significant decrease of perfusion in the right cerebellar hemisphere as well as crossed cerebrocerebellar diaschisis, reflected by a hypoperfusion in the medial and lateral regions of the prefrontal left hemisphere.