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# Apraxic agraphia following thalamic damage: Three new cases

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ABSTRACT

Apraxic agraphia (AA) is a so-called peripheral writing disorder following disruption of the skilled movement plans of writing while the central processes that subserve spelling are intact. It has been observed in a variety of etiologically heterogeneous neurological disorders typically associated with lesions located in the language dominant parietal and frontal region. The condition is characterized by a hesitant, incomplete, imprecise or even illegible graphomotor output. Letter formation cannot be attributed to sensorimotor, extrapyramidal or cerebellar dysfunction affecting the writing limb. Detailed clinical, neurocognitive, neurolinguistic and (functional) neuroimaging characteristics of three unique cases are reported that developed AA following a thalamic stroke. In marked contrast to impaired handwriting, non-handwriting skills, such as oral spelling, were hardly impaired. Quantified Tc-99m ECD SPECT consistently showed a decreased perfusion in the anatomoclinically suspected prefrontal regions. The findings suggest crucial involvement of the anterior (and medial) portion of the left thalamus within the neural network subserving the graphomotor system. Functional neuroimaging findings seem to indicate that AA after focal thalamic damage represents a diaschisis phenomenon.



## 1. Introduction

Writing is a highly complex skill that requires the mastery and integration of a range of subskills involving cognitive operations, linguistic processing and sensorimotor functioning. Cognitive models of spelling and writing (Caramazza, Miceli, Villa, & Romani, 1987; Ellis, 1988, 1992; Margolin & Goodman-Schulman, 1992; Patterson & Shewell, 1987) distinguish between the central processes (linguistic: phonological and lexical routes, graphemic buffer) involved in spelling, whatever the modality of output, and peripheral processes (motor: allographic system, graphomotor processing) that are specific to one particular output modality. In contrast to the central agraphias (e.g. surface (or lexical) agraphia, phonological agraphia, deep (or semantic) agraphia, graphemic buffer agraphia), the peripheral agraphias (e.g. afferent (or spatial) dysgraphia, micro/macrographia, apraxic agraphia, neglect dysgraphia, allographic dysgraphia) are characterized by a marked qualitative dissociation between inferior handwriting and superior non-handwritten forms of spelling, i.e. mental spelling, typing or block spelling (Heilman, Coyle, Gonyea, & Geschwind, 1973; Heilman, Gonyea, & Geschwind, 1974; Mariën et al., 2013; Valenstein & Heilman, 1979). Apraxic agraphia (AA), a subtype of peripheral dysgraphia, results from the loss of or impaired access to the graphomotor engrams that contain information about the spatio-temporal characteristics of the hand movements necessary to form letters, i.e. relative size, position and order of strokes, but not their absolute size and duration or how they will be effected (Rapcsak & Beeson, 2000; Valenstein & Heilman, 1979). Distorted graphomotor output in AA cannot be attributed to sensorimotor, extrapyramidal or cerebellar dysfunction affecting the writing limb (Hillis, Chang, Breese, & Heidler, 2004).

A third causative factor of AA might be impaired transmission of graphomotor patterns into movements necessary to produce letters (Lorch & Barrière, 2003). AA is either isolated or associated with symptoms that cannot explain the writing impairment and is characterized by hesitant, incomplete and imprecise movements leading to illegible scrawls in severe cases (Rapcsak & Beeson, 2000; Valenstein & Heilman, 1979). Grapheme formation may improve during copying, as an effect of task-difficulty (spontaneous writing requires the expression of ideas while copying and writing to dictation has no such demands (Troyer, Black, Armilio, & Moscovitch, 2004)), but is characterized by stroke-by-stroke

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execution (Rapcsak & Beeson, 2000). Croisille, Laurent, Michel, and Trillet (1990) stated that pure agraphia without any accompanying neuropsychological deficits is extremely rare and its clinical features as well as the anatomical lesions are heterogeneous. Roeltgen (2003) proposed a further subdivision of AA in two subtypes: (1) AA with ideomotor apraxia and (2) AA with normal praxis. Semiologically, both subtypes are marked on the graphomotor level by illegible writing, spontaneously as well as to dictation.

AA has been documented in a variety of etiologically heterogeneous neurological conditions and is typically associated with causative lesions located in the dorsolateral and medial part of the prefrontal cortex (conversion of graphomotor plans to motor commands) or in the superior parietal lobe (storage of graphomotor plans) of the language dominant hemisphere. However, lesions in several other brain areas have also been reported to cause AA. Exner (1881), Aimard, Devic, Lebel, Trouillas, and Boisson (1975), Coslett, Gonzales Rothi, Valenstein, and Heilman (1986), Rapcsak, Arthur, and Rubens (1988), Anderson, Damasio, and Damasio (1990), Hodges (1991) and Toghi, Saitoh, and Takahashi (1995) documented AA after lesions of the left *prefrontal* cortex. Rubens (1975) and Watson, Fleet, Rothi, and Heilman (1986) described AA due to a lesion in the left *supplementary motor area* (*SMA*), while Hillis et al. (2004) suggested that *Broca's area* plays a role in accessing orthographic representations. Left *parietal* lesions may also induce AA (Alexander, Fischer, & Friedman, 1992; Auerbach & Alexander, 1981; Basso, Taborelli, & Vignolo, 1978; Friedman & Alexander, 1983; Kapur & Lawton, 1983; Otsuki, Soma, Arai, Otsuka, & Tsuji, 1999; Roeltgen & Heilman, 1983). Magrassi, Bongetta, Bianchini, Berardesca, and Arienta (2010) showed that damage to the left *superior parietal gyrus* (*SPG*) may lead to distorted grapheme production. The left SPG plays an essential role in sensorimotor integration but is not involved in language; rather it is involved in the initiation of on-line updating for early movement corrections (Tunik, Ortigue, Adamovich, & Grafton, 2008). Lesions of the superior portions of the left *supramarginal* and *angular gyri* have been associated with AA (Fischer, McGrath, Bloch, Reinhalter, & Otto, 1995; Otsuki et al., 1999; Rapcsak & Beeson, 2000). AA has been documented following damage to the left *temporal* lobe (Rosait & De Bastiani, 1979; Soma, Sugishita, Maruyama, Kitamura, & Tsubaki, 1988; Yokota, Ishiai, Furukawa, & Tsukagoshi, 1990). In addition, there have been reports of subcortical lesions leading to AA. Laine and Martilla (1981) reported a 34-year-old ambidextral man with AA after a hemorrhage in the left *caudate nucleus* and *internal capsule*. Watson and Heilman (1983) described a 43-year-old right-handed woman who presented with AA due to vascular damage of the *corpus callosum*. Croisille et al. (1990) reported a 41-year-old right-handed man with a hemorrhage in the left *centrum semi-ovale* who presented with impaired grapheme production. The lesion spared both the frontal and parietal cortex, but involvement of the body of the caudate nucleus could not be excluded. Nagaratnam, Plew, and Cooper (1998), Assmus, Buss, Milkereit, Meyer, and Fink (2007) and Krisnan, Rao, and Rajashekar (2009) also found AA following vascular damage to the left centrum semi-ovale. Mariën et al. (2007) reported a 72-year-old right-handed man with AA, mild aphasia and dysexecutive disorder following right *cerebellar* damage. Mariën et al. (2007) hypothesized that AA, as documented by single photon emission computerized tomography (SPECT), resulted from crossed cerebello-cerebral diaschisis affecting the anatomoclinically suspected prefrontal language regions. In a recent review of 25 cases of vascular AA, De Smet, Engelborghs, Paquier, De Deyn, and Mariën (2011) confirmed that AA can be associated with lesions outside the language dominant parietal and frontal region. In their review three cases of cerebellar-induced AA were discussed.

During the last decades, a wealth of studies (e.g. Crosson, 2013; De Boissezon et al., 2005; Hillis, 2008; Schmahmann, 2003) has shown that the *thalamus* is crucially involved in language and cognition. De Witte et al. (2011) critically reviewed a study corpus of 465 patients with vascular thalamic lesions published between 1980 and 2008. The taxonomic label of thalamic aphasia was applied to 63.6% of the subjects with left thalamic damage. In addition, 65% of patients with left thalamic damage showed writing difficulties, i.e. paragraphias (Gorelick, Hier, Benevento, Levitt, & Tan, 1984; Raymer, Moberg, Crosson, Nadeau, & Rothi, 1997), perseverations (Archer, Illinsky, Goldfader, & Smith, 1981; Ciemens, 1970) or kanji agraphia (Maeshima et al., 1992). Unfortunately, in several cases (Alexander & LoVerme, 1980; Cappa, Pagagno, Vallar, & Vignolo, 1986; Cohen, Gelfer, & Sweet, 1980; Fassanaro et al., 1987; Kumar, Masih, & Pardo, 1996; Mori, Yamadori, & Mitani, 1986) only the severity level (ranging from mild to severe) of the writing disturbance was reported. Ohno, Bando, Nagura, Ishii, and Yamanouchi (2000), Ikegami, Kojima, Maeda, Hojo, and Fujihima (2006), Toyokura, Kaboyashi, and Aono (2010), Sakurai, Yoshida, Sato, Sugimoto, and Mannen (2011) and Osawa et al. (2013) explained both central and peripheral agraphia following thalamic damage by diaschisis phenomena of the left prefrontal or parietal cortex, reflecting the functional impact of a lesion in a distant but functionally connected region.

Besides clinical studies, brain-imaging studies using SPECT (Decety, Philippon, & Ingvar, 1988), positron emission tomography (PET) (Petrides, Alivisatos, & Evans, 1995), functional magnetic resonance imaging (fMRI) (Beeson, 2004; Katanoda, Yoshikawa, & Sugishita, 2001; Longcamp, Anton, Roth, & Velay, 2003; Matsuo et al., 2003), diffusion weighted imaging (DWI) (Hillis, 2008) and intraoperative cortical mapping (Roux, Boetto, Sacko, Chollet, & Trémoulet, 2003) tried to elucidate which regions are necessary for writing and which could possibly modulate this process. For example, Magrassi et al. (2010) noted that direct bipolar cortical stimulation in a limited area of the left anterior superior parietal gyrus induced complex writing deficits that were typical of both central and peripheral agraphias. They reported a full spectrum of alterations of writing, spanning from spelling errors with no or only slightly altered grapheme production to profound distortions of grapheme production, or even a complete writing stop. The writing impairment occurred without any associated spoken language, reading or calculation deficits. Magrassi et al. (2010) suggested that at least some of the patterns of deficits in these patients could be due to incomplete and unbalanced alterations in the function of the underlying neural circuits. Variations in the typology of the observed alterations in writing induced by stimulation of the same cortical area have also been described in studies in which the left frontal (Morris, Lüders, Lesser, Dinner, & Hahn, 1984) and left supramarginal gyrus were stimulated (Roux et al., 2003). Following these stimulation studies, it could be hypothesized that at the thalamic level central and peripheral functions are deeply interwoven in such a way that incomplete or unbalanced perturbation of the activity of the local circuits generates a complex spectrum of agraphias ranging from the central to the peripheral types.

In the literature only a handful of cases, mostly involving Japanese subjects, exists in which AA was induced by a thalamic lesion (Maeshima et al., 2012; Ohno et al., 2000; Vandenborre, van Dun, & Mariën, 2015). Ohno et al. (2000) described a 78-year-old right-handed man who could not write in the alphabetic script (Roman alphabet), the non-alphabetic script (Kanji (ideograms) and Kana (phonograms)) or Arabic numerals with either hand due to a left thalamic infarction in the dorsomedial nucleus. Copying, letter imagery and oral spelling of Kanji was intact. The majority of errors involved the partial omission or addition of characters. Scrawling, no reaction, neographism and complete substitution were not observed. Ohno et al. (2000) explained the AA from two different