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Cognitive and Psychiatric Manifestations of Spinocerebellar Ataxia: Impact on Quality of Life

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ABSTRACT

Spinocerebellar ataxia (SCA) is a relatively rare subset of Cerebellar Ataxia disease and inherited disease due to an autosomal dominant mutation. This results in a progressive neurodegeneration of the cerebellum, leading to a variety of health factors such as (but not limited to) saccadic visual pursuit, coordination alterations, hyperreflexia, weakness of extremities and more. These symptoms of disease vary between individuals and types of ataxia with more than 40 known forms of spinocerebellar ataxia. The effects of SCA are not only limited to physiological effects but also include cognitive and psychiatric impairments that impact quality of life (QoL). While often overlooked, the cognitive and psychiatric manifestations of SCA are essential parts of delivering comprehensive care to patients. Neuroimaging studies showed functional and structural changes in brain regions beyond the cerebellum to include the frontal and temporal lobes, which may contribute to these manifestations. Additionally, genetic factors and disease-specific pathophysiological mechanisms may underlie the observed cognitive and psychiatric profiles in SCA. The article presents an overview of the cognitive deficits and highlights the complex interplay between these manifestations, disease progression, and the overall well-being of patients. The article underscores the need for comprehensive assessment, early detection, and multidisciplinary interventions to improve the QoL of individuals living with SCA.

Introduction

Spinocerebellar ataxia (SCA) affects approximately 1-5 out of 100,000 Americans each year. Due to the rarity of the disease, research in the treatment of SCA is still mostly in developmental and testing stages. The subset types of SCA are numbered, such as SCA1, SCA2, etcetera. The differences between the different subsets of SCA is the loci on which the gene responsible for the mutation that caused the SCA is found. Due to the difference among types, the effect of disease also occurs on different parts of the nervous system. For example, SCA6 restrictively affects the cerebellum, while SCA2 has no effect on the cerebellum. These differing types of SCA make defining a singular and all-encompassing etiology difficult. However, a common etiology definition involves a repeated CAG expansion in new generations in SCA, types 1, 2, 3, 6, 7, 8, 12, and 17. Other rarer subtypes of SCA involve varying expansion sequences or singular nucleotide missense mutations, or frameshift mutations like insertion or deletion.

Despite a well understood phenotypic presentation of the disease, the exact pathogenesis remains unclear due to limited research of SCA. Current evidence supports that SCA interferes with typical transcriptional regulation and clearance. Furthermore, ubiquitin-protestarom system appears to be altered along with the setpoint and homeostasis of calcium which is effectual on neuronal loss that occurs in SCA disease progression. While the current research has only identified the previous molecular routes, new novel discoveries are anticipated that further the understanding of the pathogenesis of SCA. Despite limited understanding of pathogenesis, the phenotypic presentation of SCA follows a regular pattern and can be a strong indication of the disease. Hallmarks such as loss of coordination, balance, nerve pain in extremities and more all contribute to a physician's opinion of the presence of the disease. However, only a genetic testing that specifically observes the mutations of the cerebellar loci can provide a definitive answer.

Due to the relatively unknown nature of the disease, a large emphasis of SCA treatment revolves around the clinical pathogenesis such as clinical trials for drug treatments. What is less researched is the cognitive and psychiatric

impairments of the disease. Understanding the effects of the physical and terminal aspects of the disease are important to obtaining a comprehensive and holistic understanding of how SCA affects people–more than just physically, SCA creates large psychological burdens and can create serious psychiatric-based cognitive impairment difficulties as well. Furthermore, by understanding the holistic nature of the disease, the ability of the physician increases to care for all aspects of the person and can better improve quality of life. As there are no currently known curative treatments for SCA, treatments are largely targeted at managing an individual's QoL and thus being able to understand the often overlooked cognitive aspect of the illness will better allow physicians to give personalized and effective care. Effective management of the cognitive and psychiatric symptoms leads to targeted interventions and therapies. By inciting more research in this area, more pharmacological and nonpharmacological approaches can be created that serve as a driver for innovation. Targeted treatment strategies create improvement in symptom management, slow disease progression, and enhance QoL for individuals with SCA. Additionally, cognitive and psychiatric symptoms in SCA can present before or alongside motor symptoms. This matching timeline indicates potential for these markets to serve useful in early detection and diagnosis. Understanding the relationship between cognitive and psychiatric profiles and disease progression can aid in predicting outcomes and tailoring interventions for individuals with SCA.

The main cognitive manifestations of SCA that this article will address are the ones that have direct impact on the QoL. These impairments include attention span, working memory, and visual spatial abilities. These four impairments are usually four of the most pronounced effects of SCA on cognitive functioning. Prevalent psychiatric manifestations of SCA can often appear as depression and anxiety. These symptoms of SCA are important to address as they are directly linked to QoL of the patient and their caregivers. Due to the main focus of SCA being primarily on a curative or symptom-managing treatment, limited research has been performed on the effects and solutions of the cognitive and psychological toll of patients with SCA. While past research has proven the existence of such manifestations, future research directly targeting the cognitive and psychological effects should be further investigated in order to better QoL.

Cognitive Manifestations of Spinocerebellar Ataxia

While the entire array of cognitive manifestations of SCA are relatively unknown, common ones include impairments in attention, working memory and visual-spatial abilities.

In clinical research (2014, Ma et. al) conducted using 18 subjects with SCA1 of Han descent and subjects with SCA2 and SCA3 of Kazakh descent, a positive correlation was observed between a declining visual-spatial functioning and an increase in SCA severity. The study supported that visuospatial abilities were found to decrease in a statistically significant margin in correlation with the degeneration due to SCA's affect on diminishing cerebellum functioning. Spinocerebellar ataxia's cerebellar degeneration and disrupted cerebellar-brain connectivity results in various regions of the brain involved in visual processing thus resulting in cognition being affected. This altered communication affects the combining of visual information with other sensory cues necessary for spatial awareness.

Furthermore, SCA has been shown to have a positive correlation with attention deficits that alter an individual's ability to maintain focused and sustained attention, shifting attention or selectively attending to relevant information. Like the disrupted connections between the cerebellum that resulted in a visual-spatial impairment, similar problems arise in regards to attention span. The loss of sensory integration abilities in the cerebellum may lead to disruptions in sensory integration that may affect attentional processes that rely on the filtering of sensory information or accurate sensory perceptions. The cerebellum which plays a role in cognitive processes being degenerated can disrupt attentional networks and thus result in attentional difficulties. Furthermore, the complex motor deficits and coordination deficits associated with SCA can also demand cognitive resources which produces the phenomenon of cognitive overload. Cognitive overload resulting from depleting attention to be used in managing other symptoms of SCA results in a general loss of attention span or increased difficulty in attention span.

Likewise, the attention deficits and visual-spatial deficits working memory is affected by the degeneration as well. Due to the previously discussed visual-spatial deficits, SCA may create problems within visuospatial processing

regions of the brain. This can later impact on working memory tasks that may require a mental manipulation of visual or spatial information. Difficulties in mentally rotating objects, mentally tracking spatial relationships, or mentally navigating through a spatial layout can all affect working memory performance. The established attention span deficits such as problems with sustaining attention and selective attention can alter working memory. Working memory which is dependent on selective encoding of attentional processes makes maintaining relevant information critical. Attentional deficits in SCA can make it challenging to focus on and retain information in working memory, resulting in a reduced working memory capacity and performance.

All of the different components of cognitive manifestations like memory, attention span and visual-spatial abilities are important in maintaining a patient's quality of life. Visual-spatial abilities allow for greater independence and freedom in daily activities. A strong working memory supports cog cognitive flexibility, problem-solving, and efficient information processing. Longer attention spans allow for continued focus and thus the ability to complete tasks effectively. Therefore, challenges with cognitive deficits directly impairs QoL by hindering performance, productivity, learning, and engagement in activities, potentially impacting an individual's sense of competence, independence, and overall well-being. Furthermore, it is important to recognize individual variations and the impact of cognitive functions of the QoL can vary among individuals due to their unique strengths, challenges, and the context in which they operate. By addressing and supporting these cognitive functions, physicians would be able to help optimize an individual's QoL by understanding how to give appropriate interventions, strategies, and accommodations to enhance cognitive functioning and overcome limitations.

Psychiatric Manifestations in Spinocerebellar Ataxia:

Like the cognitive manifestations of SCA, psychiatric disorders like depression and anxiety have also been seen to be prevalent as well.

Previously conducted research (2018, Ling et. al) has strongly supported the positive correlation between depression and SCA. In the study which observed 104 patients with molecularly confirmed SCA3, a 57% (60/104) prevalence rate of depression was observed, accounting for sex and genetic predispositions yielded a statistically significant correlation between the two. These findings support that depression was a part of the neurodegeneration due to SCA3. While the study had limited scope as it used only patients diagnosed with SCA3 which makes the study pool not necessarily applicable to all types of SCA, the results may be able to be generalized to most types of SCA as the general pathology and progression of the disease remains similar. These findings may be a result of neurochemical imbalances as the degeneration of the cerebellum in the pathogenesis of SCA may disrupt normal functioning of neurotransmitters like serotonin, dopamine and more. Furthermore, the psychological impact of motor impairment may also lead to frustration with gait disturbances, balance problems, and coordination difficulties. These frustrations may manifest into a reduced sense of independence and progress from there into depressive symptoms.

The linkage between SCA and anxiety is less well-known due to less amounts of dedicated research. However, in a cross-sectional study (2021, Gong et. al) an investigation of the anxiety levels of patients with SCA during the Covid-19 pandemic found statistically significant higher percentages of patients with SCA than the control group at approximately 34%. While this study has limitations due to the atypical nature of circumstances of the Covid-19 pandemic, it may still be applicable to demonstrate the comparison of ataxia patients to the general population–the prevalence is higher. Like depression, the causes of anxiety may lie in the disruption of neurochemical signaling due to the degeneration of the cerebellum or psychological impacts of loss of motor control. Another possible cause of anxiety due to SCA is the feeling of loss of control. Due to the uncontrollable, terminal and progressive nature of the disease, patients with SCA may feel emotionally as if the progression of disease is taking away their own independence and control. This emotion of being out-of-control with one’s own body evokes anxiety-like emotions and eventually progresses into clinical anxiety.

The Interconnection between Cognitive and Psychiatric Manifestations

Between cognitive and psychiatric deficits, a bidirectional relationship can be found between the two, meaning cognitive deficits contribute to the development or exacerbation of psychiatric effects and vice versa. For example, deficits in visual-spatial relationships, attention and memory can greatly decrease a patient's ability to deal with the challenges of SCA. That also means these cognitive deficits can create challenges in problem solving, decision making and emotional regulation which all can directly impact the extent of psychiatric symptoms like anxiety, depression and irritability. Furthermore, they can also manifest in communication and social integration challenges which initiates social isolation, reduced self-esteem, frustration and more–all of which contribute to the development of psychiatric conditions. Psychiatric symptoms like depression and anxiety can also be of detriment to the cognitive health of patients with SCA. Psychiatric disorders can affect attention, concentration, memory and lead to cognitive impairments. Additionally, decreased motivation, disrupted sleep patterns and more all further exacerbate cognitive deficits. However, the relationship between cognitive deficits and psychiatric symptoms in patients in SCA varies from individual to individual due to the myriad of circumstances. These manifestations are type and stage-specific as well as heavily influenced by individual cognitive reserve and psychological resilience. All of these factors impact the bidirectional relationship but understanding the overlap is the beginning for allowing doctors to comprehensively care for all the symptoms SCA may progress into.

The synergistic effects of both cognitive and psychiatric effects of individuals with SCA can also be impactful in overall QoL. Cognitive deficits like earlier mentioned as difficulties with attention, memory and executive functioning make daily tasks like household chores much more difficult. This circumstance combined with the psychiatric symptoms like depression or anxiety can often yield decreased motivation, further impaired decision making and overall decreased functioning thus resulting in a lower QoL. Continuing, the same self-doubt and decreased esteem as addressed previously can exacerbate sadness or anxiety which manifests into decreased overall well being and decreased overall QoL. These challenges can often interfere with an individual's autonomy as cognitive deficits force patients to rely on others for assistance. The presence of psychiatric symptoms may exacerbate feelings of dependency and shame and thus impact overall self-perception resulting in a low QoL.

Assessment and Management Strategies

While SCA may present cognitive and psychiatric challenges, these defitis are not unmanageable. In regard to cognitive deficits, there are several management strategies that will help increase an individual's QoL. Visual-spatial challenges can be managed similarly to that of stroke patients by enrolling patients in rehabilitation therapies. These therapies could include vision therapy and cognitive rehabilitation. Furthermore, an environmental adaptation could be performed and the addition of assistive technology would help ease the burden as well. Both working memory and attention deficits can be treated similarly with rigorous therapy to minimize the toll on the patient due to disease progression. Establishing everyday routines along with environmental adaptations will further serve to benefit patients as well as these forms of structured assistive modifications provide regular assistance.

Furthermore, many medications can be used to assist with patients suffering from depression or anxiety. Antidepressant and antianxiety medications can be prescribed to the patient by a physician in order to help alleviate some of the symptoms of depression and anxiety. Additional treatments such as psychotherapy, lifestyle changes and more can all be used to supplement as well.

Acknowledging the cognitive and psychiatric toll that SCA takes on the patient also means that the toll taken on the caregiver and support systems must be seen as well. Being the caregiver or support system of an individual with SCA comes with many challenges but recognizing the cognitive and psychiatric effects of SCA allows doctors to give more comprehensive care, thus easing the burden off of the caregiver. While these may seem as immeasurable and rather abstract changes, dealing with more than the physiological disease progression can greatly improve the

QoL of both the patient and the caregiver or support system, allowing the most maximized management of SCA possible.

Conclusion

In conclusion, the effects of Spinocerebellar Ataxia progress beyond physiological degeneration of the cerebellum and motor effects as it is most typically associated with. The cognitive and psychiatric effects of SCA must be recognized in order for physicians to comprehensively give care to their patients. Some possible cognitive deficits include attention, memory and visual-spatial deficits and common psychiatric disorders that have seen strong support for a positive correlation include depression and anxiety. To optimize patient care, more research is warranted in the front of a holistic outlook of spinocerebellar ataxia in order to deliver the maximum benefit in care for patients and their families. By further understanding the underlying mechanism and developing targeted or even curative interventions, quality of life can be greatly improved.

References

Ashizawa, T., Öz, G., & Paulson, H. (2019) Spinocerebellar ataxias: prospects and challenges for therapy development. National Library of Medicine. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6469934/

Giocondo, F & Curcio, G (2018) Spinocerebellar ataxia: a critical review of cognitive and socio-cognitive deficits, International Journal of Neuroscience. https://www.tandfonline.com/doi/citedby/10.1080/00207454.2017.1377198?scroll=top&needAccess=true role=tab&aria-labelledby=cit

Gong, Y., Chen, Z., Liu, M., Wan, L., Wang, C., Peng, H., Shi, Y., Peng, Y., Xia, K., Qiu, R., Tang, B., & Jiang, H. (2021). Anxiety and depression in spinocerebellar ataxia patients during the COVID-19 pandemic in China: A cross-sectional study. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia, 88, 39–46. https://doi.org/10.1016/j.jocn.2021.03.004

Jutai, J., Bhogal, S., Foley, N., Bayley, M., Teasell, R., & Speechley, M. (2003) Treatment of Visual Perceptual Disorders Post Stroke, Topics in Stroke Rehabilitation, 10:2, 77-106, https://www.tandfonline.com/doi/abs/10.1310/07BE-5E1N-735J-1C6U

Lin, M., Yang, J., Chen, P., Qian, M., Lin, H., Chen, X., Shang, X., Wang, D., Chen, Y., Jiang, B., Chen, Y., Chen, W., Wang, N., & Gan, S. (2018). Bidirectional Connections between Depression and Ataxia Severity in Spinocerebellar Ataxia Type 3 Patients. https://karger.com/ene/article-abstract/79/5-6/266/125926/Bidirectional-Connections-between-Depression-and?redirectedFrom=full text

Ma, J., Wu, C., Lei, J., & Zhang, X. (2014). Cognitive impairments in patients with spinocerebellar ataxia types 1, 2 and 3 are positively correlated to the clinical severity of ataxia symptoms. International journal of clinical and experimental medicine, 7(12), 5765–5771. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4307551/

Okamoto, N., Ogawa, M., Murata, Y., Sakamoto, K., Nagai, T., Yamada, M., & Higuchi, T. (2010). Major Depressive Disorder Complicated with Spinocerebellar Ataxia: Report of 2 Cases. Case reports in neurology, 2(2), 52–56. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2905581/

Yahikozawa, H., Miyatake, S., Sakai, T., Uehara, T., Yamada, M., Hanyu, N., Futatsugi, Y., Doi, H., Koyano, S., Tanaka, F., Suzuki, A., Matsumoto, N., & Kunihiro Yoshida (2018). A Japanese Family of Spinocerebellar Ataxia Type 21: Clinical and Neuropathological Studies. https://link.springer.com/article/10.1007/s12311-018-0941-6#cities