Although we do not yet know the mechanism by which TMS works, we are very much interested in the increase in cerebellar blood flow after TMS. This finding suggests that TMS over the cerebellum may activate the decreased cerebellar function. This effect may be caused by direct stimulation to the cerebellum as we used the maximum strength of stimulation at 2.5 times the motor threshold. Another possibility is that sensory input from the contracted muscles by TMS might occur.

After the TMS trial we continued TMS in some patients. Patients receiving TMS once or twice a week kept their improved condition at least for 6 months, but patients receiving TMS every 2 weeks returned to their baseline in 2 weeks. Therefore, we think that the effects of TMS with our method are maintained for about 1 week. We conclude that TMS over the cerebellum is a promising treatment for spinocerebellar degeneration.

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Agraphia in Kanji after a contusional haemorrhage in the left temporo-occipital lobe

The Japanese language has two different writing systems, Kana (Japanese syllabograms) and Kanji (Japanese ideograms), and Japanese sentences usually consist of combinations of both. Recently, there has been speculation that different pathways are involved in Kanji and Kana reading and writing.[1] It has been suggested that the processing of Kanji and Kana involves different intrahemispheric mechanisms, as judged mainly through studies on patients with alexia and agraphia.[2] Wernicke's area and its surrounding left middle temporal lobe may play the most important part in Kanji reading when visual information is transmitted by any pathway. We recently had the opportunity to examine a patient who had mild transient aphasia and persistent agraphia of Kanji after a discrete contusional haemorrhage in the left temporo-occipital lobe.

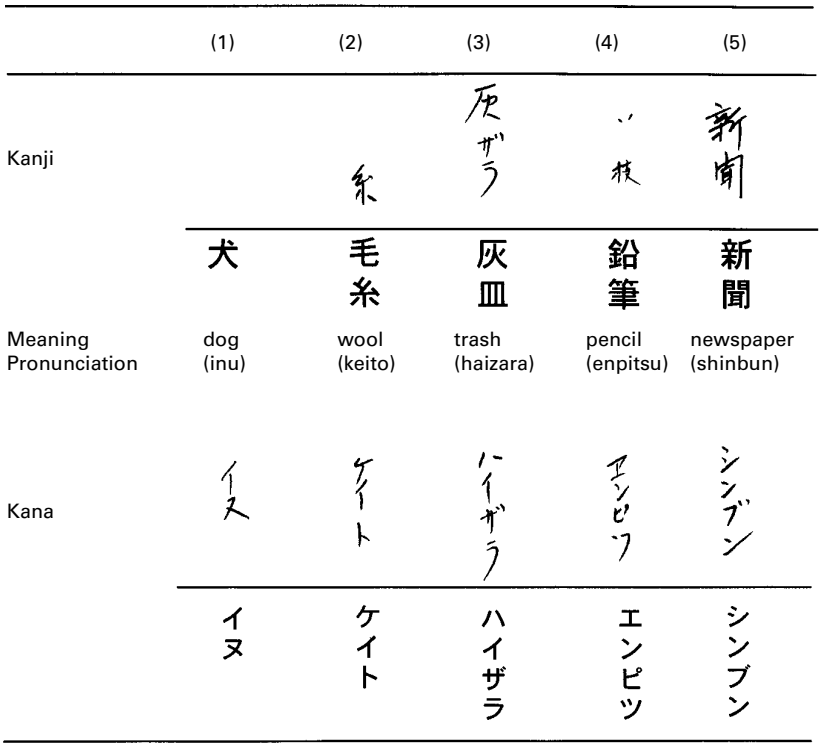

Figure 1 Examples of dictation. This patient showed intact Kana writing and difficulties in Kanji writing: 1, no response; 2, partial completion; 3, partial substitution; 4, neographism; 5, correct.

A 66 year old right handed man (pensioner) with 12 years of school education was involved in a traffic accident and sustained a closed head injury. He was admitted to our hospital the next day. He had no history of neurological problems. His parents, brothers, and sisters are all right handed. On examination, he was alert and cooperative. Neurological examination disclosed no motor or sensory disturbance.

Formal language assessment was undertaken 3 days after injury using the standard language test for aphasia (SLTA). His spontaneous speech was fluent. He had no difficulty initiating speech, articulated normally, and did not have logorrhoea. Echolalia was not seen and phonological structure was clear. Object naming was moderately impaired, with considerable paraphasia. Word fluency (animal naming) was 3/min. Repetition was excellent. Reading aloud was good; however, writing of both Kanji and Kana was impaired, and considerable paragraphia was evident.

In addition, he demonstrated constructional apraxia using figure copying of a three dimensional cube but not oral, ideomotor, or ideational apraxia. There were no signs of motor impersistence or unilateral spatial neglect. The score on Raven's coloured progressive matrices was 26/36.

Brain CT on admission showed an area of high density consistent with contusional haemorrhage in the left temporo-occipital lobe. Brain MRI 5 days after admission showed contusional haemorrhage in the left temporo-occipital lobe involving the posterior part of the temporal cortex and the adjacent white matter. There were no abnormalities in the left angular gyrus.

Aphasia was gradually resolved, his scores on SLTA 8 weeks after the onset becoming normal. Despite this, his writing ability remained clearly disturbed. We asked him to read and write on dictation 221 Kanji and 76 Kana, all of which are taught in the first 2 years of primary school in Japan. He was unable to write 83 of the 221 Kanji (37.6%), which he reported that he knew but could not recall. He tended to have difficulty with Kanji characters, which were more complex and had been learnt later (fig 1). Error types included partial substitution (two), partial completion (seven), neographism (29), and no response (45). On the other hand, he made no mistakes in reading Kanji or in reading and writing Kana letters. On the revised Wechsler adult intelligence scale (WAIS-R), his verbal intelligence quotient (IQ) was 105 and his performance IQ was 101, with an overall IQ of 103. Brain MRI 3 months after admission showed a subcortical lesion in the left temporo-occipital lobe (fig 2).

Although this patient experienced aphasia immediately after cerebral contusion, the aphasia resolved over a subsequent 8 week period. He was left with an isolated disturbance of Kanji writing. In the absence of any dementia, aphasia, or disturbance of consciousness, his condition was classified as one of pure agraphia.

Soma *et al*[2] described "pure agraphia of Kanji" in three patients, who had a lesion in the left posterior temporal area extending to the angular gyrus on CT. Although they

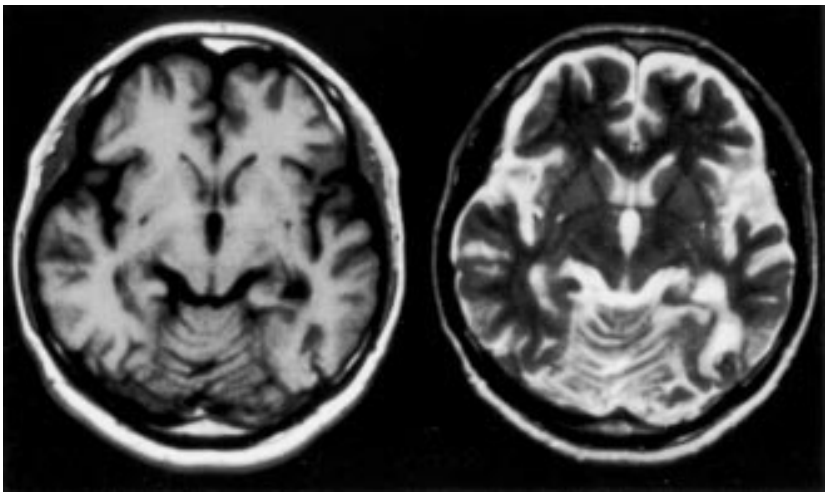

Figure 2 Brain MRI 3 months after admission showed the subcortical lesions in the left temporo-occipital lobe.

exhibited amnestic aphasia, alexia, and agraphia in the acute phase, disturbances other than agraphia of Kanji disappeared in a few months. Yokota *et al*[3] also reported a case with pure agraphia of Kanji, and suggested that the process of writing Kanji involves a different pathway from that which mediates Kanji reading in the left temporal lobe.

Iwata[1] proposed a hypothetical neuronal mechanism in the writing of Kanji and Kana as follows: the Broca's and motor association areas are the final coordination centres, but the angular gyrus plays an important part in sending the graphic information to the motor areas. However, spontaneous writing and responses to dictation are usually initiated by Wernicke's area, which gives rise to two different pathways to the angular gyrus. One is the auditory somaesthetic association pathway leading directly from Wernicke's area to the angular gyrus; Kana writing mainly depends on the intactness of this route. The second pathway is from Wernicke's area to the occipital lobe by way of the posterioinferior temporal area. This is the pathway involved in selecting the correct Kanji graphemes according to the meaning of the word, and thus recalled visual engrams of letters are sent to the angular gyrus.

Our patient demonstrated that initial amnestic aphasia, and agraphia of Kanji were associated with a lesion in the left temporal lobe. Because the posterior temporal region is located in close proximity to the angular gyrus and Wernicke's area, the pathological process in the first area affects the second two regions in its acute phase. We conclude that the persistent symptom of pure agraphia for Kanji in this study was caused by the left posterior temporal lesion which disconnected the pathway for Kanji writing selectively.

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Successful autologous stem cell transplantation in a patient with chronic inflammatory demyelinating polyneuropathy

A patient with chronic inflammatory demyelinating polyneuropathy is reported on who never had spontaneous remissions for 10 years, but who is in remission for 2 years after an autologous stem cell transplantation (ASCT). Before ASCT he needed at least 20 mg prednisone/day and in addition intravenous immunoglobulin (IVIg) treatment at regular intervals. An ASCT was considered in this patient because of serious side effects of immunosuppressive treatment.

Chronic inflammatory demyelinating polyneuropathy (CIDP) is characterised by weakness with sensory impairments in the arms and legs. The reflexes in the arms and legs disappear. The onset is insidious. There may be progressive deterioration or a course with remissions and exacerbations. Routine blood examination is usually normal. Protein in CSF is increased in most patients. Electrophysiological studies may show slow nerve conduction velocities, conduction blocks, or dispersion.[1] Inflammatory demyelinating polyneuropathy is considered to be an autoimmune disease which is supported by the presence of inflammatory cells in sural nerve biopsies and the beneficial response to immunosuppressive treatment in most patients.[2] We describe a patient with CIDP who has had this disease for 10 years without spontaneous remissions. He responded to immunosuppressive therapy, but needed high doses and had severe side effects. Therefore, we decided to try to induce a long lasting remission by autologous stem cell transplantation (ASCT).

This patient was 38 years old when, in 1988, he began to have tingling and numbness in his fingers. The sensory symptoms progressed to his arms and legs, followed by weakness. Initially his symptoms were attributed to too much stress but at the end of 1990 when weakness had worsened to such an extent that he was no longer independent in his daily activities, it was decided that it was time for a neurological evaluation. At that time he had weakness of his arms and legs, MRC grade 4. There was atrophy of his intrinsic hand muscles and fasciculations were seen in the muscles of his arms. Except for diminished knee reflexes, there was areflexia. He had numbness of his arms and legs in a glove and stocking distribution. Electrophysiological studies showed slowed nerve conduction velocities of the median, ulnar, tibial posterior, and peroneal nerves in the range of 15–25 m/s with prolonged distal latencies and F wave responses. The distal compound muscle action potentials were small. Few muscles had signs of denervation. Blood examination was unremarkable and CSF total protein was 0.67 g/l without cells. Sural nerve biopsy was consistent with CIDP, showing inflammatory cells and demyelination.

In 1990 he was started on 60 mg/day prednisone. After 2 weeks improvement began. This improvement continued to normal strength leaving only slight numbness in his fingers. During tapering off of the prednisone dose he had mood disturbances at every change of dose. Repeatedly he had a relapse at doses lower than 20 mg/day. Subsequently we tried to replace prednisone by 150 mg/day azathioprine but after 2 years of treatment with azathioprine it was still not possible to decrease the dose of prednisone to less than 20 mg/day. Azathioprine was replaced by methotrexate (7.5 mg/week) for 6 months without a beneficial response. Thereafter he was treated with IVIg. After two cycles of 30g/day IVIg for 5 days he needed infusions every other week to maintain his improved condition. We tried to prolong these intervals by adding prednisone. With 20 mg/day prednisone he remained free of relapses for about 4 months. However, these intervals became gradually shorter; he developed arthralgias after administration of IVIg, and had repeated gastric pain. After 8 years of immunosuppressive treatment, without spontaneous remissions, we discussed the possibility of autologous stem cell transplantation (ASCT).

In May 1998 peripheral blood stem cells were harvested by leukopheresis after mobilisation with cyclophosphamide (4 g/m^2) and granulocyte colony stimulating factor (G-CSF; 5 μg/kg). CD 34+ cells were positively selected by immunomagnetic beads (Clinimax®, purity 98.7%) and cryopreserved. Before this procedure the patient had had IVIg every other week together with 20 mg/day prednisone. With this regular IVIg treatment he was in an optimal condition: he had no weakness and only mild sensory impairment of his fingers. After the mobilisation procedure, prednisone could be tapered off to 8 mg/day. Even without IVIg he remained in this improved condition for 5 months before he relapsed. Weakness in the arms and legs returned together with sensory impairment. Electrophysiological studies were repeated. We decided firstly to improve his neurological condition by IVIg treatment before myeloablative treatment was started. This treatment resulted in considerable improvement; only mild sensory impairment of the fingers remained.