Spinocerebellar ataxias in Asia: Prevalence, phenotypes and management

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ABSTRACT

This paper reviews and summarizes three main aspects of spinocerebellar ataxias (SCA) in the Asian population. First, epidemiological studies were comprehensively reviewed. Overall, the most common subtypes include SCA1, SCA2, SCA3, and SCA6, but there are large differences in the relative prevalence of these and other SCA subtypes between Asian countries. Some subtypes such as SCA12 and SCA31 are rather specific to certain Asian populations. Second, we summarized distinctive phenotypic manifestations of SCA patients of Asian origin, for example a frequent co-occurrence of parkinsonism in some SCA subtypes. Lastly, we have conducted an exploratory survey study to map SCA-specific expertise, resources, and management in various Asian countries. This showed large differences in accessibility, genetic testing facilities, and treatment options between lower and higher income Asian countries. Currently, many Asian SCA patients remain without a final genetic diagnosis. Lack of prevalence data on SCA, lack of patient registries, and insufficient access to genetic testing facilities hamper a wider understanding of these diseases in several (particularly lower income) Asian countries.

1. Introduction

Spinocerebellar ataxias (SCAs) represent a group of rare, autosomal dominantly inherited neurodegenerative disorders. Currently, almost 50 subtypes have been identified [1]. A systematic review previously estimated the worldwide prevalence of SCA to be 2.7 cases per 100,000 [2]. Given the fact that approximately 60% of the world population is living on the Asian continent [3], one would extrapolate that a majority of the SCA patients is of Asian origin and/or inhabitant of the Asian continent. Despite this, there is a clear underrepresentation of scientific data on SCA coming from Asian countries. The majority of studies come from a limited number of countries like Japan, China, India, and South Korea, while many other countries are not represented in the current literature. This means that there is insufficient knowledge on SCA prevalence, genetic subtypes, and disease manifestations for many of the Asian countries.

As there are new treatment options at the horizon for SCAs, some of which are highly selective for certain genotypes, it is becoming increasingly important that SCA patients are recognized early and that a definite SCA genotype is established. Lack of knowledge on Asian-specific disease characteristics, as well as registries and genetic testing facilities for SCA, pose clear challenges towards optimal diagnostic and therapeutic strategies in many Asian countries. This review 1) summarizes the known epidemiological data of SCAs in Asia, 2) highlights Asian-specific phenotypic aspects of SCA subtypes, and 3) provides survey data on SCA-specific healthcare resources in Asian countries.

2. Methods

First, a systematic search on PubMed was conducted in December 2020, using a combination of keywords and Mesh terms that focus on studies reporting on relative frequencies of SCA subtypes in Asian countries (see Appendix 1 for the complete search strategy). Seven additional studies were found after reviewing reference lists of included studies. The complete systematic search yielded 175 studies. To be included in the systematic review, studies were required to be in English language, published after 01-01-1995, and report on relative frequencies of SCA genotypes in specific Asian countries. See Fig. 1 for a flowchart on the systematic search and final selection of articles (see also Appendix 3 for a full list of included studies). Relative frequencies and absolute patient numbers of SCA subtypes were extracted from the
included studies as well as other relevant study information (cohort size and characteristics, absolute patient numbers, and proportions of patients with unknown genetic etiology). All data were clustered based on country (and specific region within a country, if applicable) and genetic subtype. We performed a descriptive analysis, by describing highest and lowest reported relative frequencies as well as calculating median relative frequencies for each SCA subtype and the median proportions of SCAs with an unknown genetic cause for all countries. For this analysis, we only included studies reporting on frequencies of several SCA subtypes (see Fig. 1.) in order to be able to reliably assess relative frequencies.

Second, we reviewed the literature on Asian-specific genotypes and phenotypic variations. Our systematic search on relative frequencies of SCA subtypes already provided several studies reporting on country-specific genotypes and related phenotypes. Reference lists of these studies were screened for all potentially relevant references cited, as well as studies citing the study on PubMed. We continued our literature search for Asia-specific phenotypic aspects using a citation-based search, rather than an additional broad literature search as we expected that it would result in a rather small selection of studies. Two recent studies were used as a starting point [4,5]. Other studies suggesting Asia-specific elements within a SCA subtype were reviewed and included.

Thirdly, we conducted a survey on various aspects of SCA-related expertise, facilities, resources, and management in various Asian countries. Key opinion leaders of several Asian countries (China, India, Indonesia, Japan, Laos, Malaysia, Philippines, Singapore, South Korea, Taiwan, Thailand, Vietnam) were invited by the authors to participate in an online survey. The invited authors were encouraged to forward the invitation to other colleagues. The survey was designed and distributed via the online survey tool Limesurvey, hosted by the server of the Radboudumc Health Academy and was divided into four sections: section 1, characterization of the participants (i.e. name, country, qualifications); section 2, characterization of the country in relation to SCA (i.e. SCA experts and tertiary centers, accessibility, patient associations, training possibilities); section 3, focus on availability of diagnostics; section 4, focused on availability of treatment options. A total of 37, mainly close-ended questions (yes/no, easily accessible/accessible with some difficulty/not available) were included, but respondents were encouraged to provide additional free text comments (Appendix 2 shows the survey questions). All survey data were exported from the online survey tool and responses were clustered based on their originating country. In case of contradictory answers between respondents from the same country, the respondents were approached by e-mail to provide additional comments on their answer. If despite these efforts uncertainty remained with regards to specific questions, the final answer was set as uncertain.

3. Results

3.1. Part 1: Relative frequency of SCA genotypes and geographical distribution in Asia

Fifty-one studies that reported on relative frequencies of SCA genotypes in Asian countries were included. These studies came from 10 different Asian countries (Fig. 1). The majority of these studies were from China (n = 13), Japan (n = 13), and India (n = 10), while several Asian countries had not published any (prevalence) studies on SCA.

Fig. 1. Flowchart of systematic review and nationwide overview of Asian studies reporting on relative frequencies of SCA subtypes.
Most included studies reported on relative frequencies of (several or specific) SCA subtypes and were based on numbers of patients diagnosed within tertiary ataxia centers. Some studies focused on relative frequencies within a cohort of sporadic SCA cases, while other studies reported relative frequencies within a cohort of known dominant ataxia families, a combined sporadic and familial cohort, or a cohort of ataxia patients in whom the most common repeat-expansion SCAs were excluded. Where some papers were able to provide estimates on nationwide prevalence rates, other studies covered specific districts within countries. These different methodological approaches result in large heterogeneity and scattering of results, both within and between countries. Therefore, country-specific prevalence rates for the various SCA subtypes cannot currently be estimated accurately. Table 1 illustrates the heterogeneity in reported relative frequencies, showing highest reported relative frequencies, lowest reported frequencies, and calculated median relative frequencies in all Asian countries of which more than one prevalence study was available.

Still, based on these data, the relatively common SCA subtypes for various countries could be extracted (Fig. 2). SCA3 is the most common subtype in China [6-11], Thailand [12,13], Taiwan [14,15], Singapore [16,17], and Malaysia [18]. SCA2 is the most common subtype in India [19-26] and South Korea [27-30]. In Japan, SCA6 and SCA3 are the most common subtypes [31-41]. DRPLA is also relatively more common in Japan compared to other Asian (and also Western) countries. SCA1 was the most commonly observed genetic subtype in a single prevalence study from Sri Lanka [42]. A case report from Mongolia reported on one SCA1 patient, the first genetically confirmed SCA patient in this country in 2019 [43]. Another case report from the US reported on four Cambodian families originating from the same region in Cambodia, who immigrated to the United States and were diagnosed with SCA3 [44]. In Hong Kong, only one cross-sectional study was published on the distribution of SCA1 (3/16), SCA3 (12/16), and DRPLA (1/16) in a group of 16 patients with a genetically confirmed SCA [45]. Other Asian countries did not report any SCA prevalence data in the English literature.

Specific subtypes of SCAs appeared to be very prevalent in certain regions within countries, probably due to founder effects within these regions. For example, SCA31 is a relatively frequent subtype in the Nagano district of Japan [46] (up to 48.1% in a group of ataxia patients in whom other common SCA types were ruled out). SCA12 is very common in a specific ethnic population in Northern India [47]. A Thai study analyzed a cohort of 82 ataxia patients in whom several repeat-expansion SCAs (SCA1, SCA2, SCA3, SCA6, SCA7, DRPLA) were already genetically excluded. Less common repeat-expansion SCAs (SCA8, SCA10, SCA12, SCA17) as well as SCA19 were tested. A large proportion (almost 10%) carried SCA17 expansions, suggesting that SCA17 might be a relatively common genotype in Thailand alongside SCA3, SCA1 and SCA2 [48].

Prevalence studies in all countries indicate high numbers of SCA patients without a known genetic etiology. When comparing the studies that investigated the relative prevalence of several SCAs, the median proportions of SCAs with an unknown genotype were 33.3% in Chinese studies, 23.4% in Japanese studies, 38.5% in Indian studies, 30.5% in Korean studies, 57% in Thai studies, and 38% in Taiwanese studies. Again, available studies indicate marked heterogeneity of rates per country. In almost all prevalence studies, genetic analysis was only performed for (common) repeat-expansion SCAs. Occasionally, additional conventional mutations were targeted specifically (i.e. SCA14, SCA19, SCA35). Only one study of Chinese origin screened for a panel of conventional SCA mutations [8].

3.2. Part II: Phenotypic differences compared to other continents & Asia specific phenotypes

For most SCA genotypes, a ‘classic’ phenotype can be recognized, reflecting the key symptoms and signs frequently observed for a certain genotype. Progressive ataxia is a hallmark and overlapping characteristic for all SCAs, but many SCAs are accompanied by a wide spectrum of other, non-ataxia symptoms. Previous studies have shown that this spectrum of additional symptoms depends partially on the ethnic background and geographical origin [49], resulting in SCA phenotypes with distinctive features in specific geographic locations [4]. Also, some phenotypes are associated to genotypes that occur only in very specific Asian regions (see part I).

Worldwide, parkinsonism is a relatively common non-ataxic manifestation in SCA, especially in SCA2, SCA3, and SCA17 [50,51]. In these three SCA subtypes, parkinsonism can be the dominant feature and can
be indistinguishable from idiopathic PD, with levodopa-responsive bradykinesia, rigidity, resting tremor, and sometimes levodopa-induced dyskinesia. In most of these cases, only mild cerebellar signs were present or developed only years later in the disease course, although cerebellar atrophy on brain MRI was also reported in 30% of ‘pure’ Parkinsonian cases [50]. In some SCA2 and SCA17 patients, age of onset was relatively late and parkinsonism was accompanied by autonomic dysfunction, therefore mimicking MSA-P. SCA2 cases with this MSA-P mimic showed mild cerebellar atrophy on brain MRI [51].

Some studies have suggested that this Parkinson’s disease (PD)-like phenotype might be relatively frequent, especially in SCA2 and SCA17, in patients from Asian countries [51,52]. The first levodopa-responsive PD-phenotype of SCA2 was described in a Chinese family in 2000 [53]. However, only a few Asian studies have actually reported on the frequency of parkinsonism or other movement disorders in SCAs. A Taiwanese study found that parkinsonism was the most common non-ataxic manifestation (21.1%) in a cohort of 90 SCA1, SCA2, SCA3, SCA6, and SCA17 patients [5]. Studies from other Asian countries reported a lower prevalence of parkinsonism. In a cohort of SCA patients from India, 5.26% of the patients showed co-existing parkinsonism [54]. A study from Thailand did not find any patients with co-existing parkinsonism in a cohort of 131 SCA1, SCA2, SCA3, and SCA6 patients [12].

The pathophysiological mechanism for the occurrence of a PD-like phenotype has been studied and for both the SCA2 and SCA17 parkinsonian phenotype an association with an interrupted and shorter/intermediate CAG repeat was found [55,56]. This association might be partly related to structural changes in the expanded SCA alleles, caused by CAA-interruptions. For SCA2 it was suggested that these structural changes in the expanded allele might result in brain structure specific toxicity, either by disruption of cell-specific function or by preventing the occurrence of somatic mosaicism [55].

Several studies worldwide have, conversely, investigated the role of SCA2 and SCA17 in familial parkinsonism cases. The reported frequency of cases with a pathogenic trinucleotide expansion in the SCA2 or SCA17 gene in familial parkinsonism are higher compared to studies in countries from Europe or North or South America [51]. A study from Taiwan showed that SCA2 mutations were present in up to 8.7% of familial parkinsonism in Taiwan [57]. In Korea, SCA17 mutations occurred in up to 7% of familial parkinsonism cases [56]. Even in a large cohort of sporadic parkinsonian patients in Korea, a SCA17 mutation was detected in 0.9% of cases [56]. No other Asian countries reported on the results of such screens.

Furthermore, several studies have investigated CAG-repeat lengths of various SCAs in cohorts of idiopathic PD patients with contradictory results. The largest world-wide, multicenter study that also included an Asian cohort, did not observe a major contribution of pathogenic or intermediate repeat expansions in the SCA2, SCA3, SCA6, and SCA17 genes for idiopathic PD, neither in Caucasian or Asian populations [58].

Recently, one study suggested the existence of a specific ‘Asian’ SCA3 phenotype [4], with a later age of onset and a relatively mild ataxia phenotype, compared to those with other ethnic backgrounds. However, the findings of this study have to be interpreted cautiously since there were relatively small numbers of Asian SCA3 patients in the cohort compared to patients of different ethnicity.

3.2.1. Phenotypes of Asian-predominant genotypes

As mentioned earlier, SCA12 is relatively frequent in India as a consequence of a founder effect in a specific northern Indian endogamous community [47] and is caused by a repeat expansion in the PPP2R2B gene. This SCA subtype type is very rare in other countries. In Asia, it has been also identified in China and Singapore, but in a very limited number of cases [59]. SCA12 has specific disease characteristics as it is predominantly and initially a coarse action tremor of hands and head, while cerebellar signs typically develop at a later stage of the disease [59]. Its initial presentation can mimic essential tremor [60].

A second type of SCA that is rather specifically connected to a certain area in Asia is SCA36. This subtype was detected independently in two regions: Western Japan, were it was initially named ‘Asidan’ ataxia [61,62] and Galicia in Spain, were it was named ‘Costa del Morte ataxia’ [63]. SCA36 is now seen worldwide, but most cases are still found in

Fig. 2. Overview of relatively common SCAs in Asian countries.
Western Japan and Spain [64]. SCA36 is caused by a hexanucleotide repeat expansion in the NOP56 gene. Its phenotype is characterized by a late-onset cerebellar ataxia combined with signs of progressive upper and lower motor neuron involvement, including skeletal and tongue muscle atrophy and fasciculations [61]. In Galicia, sensorineural hearing loss was frequently described as an early feature and as this observation was later confirmed in Japanese patients, this is a distinguishable feature for SCA36 [65].

Finally, SCA31 is largely restricted to the Nagano district of Japan [66]. It is caused by a penta-nucleotide (TGGAA)n repeat insertion located in an intron of the BEAN gene [67]. The phenotype of SCA31 is characterized by a pure cerebellar syndrome [68], making it difficult to distinguish from other, more commonly reported SCA subtypes in Japan, such as SCA6.

3.3. Part III: Diagnostics and management resources

To map SCA-related resources and management within the various Asian countries, we conducted a survey that was completed by 21 respondents (neurologists and residents) who represented 12 (East) Asian countries. Table 2 presents a summary of general aspects of these resources and management aspects in Asian countries. We also included the Sociodemographic Index (SDI) for every country, serving as a measure for the developmental status. This is a composite average developed by researchers of the Global Burden of Disease Study [69] and comprises incomes per capita, average educational attainment, and fertility rates in countries.

Accessibility of SCA patients to SCA experts is classified as difficult in most Asian countries, except for Singapore, Japan, Taiwan, and South Korea. These four countries all have notably higher SDI indices, reflecting a better economic situation, compared to the other Asian countries. Some countries reported a complete lack of ataxia experts or ataxia tertiary centers (Laos, Philippines, Vietnam), while in other countries (India, Indonesia, Malaysia, South Korea) difficulties in accessibility were mainly related to travel difficulties (long distances and high costs), especially in rural areas since ataxia centers are mainly located in larger cities.

All countries participating in the survey reported a lack of awareness on SCA. Most respondents mentioned the low prevalence of SCA as the main reason for this. In relation to this, the survey results showed that only China and Japan have a national SCA association. A limited number of countries offer training in ataxia to neurology residents, rehabilitation specialists, and allied healthcare workers. Some respondents were not aware of training possibilities reported by other respondents from the same country, suggesting a possible lack of awareness of these training opportunities in some professionals. Almost all countries reported ongoing research projects on SCA.

Several respondents reflected on the existence of possible social and cultural aspects that complicate medical management. These included false beliefs related to SCA, reluctance to visit the hospital, and hesitance within families regarding genetic testing. Furthermore, the perception that SCA is untreatable also contributes to the reluctance to visit the hospital. The results on availability of diagnostic facilities show large differences between Asian countries. Neuroimaging and nerve conduction studies are widely and easily available in almost all Asian countries. Contrarily, the availability of genetic testing facilities showed marked differences: Japan, China, and Singapore reported that repeat expansion testing and next generation sequencing for SCAs are easily accessible. In Vietnam and Laos, however, neither of these facilities is available. All other participating countries reported that genetic testing facilities are partly available. Access is dependent on location (limited to large cities) and tests are indicated to be very expensive. In some countries, blood samples can be sent overseas to other centers for testing, but that this is a costly and complicated procedure.

With regards to treatment, most countries reported the availability of

<table>
<thead>
<tr>
<th>Country</th>
<th>SDI</th>
<th>Social-demographic Status</th>
<th>Tertiary - Ataxia centers</th>
<th>Training in movement disorders/ataxia</th>
<th>Research funding allocation for residents</th>
<th>Genetic testing facilities</th>
<th>Access to SCA experts</th>
<th>Training in ataxia</th>
<th>Rehabilitation specialists/Allied healthcare workers</th>
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<td>China</td>
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<td>Yes</td>
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<td>Yes</td>
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<td>Yes</td>
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<tr>
<td>Japan</td>
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<td>Unsatisfactory</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Laos</td>
<td>0.97</td>
<td>Unsatisfactory</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Singapore</td>
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<tr>
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<tr>
<td>Vietnam</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
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</tr>
</tbody>
</table>

Table 2: Overview of general aspects of SCA resources, diagnostic facilities and management in Asian countries.
allied healthcare interventions such as physiotherapy, occupational therapy, or speech therapy. Rehabilitation specialists are accessible in most countries, but both allied healthcare workers and rehabilitation specialists are often not specifically trained for treating patients with ataxia or other neurological conditions. The availability of more invasive treatment options varied: botulinum toxin injections for treatment of co-existing dystonia and spasticity is available in all countries, except for Indonesia and Laos. Deep brain stimulation, for the treatment of refractory tremor, is less easily accessible. Intrathecal baclofen for the treatment of spasticity is only easily accessible in Singapore and China. A role for traditional medicine was reported in China, South Korea, Taiwan, Singapore, and India.

4. Discussion

The overview of currently available SCA prevalence data for Asia firstly revealed that many Asian countries remain without published prevalence data on SCA. There are at least two important reasons for this. First, as supported by our survey findings, genetic testing facilities are limited or access is difficult or limited due to cost in many (low-income) Asian countries, often without appropriate funding allocated to conduct these genetic diagnostic tests. Consequently, only a subset of patients is genetically tested in comparison to higher income countries and prevalence data might be partially biased towards those who could afford the testing. Secondly, there is lack of coordinated SCA registries in most Asian countries, impeding the composition of regional or nationwide SCA cohorts and joint publications on cohorts of genetically confirmed SCA cases. In this study, we focused only on prevalence studies published in the English language. This might have led to an incomplete picture, as authors may have published prevalence data in their native language.

Secondly, in countries with available prevalence data on SCA, a large proportion (range 23%-57%) of patients still remains without a genetically confirmed SCA diagnosis. In the majority of studies in this systematic review, only the most common repeat expansion-SCAs were tested. SCAs caused by conventional, non-repeat mutations (or less frequent repeat expansions, such as SCA12 and SCA36) were often not included in the testing panel, as this requires more advanced molecular techniques and these facilities are not widely available. Besides, in countries where advanced molecular techniques might have become available over the last few years, scarcely any papers on SCA prevalence have been published since then. Although the median proportion of patients within Asian ataxia cohorts without a final genetic diagnosis is comparable to other (mainly European) series [70], this selective testing will have influenced relative prevalence rates and leads to an incomplete picture of the genetic background of Asian SCA patients.

Furthermore, it seems that Asian SCA patients can present with somewhat unique phenotypes, in part related to genetic subtypes that are more often or almost exclusively found in Asia or specific Asian regions. These include for example the motor neuron phenotype in SCA36 and the tremor presentation in the early disease stages of SCA12. For the more common SCAs, the relatively frequent occurrence of the parkinsonian phenotype in SCA2 and SCA17 in South Korea, China and Taiwan, should be noted. This knowledge serves towards an earlier recognition of SCA patients in case of deviant phenotypes.

Our survey results on the current healthcare facilities for SCA patients in Asian countries indicate that the accessibility of SCA patients to ataxia experts, but also the availability of diagnostic and treatment facilities, is highly dependent on the socio-economic situation in Asian countries. High-income countries show adequate accessibility and the provision of educational programs to patients and family members could be helpful in increasing awareness and change certain perceptions of patients and families that influence disease management.

To our knowledge, no other studies have previously reported on differences in SCA resources between Asian countries. We here aimed to provide a first impression of these differences. A limitation is, obviously, the number of respondents. Besides, some specific questions on availability of ataxia training or treatment facilities might have been interpreted differently between respondents, as we did not predefine any criteria for those aspects. Our results, therefore, have to be interpreted cautiously and might not be generalized as the results represent only small numbers of ataxia experts in Asian countries and several, mainly low-income countries are not represented. However, the respondents were all movement disorder neurologists and mostly specialized in ataxia, so are believed to have good knowledge on SCA-related healthcare aspects in their countries. The lack of response from several (low-income) countries might reflect the lack of specialized physicians in these countries.

As new symptomatic and disease-modifying therapies are in development, an early and conclusive genetic diagnosis for SCA patients becomes increasingly important as new treatments might be highly genotype specific. Our results indicate that currently, this diagnostic process is clearly challenging for many neurologists in low-income Asian countries. Next steps towards an optimal diagnostic and therapeutic process for SCA patients in these countries should include: 1) development of education and training programs for patients, neurology residents, and allied healthcare workers to increase awareness on SCA, 2) further development of genetic testing facilities, allowing to find a genetic diagnosis in a larger proportion of patients, and 3) coordinated registry of confirmed SCA cases, gaining more insight in country- or region-specific prevalence numbers, addressing specific phenotypic characteristics of SCA in Asia, and allowing Asian patients to participate in future interventional trials.

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Appendix A. Supplementary data

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References


[23] N. Mohamed Ibrahim, et al., Frequency of spinocerebellar ataxia type 1, 2, 3, 6 and 7 and clinical profile of spinocerebellar ataxia type 3 in Malaysia, Cerebellum Ataxias 7 (2020) 11.


