Clinical/Scientific Notes

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FAMILIAL CONGENITAL MIRROR MOVEMENTS: REPORT OF A LARGE 4-GENERATION FAMILY

Mirror movements (MM) are synkinesias occurring in the opposite side during the intentional use of a limb. They are occasionally present in children, but persistence after age 10 is abnormal.[1,2] We have found a large 4-generation family with congenital mirror movements not associated with other neurologic abnormalities.

Methods. Nineteen members (11 affected and 8 unaffected) of a 4-generation family with individuals affected with congenital MM were interviewed in a systematic questionnaire that queried perinatal history, development, presence of learning disabilities, and other medical history. Information regarding the onset, distribution, suppressibility, and functional and social impact of MM was obtained. A videotaped examination was performed, and subjects underwent diadochokinesimeter measurement of rapid alternating pronation-supination movements at 2 different velocities. The diadochokinesimeter consisted of 2 hand-held plastic spheres connected to optical encoders, which recorded amplitude and velocity of movement in each hand.[3] This project was approved by the Institutional Review Board of the Centre Hospitalier de l'Université de Montréal.

Results. This French Canadian family originates from the Lanaudière region of Quebec. There is no known consanguinity. Transmission is autosomal dominant with high but incomplete penetrance. Penetrance is higher in males (figure).

The index case first sought neurologic attention for episodes of fatigue, and MM were incidentally noted on examination. They had been present since childhood, and had never resulted in functional or social impairment. The remainder of the neurologic examination was normal. MRI of the brain and cervical cord was normal.

Questionnaire results and clinical features are presented in tables e-1 and e-2 on the *Neurology*® Web site at www.neurology.org. More men than women were affected (M:F = 9:2). Perinatal and developmental histories did not differ between affected and unaffected individuals. MM were present in hands, fingers, and forearms of all affected individuals: upon voluntary activation of one hand, the contralateral hand would mirror both simple and complex movements such as writing, typing, and tapping. Three individuals reported MM in the toes and feet, which were observable during foot tapping and movement of the toes. In most, MM were noted at birth or infancy, and persisted unchanged throughout life. Half could partially suppress the movements. Despite often high amplitude and easily observed movements, patients functioned essentially normally. One patient worked successfully as an electrician performing high precision bimanual tasks, and another worked as a secretary and could type rapidly. Three reported mild clumsiness during childhood. Several reported social impairment, stating they felt conspicuous or embarrassed by their MM.

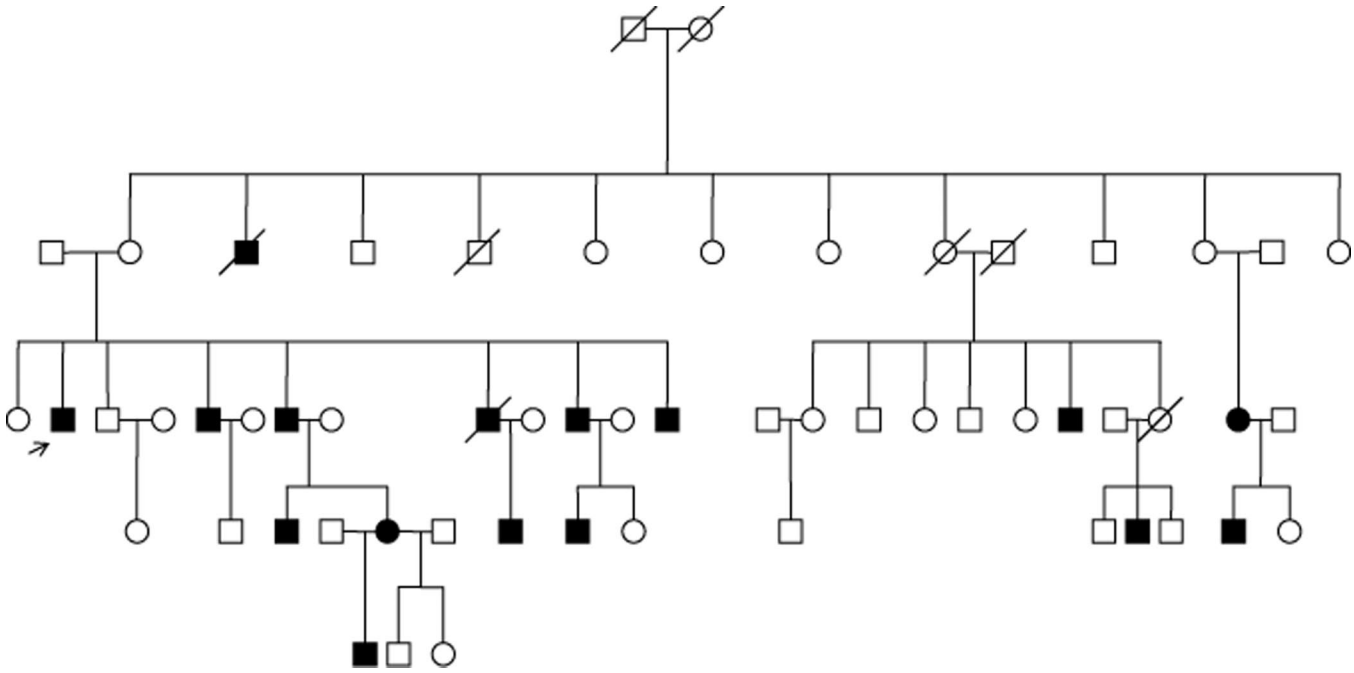
Neurologic examinations were otherwise normal in all. Specifically, there was no anosmia, parkinsonism, motor asymmetry, or dysmetria. An example of the MM is shown on the video. Results of the quantitative testing confirmed clinical diagnosis. In affected members, MM showed amplitudes and velocities ranging from 4% to 26% and 5% to 43% of the values observed in the voluntary hand at normal and fast pace. There were no differences between left and right hand MM. Unaffected members did not show any MM movements.

Discussion. This report of a large 4-generation family with familial congenital MM not associated with neurologic abnormalities provides definite evidence that MM can be familial, with an autosomal dominant inheritance with incomplete penetrance. There have been sporadic case reports of congenital MM in 2 or 3 members of a family, and a recent report suggested potential for multigeneration involvement, although a very limited cohort was examined.[2,4]

The pathophysiology of familial congenital MM is uncertain. MRI of brain and upper cervical spine shows no abnormalities of the corpus callosum, brainstem, or upper cervical cord, as seen in Klippel-Feil syndrome, Joubert syndrome, or Chiari type 1.

Supplemental data at www.neurology.org

Figure Pedigree of the family with congenital mirror movements illustrating autosomal dominant inheritance with incomplete penetrance



There have been no pathology reports of familial congenital MM.

In individuals with familial congenital MM, there is evidence of fast-conducting corticospinal pathways connecting M1 with both sides of the spinal cord. Transcranial magnetic stimulation (TMS) studies have shown that stimulation of either M1 can elicit bilateral motor evoked potentials of normal and symmetric latency in resting hand muscles in MM patients.[5,6] This is in contrast to physiologic MM in children, where evoked responses are not simultaneous and have a long latency, probably reflecting the spread of excitation across the corpus callosum.[1,5] Therefore, the pathophysiology of physiologic and congenital MM are distinct, and there exists an abnormal ipsilateral corticospinal projection in familial congenital MM.

The origin of these abnormal ipsilateral corticospinal pathways is unclear. Hypotheses include abnormal branching of crossed corticospinal fibers to ipsilateral spinal motor neurons or presence of a separate ipsilateral corticospinal projection.[1,7] Dysfunctional inhibitory transcallosal projections (i.e., from premotor regions) affecting M1 contralateral to the MM may also contribute to the MM. Further genetic studies are underway in this family to clarify the underlying genetic basis of this disorder.

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AKINETOPSIA IN THE POSTERIOR CORTICAL VARIANT OF ALZHEIMER DISEASE

Akinetopsia is a rare condition in which patients cannot perceive motion.[1] Akinetopsia has occurred from bilateral cortical lesions involving the temporo-parieto-occipital junction.[1,2] This report describes 2 patients with akinetopsia from neurodegenerative disease. They had double vision, and proved to have directional akinetopsia with persistence of successive stills from moving images as part of posterior cortical atrophy (PCA) or visual variant Alzheimer disease (AD).[3,4]

Case reports. ***Case 1.*** A 71-year-old right-handed woman had a 3-year progressive decline in the ability to visually localize objects. She could not find objects in her home, on countertops, in her wallet, or if dropped. She also had double vision. Leftward moving objects were perceived as 2 or more successive images occurring side by side. She did not have polyopsia on viewing static objects or on moving her eyes.

The patient also had a decline in recent memory, numerical ability, and instrumental activities of daily living. Past medical history included recent cataract surgery in an attempt to fix her visual problems, and her medications were donepezil and memantine.

On examination, she scored 21/30 on the Mini-Mental State Examination (MMSE). Language was fluent with good auditory comprehension, repetition, and naming. On a verbal learning task, the patient recalled 0/10 words after a 15-minute delay, and subsequent neuropsychological testing confirmed a prominent deficit in episodic memory. Praxis and abstraction were intact, but calculations and right–left discrimination were abnormal.

On neurologic examination, cranial nerves, including visual acuity, visual fields, voluntary saccades, and range of extraocular movements, were normal except for saccadic pursuit. Akinetopsia was elicited with fingers or objects moving toward the left and was not eliminated with alternate eye cover and uncover. There were no abnormalities on gait, motor, sensory, and reflex examinations. Neuroimaging showed bilateral parieto-occipital changes (figure).

Case 2. A 61-year-old man had 18 months of progressive difficulty finding objects. He would lose objects that he put down, often walking by them multiple times without seeing them. Localization was particularly difficult in the left visual field, and he had significant dressing apraxia. This patient further described a sensation of double or multiple images when objects moved in a leftward direction, but not on moving his eyes.

He had a decline in memory, reading, writing, and the use of numbers, and was depressed over his condition. Medical history included polyarthritis and a left knee replacement, and his medications were donepezil, memantine, and bupropion.

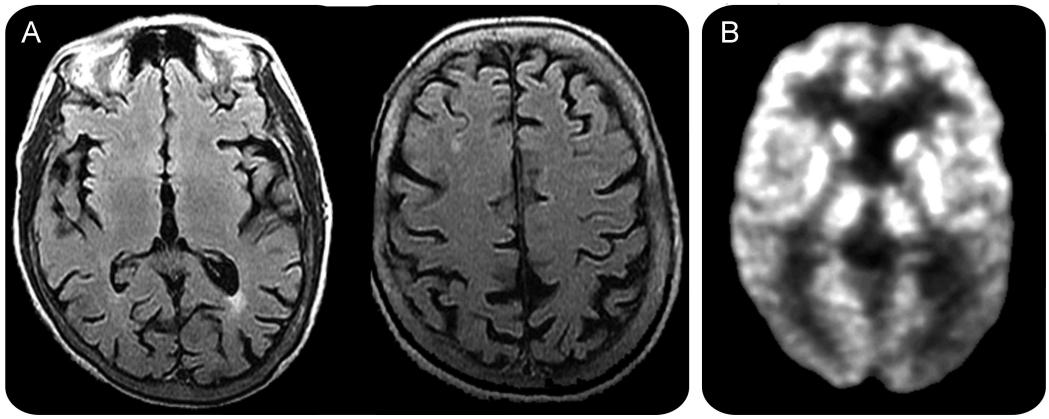
On examination, his MMSE score was 21/30. His language was fluent with good auditory comprehension, repetition, and naming. He recalled 2/10 words at 15 minutes; this memory deficit was confirmed on neuropsychological tests. Further testing showed difficulty in reading and number use, but no apraxia.

On neurologic examination, cranial nerves, including visual acuity, visual fields, voluntary saccades, and range of extraocular movement, were intact except for left hemispatial neglect and saccadic pursuit. Akinetopsia was elicited with fingers or objects moving to the left and was not eliminated with alternate eye cover and uncover. There were no abnormalities on the rest of his neurologic examination, and MRI showed atrophy especially in parietal regions.

Complex visuospatial tests. Both case 1 and case 2 had decreased visuospatial constructions (Rey-Osterreith), figure-ground discrimination (cross-hatched and overlapping figures), visual synthesis (Hooper and Gollin figures), visual search (picture and dot localization), and monocular depth discrimination (relative size and perspective). Both had intact color naming, object recognition, and famous face recognition.

Discussion. These patients had akinetopsia from the posterior cortical or visual variant of AD.[3,4] They presented with double vision, and proved to have akinetopsia on perceiving object motion toward the left. Their double vision was consistent with polyopsia due to brief persistence of the successive images from dysfunction of the contralateral parietal cortex.[5]

Figure Case 1: (A) MRI horizontal images of the brain showing mild white matter changes and atrophy, most prominent in the parietal regions; (B) fluorodeoxyglucose PET scan showing cortical hypometabolism in the posterior parieto-occipital regions



Akinetopsia or motion blindness results from damage affecting the temporo-parieto-occipital cortex (area MT/V5 in monkeys corresponds to the junction of Brodmann areas 19 and 37).[1,2] Area MT/V5 contains neurons sensitive to the direction, speed, and orientation of motion.[1,2] The most characteristic feature of primate MT/V5 neurons may be their preference for one direction of motion, corresponding with the leftward directional akinetopsia in these 2 patients.[6]

PCA results in progressive complex visual disturbances and most commonly represents a visual variant AD with or without prominent memory impairment.[3,4] On tests, AD is associated with impairment of visual motion perception independent of the degree of memory impairment.[7] These 2 patients illustrate akinetopsia presenting as double vision in PCA/AD and suggest that this disorder involves the dorsal (parietal) visual stream for visuospatial localization.

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