

Correspondence

ASSOCIATION BETWEEN ALZHEIMER DISEASE AND AMYOTROPHIC LATERAL SCLEROSIS?

To the Editor:

I read with interest the recent article by Frecker et al¹ discussing the possible association between Alzheimer disease (AD) and amyotrophic lateral sclerosis (ALS).

To date, 617 consecutive, unrelated index cases attending the Clinic for Alzheimer Disease and Related Disorders have had detailed family histories taken using the family history method with multiple informants.² Three relatives of 2 out of 233 (0.86%) index cases with a diagnosis of "probable" AD according to recognized criteria³ possibly had ALS.

Family "A" was of Norwegian ancestry. The index case, the eldest of 2 children, had the onset of her dementia at approximately age 50. She is still alive at age 55. Her sister, aged 44, is alive and well. Her father died at age 66 from a brain tumor and was mentally alert. Her mother died at age 62 and the diagnosis of ALS in this lady was confirmed by autopsy. There was one maternal uncle (brother of the index case's mother) who reportedly suffered from dementia and ALS. An autopsy performed in 1974 confirmed the diagnosis of ALS, but the etiology of the dementia was not resolved.

Family "B" was of English ancestry. The index case, the youngest of four children, had the onset of her dementia at age 72. She is still alive at age 79. One of her brothers died at age 18 during World War II and another brother died at age 75 from heart problems and was mentally alert until his death. Her sister also developed dementia at age 72 and died at age 77 with a neuropathologically confirmed diagnosis of AD. The index case's father died at age 86 and was mentally alert until his death. Family informants reported that her mother had a "neurological condition", but all relevant clinical records on this lady have been destroyed. However, clinical records on the index case's sister were obtained. These stated that "her mother died at age 67, secondary to some neurological disease that sounds similar to ALS".

One hundred forty-six index cases seen at the Clinic are presently diagnosed as "possible" AD.³ Of these, informants for one family reported a relative with ALS. Family "C" was of German, Dutch and English ancestry. The index case, the second of four children, had the onset of her dementia at age 62 and is still alive at age 67. Her eldest sister died in her mid-fifties from a brain tumor. Another sister is alive and well at age 65. Her only brother died at approximately age 60 from ALS, diagnosed clinically but there was no autopsy.

In summary, out of 379 consecutive, unrelated index cases with a diagnosis of "probable" or "possible" AD,³ 3 (0.79%) had a total of 4 first- or second-degree relatives reported to have ALS. Assuming a prevalence for ALS of 1 in 100,000,⁴ this is more frequent than expected. We therefore agree with Frecker and colleagues¹ that further investigation is warranted on the possible association between ALS and AD.

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POSSIBLE INTERACTIONS BETWEEN DEPRENYL AND PROZAC

To the Editor:

Fluoxetine (Prozac) and Selegiline (Deprenyl), are two new medications which have only recently been introduced on the North American market. There is limited experience using these medications in combination, and we would like to describe two patients in which there may have been an interaction between these two drugs.

The first patient is a 46-year-old woman, with moderately severe, left sided Parkinson's disease, who was maintained on Prolopa 15/12.5 every two hours and bromocriptine 10 mg t.i.d. She was also taking amitriptyline 50 mg hs for depression, which over the years had been considered to be an atypical depression. She had taken selegiline for a month in the fall of 1989, but discontinued it because of lack of perceived benefit.

In January of 1990, because of anticholinergic side-effects, the amitriptyline was discontinued and fluoxetine 20 mg q.a.m. initiated. Selegiline was re-started about ten days later. Initially, the patient felt much better. However the next month, she became increasingly hyperactive, over communicative, elated and creative. Her actions and judgement appeared grossly impaired, and her physicians thought her to be manic. Both the selegiline and fluoxetine were discontinued, and the patient slowly improved, over the next 2 months.

Fluoxetine has previously been reported to cause mania^{1,2} although usually at higher doses than 20 mg a day, and manic symptoms resolved quickly with discontinuation of fluoxetine. Selegiline is metabolized to 1-amphetamine and 1-methamphetamine, and may cause agitation in some patients. In one case, selegiline alone was reported to cause manic behavior.³ Thus, the severe prolonged mania seen in this patient may have been due to the concomitant use of selegiline and fluoxetine.

The second patient, a 56-year-old woman, with moderate

Parkinson's disease, had selegiline 5 mg q.a.m. added to her previous regime of Parlodel 5 mg t.i.d. and Sinemet 100/25, 8 tablets per day in January of 1990. She was also on amitriptyline, for depression which was discontinued in March of 1990 because of urinary hesitancy. The patient was started on fluoxetine 20 mg q.a.m.

Several days after starting the fluoxetine, the patient started to develop episodes, during which she would shiver and break out into a cold sweat. The episodes would start in midafternoon, and last for several hours. On these occasions, she would feel very clammy, and her hands would be cold. She was seen in the office for assessment one month later. At that time, it was noted that she was very diaphoretic. Her hands were severely vasoconstricted, and the fingers were blue and mottled. Her blood pressure was 200/120.

Previously, the patient had had transient elevations of blood pressure, which were usually induced by stress, but she did not feel under stress on this occasion. The selegiline and fluoxetine were both discontinued, and she recovered over the next few days. Her blood pressure returned to normal (120/90). She did not have any further diaphoretic episodes. She has since restarted fluoxetine with no side-effects.

This patient developed a very unusual reaction, which has not been reported previously with either selegiline or fluoxetine. As she was able to tolerate both medications independently, it would appear to be specifically due to this combination.

Selegiline, a selective MAOB inhibitor at low doses (5-10 mg a day) has been reported to cause hypertension, when taken in high doses, due to loss of selectivity.⁴ However, this patient was taking only 5 mg a day and use of deprenyl alone did not cause any elevation of BP on previous visits. Several reports have suggested that administration of tranlycypromine, a non selective MAO inhibitor together with fluoxetine, may result in a "serotonin syndrome" characterized by shivering, diaphoresis, diplopia, nausea and confusion.⁵ The temporal sequence of this patient's symptoms, suggests that the episodes of diaphoresis and hypertension may have been due to the combination of fluoxetine and selegiline, and may be similar to the serotonin syndrome reported previously.

No previous reports of a possible interaction between Deprenyl and Prozac have been reported in Canada to this date. However representatives from the manufacturer of Prozac have indicated that they are aware of several reports in the U.S. and that they are recommending that Selegiline and Fluoxetine not be used in combination.

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DR. MCKENZIE'S YEAR WITH DR. CUSHING

To the Editor:

Dr. Kenneth McKenzie and his many contributions to the art of neurosurgery are long remembered even after half a century. After receiving a degree in medicine from the University of Toronto in 1914, he joined the British Royal Medical Corps when World War I was declared. After the war, he returned to the University of Toronto for postgraduate surgical training with Dr. Clarence L. Starr, the Professor and Chief of Surgery there. When Dr. Harvey Cushing was awarded the Charles Mickle Fellowship by the University of Toronto in 1922, he invited Dr. Starr to send a man to Boston to train with him in neurosurgery. Dr. McKenzie was selected for the position and given a \$1000 scholarship.¹

Dr. McKenzie's contributions during his career were numerous and included operative modifications and improvements in the treatment of chronic subdural hematomas and gliomas. He seemed to take particular interest in pathological conditions affecting the cranial nerves. For example he studied and wrote about Menier's disease, acoustic neuromas, and spasmodic torticollis. In reviewing the surgical histories of the Peter Bent Brigham Hospital (PBBH) from 1922 to 1923, we have found that Dr. McKenzie was also interested in the treatment of trigeminal neuralgia. During Dr. McKenzie's training period in Boston, Dr. Harvey Cushing and Dr. Gilbert Horrax performed many operations for the treatment of trigeminal neuralgia. Dr. McKenzie performed admission neurological examinations on most of these patients and recorded both objective and subjective findings for each cranial nerve. He then documented many of his post-operative neurological examinations with diagrams sketched by himself. We report one of the trigeminal neuralgia cases well documented by Dr. McKenzie and show a typical sketch.

AD was a 70-year-old white male who presented with pain involving the entire left side of the face. His problem began 10 years prior to admission; one day while dressing he was seized with a sharp, twisting, shooting, pain in his left forehead lasting for about 30 seconds. He had several more episodes of the same type of pain confined to the left forehead at intervals over 2-3 months. Eight years prior to admission, he developed intermittent paroxysmal pain in the left lower mandibular area which frequently radiated to the left infraorbital region, never crossing the midline. These attacks usually lasted from 15 to 60 seconds and disappeared suddenly. His symptoms gradually worsened both in frequency and severity. A slight jar, chewing, yawning, swallowing, walking without rubber heels or riding over a rough surface could bring on a paroxysm of pain. Neurological examination performed by Dr. McKenzie showed a decreased corneal reflex in left eye but normal sensation in the face.

An avulsion of the third division of the left trigeminal nerve was performed by Dr. Horrax on January 19, 1923. His operative note states: "This case was a very easy and simple one . . . The third division was identified and from this the dura [was] peeled back off the ganglion and sensory root and its fibers avulsed easily and completely as far as could be told. No attempt was made to save the motor division . . . brain [was] allowed to go back to its normal position by lowering the head.