

# Ocular-Motor Profile and Effects of Memantine in a Familial Form of Adult Cerebellar Ataxia with Slow Saccades and Square Wave Saccadic Intrusions

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## Abstract

Fixation instability due to saccadic intrusions is a feature of autosomal recessive spinocerebellar ataxias, and includes square wave intrusions (SWI) and macrosaccadic oscillations (MSO). A recent report suggested that the non-competitive antagonist of NMDA receptors, memantine, could decrease MSO and improve fixation in patients with spinocerebellar ataxia with saccadic intrusions (SCASI). We similarly tested two sisters, respectively of 58 and 60 years, with an unrecognized form of recessive, adult-onset cerebellar ataxia, peripheral neuropathy and slow saccades, who showed prominent SWI and also complained with difficulty in reading. We tested horizontal visually guided saccades ( $10^{\circ}$ – $18^{\circ}$ ) and three minutes of steady fixation in each patient and in thirty healthy controls. Both patients showed a significant reduction of peak and mean velocity compared with control subjects. Large SWI interrupting steady fixation were prominent during steady fixation and especially following visually guided saccades. Eye movements were recorded before and during the treatment with memantine, 20 mg/daily for 6 months. The treatment with memantine reduced both the magnitude and frequency of SWI (the former significantly), but did not modified neurological conditions or saccade parameters. Thus, our report suggests that memantine may have some general suppressive effect on saccadic intrusions, including both SWI and MSO, thereby restoring the capacity of reading and visual attention in these and in other recessive forms of ataxia, including Friedreich's, in which saccadic intrusions are prominent.

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## Introduction

Saccadic intrusions occurring during attempted visual fixation are a well-documented feature of recessive hereditary cerebellar ataxias, such as Friedreich's ataxia and spinocerebellar ataxia with saccadic intrusions (SCASI) [1,2]. Such movements comprise a range of disorders that include square-wave intrusions (SWI), macrosaccadic oscillations (MSO), saccadic pulses, and ocular flutter [3]. Of these, SWI are the most common and consist of a pair of small, predominantly horizontal saccades (typically  $<5^{\circ}$ ), the first of which takes the eye away from the fixation position and the second returns it after a period of 200–400 ms [4]. Since the eye returns to its target following each bi-saccadic intrusion, vision is usually not compromised by square-wave jerks unless they are large and frequent. Many healthy individuals have SWI, and their frequency may be as high as 20 per minute [4]. In hereditary ataxias and parkinsonian disorders such as progressive supranuclear palsy, the size and frequency of SWI may be increased, sometimes being so frequent to appear as “square-wave oscillations.” [3] Recent studies suggest that SWI form a continuum with microsaccades, which all normal subjects display, and which appear to prevent fading of vision due to sensory adaptation [5,6].

It is hypothesized that, if the size of microsaccades increases, a return movement will be triggered, giving the appearance of SWI [7,8].

Distinct from SWI are MSO, which consist of a series of predominantly horizontal saccades that oscillate the eyes across the point of fixation [9]. Although MSO also show an intersaccadic interval of 200 ms, they often degrade vision because the line of sight does not land on target, but straddles the point of fixation. MSO often co-exist with saccadic hypermetria, and occur following destructive lesions of the deep cerebellar nuclei [10]. Patients with MSO and saccadic hypermetria often complain of difficulty with reading, which can be explained by their frequently losing their place as they switch from one line of text to the next [3]. Other saccadic intrusions such as saccadic pulses and ocular flutter may also disrupt vision, but they are less common than SWI and MSO in the hereditary ataxias.

A recent report [11] suggested that the non-competitive antagonist of NMDA receptors memantine [12] could decrease MSO and improve vision in patients with hereditary ataxia. We report a similar effect of memantine in two sisters with an