A Systematic Review of Idiopathic Basal Ganglia Calcification for Possible Inclusion in the Social Security Administration’s Compassionate Allowances Program.
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Abstract

Background: The Social Security Administration launched the Compassionate Allowances List in 2008. This initiative created a mechanism for identifying diseases and other medical conditions that meet the Social Security Administration’s standards for expedited review and delivery of disability benefits. Idiopathic basal ganglia calcification or Fahr’s disease was selected for review in this study. A review of the condition’s appropriateness for inclusion in the Compassionate Allowance list was undertaken. This project was supported by Policy Research, Inc. as part of the U.S. Social Security Administration's Improving Disability Determination Process Small Grant Program. Method: Using guidance from the Cochrane methodology, a systematic review of the literature was undertaken. The following databases were searched: The Cochrane Library, The Health InterNetwork Access to Research Initiative (HINARI), MEDLINE, EMBASE, Applied Social Services Index and Abstracts, Education Resources Information Center, and PsycInfo. The Science Citation Index Expanded was searched as well as the National Technical Information Service. Articles were first identified by condition, and then narrowed down by inclusion criteria. Articles were coded and severity thresholds were examined to determine if the condition “invariably” meets the criteria for the Compassionate Allowance list or if the heterogeneous presentation among those affected makes it difficult to include the condition as a whole. Findings: This systematic review provided an in-depth examination of the extent to which Idiopathic Basal Ganglia Calcification invariably meets or fails to meet the definition of disability provided by the Social Security Administration. Given that symptomatic case are often severe, result in progressive deterioration as well as myriad symptoms affecting a variety of different bodily systems, it is recommended that consideration extend to symptomatic idiopathic basal ganglia calcification for inclusion in the Compassionate Allowance List. Given that differentiating between those who are symptomatic and those who are not may include citation of medical evidence, the Quick Disability Determination process may be a more applicable expedited review procedure. Conclusion: This study demonstrated that Idiopathic Basal Ganglia Calcification does not invariably meet the criteria for inclusion in the Compassionate Allowance List. While some experience this condition in a severe form, the presentation of the condition is too variable to universally recommend its inclusion. Some remain asymptomatic and are diagnosed through CT scans. For these people, disability benefits would be unnecessary. For those who are clinically symptomatic, however, inclusion is recommended. The Compassionate Allowances List provides a benefit to both the Social Security Administration and its respective claimants. By identifying diagnoses that invariably meet the criterion for disability, claimants may experience an expedited review time and the Social Security Administration can expect to see a decrease in their backlog of applications. This systematic review provided one example of a system to identify those diagnoses that may be considered for inclusion in this initiative.

Background:

Fahr’s Disease

Fahr’s disease is often attributed to a German neurologist, Karl Theodor Fahr. Fahr described the condition in an 81-year-old man in 1930. The condition had been first described in 1850 by Delacour. Since that time, Fahr’s disease has been known by many names, including idiopathic striopallidodentate calcinosis, non-arteriosclerotic cerebral calcification or the most common alternative, idiopathic basal ganglia calcification (IBGC). As these terms indicate, the
disease is noted for the bilateral, symmetrical calcification of the basal ganglia. The occurrence of this condition is, by definition, of unknown origin (Manyam, 2005). There have been some discrepancies in the literature, however, as some cases have been noted to be idiopathic when in fact a traumatic event, such as a car accident with head trauma, is also noted (for instance: Kim & Ha, 2008).

The diagnosis of idiopathic basal ganglia calcification requires the following:

a. the presence of bilateral calcification of the basal ganglia;

b. the presence of neurologic dysfunction;

c. the rule-out of a metabolic, infectious, toxic or traumatic cause, which might better account for the symptomology or etiology;

d. a family history consistent with autosomal dominant inheritance (Aggarwal, Kumar, Dev, & Jain, 2012).

Takagi and colleagues (2013) have expanded this criterion to note the importance of excluding parathyroid diseases as well as Albright’s signs. In addition, care should be taken to exclude DTNC or Kosaka-Shibayama disease. Interestingly, Arslan and colleagues (2013) have written about a 34-year-old woman with Fahr’s disease associated with hypoparathyroidism. Preussner and colleagues (2007) did the same regarding the death of a 65-year-old woman with hypoparathyroidism, Fahr’s disease and multiple system atrophy showing that this standard is not clear throughout the medical profession. In fact, Miklossy and colleagues (2005) include hypoparathyroidism as part of what they refer to diagnostically as the “Fahr’s triad” (p. 643). It is important to note that the calcification of the basal ganglia occurs without any otherwise abnormal calcium breakdown or uptake (Tsuhya et al., 2011).

An interesting finding arising out of the systematic review is the distinction made by some researchers between Fahr’s disease and Fahr’s syndrome. Some authors (See Kumar, Dhull, Somasekharan, & Seshadri, 2012; Modrego, Mojonero, Serrano, & Fayed, 2005) have argued that Fahr’s syndrome includes bilateral calcification of the basal ganglia secondary to another cause such as hypoparathyroidism, while Fahr’s disease is completely idiopathic in origin. Using the term Fahr’s, however, connotes an idiopathic origin therefore it stands to reason that Fahr’s secondary to another disorder would negate the use of Fahr’s as diagnosis. This is a potential diagnostic issue for further study. For the purposes of this project, cases of bilateral basal ganglia calcification of idiopathic origin will be included, while those of known origin will be excluded, per the diagnostic definition of Fahr’s disease (Aggarwal, Kumar, Dev, & Jain, 2012).

Researchers have attempted to find mutations in genes that may be responsible for IBGC. In an American family, one point of origin was mapped to 14q and has been named IBGC1. Members of this family had movement disorders and Parkinsonism. Psychosis was also an issue along with neurological deficits. Brain regions such as the pallidum, thalamus and dentate nuclei were affected. An interesting finding was a decrease in the age of onset by almost twenty years with each new generational propagation (Geschwind, Loginov, & Stern, 1999). In a South Tyrolean family, the point of origin was mapped to chromosome 2q37 and was termed IBGC2. This family presented with some differences in body structure and neuropsychiatric features. The brain region with calcification was concentrated in the pallidum. Interestingly, most of the family members affected with calcifications were clinically asymptomatic. Without radiologic evidence, FIBGC would not have been discovered (Volpato, De Grandi, Buffone, Fachieris, Gebert, et al, 2009; Volpato, De Grandi, Buffone, Pichler, Gebert, et al, 2008). In another large Chinese family, a point of origin was mapped to chromosome 8 and has been named IBGC3. The gene
responsible in IBGC3 may be SLC20A2 (Dai, Gao, Xu, Cui, Liu, et al, 2010). SLC20A2 has been identified as a causative gene as well, and is thought to cause 41 percent (Hsu, Sears, Lemos, Quintáns, Huang et al, 2013) to 50 percent of hereditary cases (Mendes de Oliveira & Fernandes de Oliveira, 2013). The causative genes are variable providing evidence of the heterogeneous presentation and causes of this disorder (Dai, Gao, Xu, Cui, Liu, et al, 2010).

While mapping these chromosomes and their links to IBGC is a step in the right direction, the chromosomes implicated in IBGC1, IBGC2, and IBGC3 have been excluded in the mappings of other families (Kostić, Lukić-Jćmenica, Novaković, Dobričić, et al, 2011). An additional chromosome, PDGFRB, which is located on 5q32, was discovered in 2013 as a potential causative gene (Nicolas, Pottier, Maltête, Coutant, Rovelet-Lecrux, et al., 2013).

The incidence of IBGC is unknown, though estimates based on radiological evidence reported in the literature range from 0.24 to 2 percent (Aggarwal et al, 2012) At autopsy, this figure hovers near 0.6 percent (Tsuhiya et al., 2011). There is a correlation between increasing age and increasing incidence of IBGC (Aggarwal et al., 2012). Though this disease does not only affect those of advanced age, it may not be discovered or symptomatic until the fourth or fifth decades of life (Panduranga & Sulaiman, 2012). Given that the familial form of IBGC is transmitted in an autosomal dominant fashion, ninety-five percent of those with the mutation will develop this condition (Sheta & Angi, 2013). Males appear to be affected more often than females, and in one study were diagnosed at a rate of 2:1 (Manyam, 2005). Some patients are asymptomatic for years until exploration of new symptoms leads to a diagnosis. If calcification is discovered during the course of testing for other conditions, and the patient is asymptomatic, treatment is not recommended. For those who are showing symptoms, antipsychotic and antiepileptic medications may be used to control the mental health or neurological symptoms. There is no cure, and treatments vary from patient-to-patient as a standard treatment does not exist (Aggarwal et al., 2012).

It is possible that IBGC predisposes patients to other conditions, which upon examination, are determined to be secondary to basal ganglia calcification (see case report: Paraskevas et al, 2012). IBGC has also been a complicating factor in other conditions such as, membranoproliferative glomerulonephritis, “mitochondrial encephalomyopathy, juvenile rheumatoid arthritis, multiple myeloma, sensory deafness, hypopituitarism, and diabetes mellitus” (Tsuchiya et al., 2011, p. 2355). IBGC has also been associated with post-polio syndrome (Mendes de Oliveira & Fernandes de Oliveira, 2012) and often produces symptoms that are Parkinson-like (Brüggemann, Schneider, Sander, Klein, & Hagenah, 2010).

**Compassionate Allowance List:**

This study examined the suitability of idiopathic basal ganglia calcification or Fahr’s disease as a condition for addition to the Compassionate Allowance List. The Social Security Administration (SSA) Compassionate Allowances List began in 2008. This program created a mechanism within the Social Security Disability department for identifying diseases and other medical conditions that by definition meet Social Security’s standards for disability benefits. The program initially identified fifty neurological, mental, and immune disorder conditions that qualified as a disability (under statutory definition provided by SSA) necessitating expedited delivery of benefits; reducing waiting time and more immediate eligibility. There are many conditions which are not included in the list of conditions set forth by the Compassionate Allowances criterion. These conditions affect one’s ability to maintain gainful employment, and
are variable depending on the level of severity. Depending on the syndrome, the needs of the individuals diagnosed may vary greatly, as would their capacity to maintain employment and their need for expedited benefits. As a result, it is hypothesized that Compassionate Allowances may be necessary for individuals diagnosed with conditions, with higher disease burdens, who have been so diagnosed for at least 12 months, experience an impact on their quality of life or their life is threatened, and are unable to maintain gainful employment beyond those included in the current listing. Currently the Compassionate Allowances List includes 200 conditions, though there are many conditions which meet the criterion, including those that are developmental in etiology.

Though only 50 conditions were originally added to the Compassionate Allowances list, the current total of conditions has risen to 200 (Social Security Administration, 2012). There are often conditions, not yet added to the list, which have been diagnosed, well-established, and verified by objective medical evidence but the benefits process is long and difficult to navigate for parents, guardians, and those affected by disabling conditions. Though the original fifty conditions were constrained to cancers, brain injuries and conditions considered “rare,” the argument that younger-onset dementias should be added to the list was propelled by the fact that those afflicted can no longer maintain employment (Fried, 2009). This opened the possibility of dialogue and research concerning other conditions that also inhibit the possibility of gainful and significant employment and are neurodevelopmental from birth or present themselves later in life.

Currently the group of claimants eligible for consideration under the Compassionate Allowances represents 6 percent (this figure includes QDD claimants as well) of all Social Security Disability Insurance and Supplemental Social Security claimants, although this would expand as additional conditions are added to the list (Social Security Administration, 2013). It does not appear that adding conditions to this list would increase the number of claimants to Social Security in general, but would rather shift the percentage of those applying for benefits through the typical process and increase the percentage of those applying for expedited review.

An alternative to using the Compassionate Allowances List in this way may include using the Quick Disability Determination (QDD) process. Under the QDD, conditions or other factors found in the initial information submitted by a claimant is flagged based on easily obtainable information to verify the condition and is highly likely to receive a favorable determination (International Social Security Association, 2009). CAL looks strictly at one’s diagnosis, whereas the QDD considers the diagnosis as well as a variety of other factors.

According to the Social Security Administration, conditions are added to the CAL based on information received from public outreach, hearings, comments received from advocacy groups, medical and scientific expert opinion, and the National Institute of Health (Social Security Administration, 2012). Beginning in 2012, information received from the Disability Determination Process Small Grant Program has also been considered. The first hearing was held in 2007, and the last was held on March 16, 2011. No hearings are currently scheduled.

In terms of evaluating this program, the Social Security Administration reports that the CAL has allowed Social Security to process more claims at a faster speed, eliminating some of the backlog. Remediyying this backlog was marked as a goal (Strategic Objective: 3) in the agency’s 2013-2016 strategic plan (Social Security Administration, 2013). The number of cases that proceeded through the CAL list increased from 3.8 percent in 2009 to 5.8 percent in 2012 (Social Security Administration, 2012, p. 71)
Methods:

Using guidance from the Cochrane Methodology Register (Higgins & Green, 2011), a systematic review of the literature was undertaken in bibliographic databases, such as The Cochrane Library, and The Health InterNetwork Access to Research Initiative. MEDLINE and EMBASE were used as sources of literature that fulfill the predefined inclusion criteria. Regional electronic databases were searched in order to gather regional or international literature that may not be indexed on MEDLINE and EMBASE. Subject-specific databases were utilized such as: Applied Social Services Index and Abstracts, Education Resources Information Center (ERIC), and PsycInfo. Citation indexes were explored, such as: the Science Citation Index Expanded. The references cited in identified publications were searched in some instances to locate other pertinent studies and assessments. Search strategies were customized for each database given their use and depth of controlled vocabulary related to the condition of concern.

The effects of symptoms of idiopathic basal ganglia calcification were compared to Social Security’s definition of disability (Social Security Administration, 2012). IBGC was also compared to the CAL criteria (of which the definition of disability is a part of) to determine if this condition, invariably, meets the criteria. Each article meeting the inclusion criteria was rated with a code of 1, 2, or 3. A rating of “1” signifies that the article demonstrates that the condition meets one of the three criteria listed previously. A rating of “2” signifies that the article demonstrates that the condition meets 2 of the 3 criteria listed previously. A rating of “3” signifies that the article meets all 3 of the criteria listed previously. From this analysis, only articles which met all 3 of the criteria were reviewed in the final phase. All articles receiving a score of “3” were reviewed to determine what, if any, severity thresholds were identified in each manuscript rated as a “3.”

This synthesis was conducted from the interpretative stance, as defined by Dixon-Woods and colleagues (2005). The end result of this synthesis was not integrative, in that it did not seek to aggregate data for analysis, but rather to focus on the conceptual themes around disease burden and severity as the condition relates to the criteria set forth by the Social Security Administration. Severity and intensity levels were compared to the CAL criteria to determine if severity indices screen in or screen out certain severity levels or the entire condition in relation to the CAL program. Using this method, 451 articles were identified through an initial search, with 109 articles reviewed after applying the inclusion criteria and filtering out repeated articles. Eleven articles were subsequently excluded as they did not refer to IBGC specifically enough. Of the 105 articles reviewed during the coding process, 35 articles were coded as a “1” (demonstrating that the condition will last beyond 12 months), 39 articles were coded as a “2” (demonstrating that the presence of the first criteria plus an impact on quality of life or death), and 35 articles were coded as “3” (demonstrating full disability criteria).

The following definitions from the Social Security Administration guided the coding process:

Disability in adults was defined as “the inability to do any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 months. To meet this definition, you must have a severe impairment(s) that makes you unable to do your past relevant work (see §416.960(b)) or any other substantial gainful work that exists in the national economy.” §416.905(a). Disability in children (under the age of 18) was defined as possessing a a medically determinable physical or mental impairment or
combination of impairments that causes marked and severe functional limitations, and that can be expected to cause death or that has lasted or can be expected to last for a continuous period of not less than 12 months.” §416.906.

Substantial Gainful Activity (SGA) was defined as “gainful activity is work activity that is both substantial and gainful: (a) Substantial work activity. Substantial work activity is work activity that involves doing significant physical or mental activities. Your work may be substantial even if it is done on a part-time basis or if you do less, get paid less, or have less responsibility than when you worked before. (b) Gainful work activity. Gainful work activity is work activity that you do for pay or profit. Work activity is gainful if it is the kind of work usually done for pay or profit, whether or not a profit is realized § 416.972. As of January 1, 2013, for individuals who are not blind the earnings guidelines are $1,040 a month, or if the individual is blind the earnings cap is $1,740 (Social Security Administration, 2012).

The Compassionate Allowances Initiative was defined as a way to “quickly identify diseases and other medical conditions that invariably qualify under the Listing of Impairments based on minimal objective medical information.” FR Doc. E9–26194 Filed 10–29–09

Results:

This study examined two research questions:

1. Given that improvement in presentation or remission of symptoms, quality of life, and employability is unlikely, what are the empirical justifications, deducted from published scientific literature, for the inclusion of idiopathic basal ganglia calcification in the compassionate allowance initiative?

2. Can severity thresholds that meet the criteria for compassionate allowances be identified for idiopathic basal ganglia calcification?

A thorough systematic review of the literature was undertaken. A threshold criterion of either mild or severe was applied to empirical cases presented in the literature. Based upon that information, a comparison with SSA criteria was determined. The results are as follows:

Severity Thresholds:

Mild:

Many people with idiopathic basal ganglia calcification remain symptom free for most of their lives, and a diagnosis is not made until they eventually become symptomatic and/or a medical event requiring a CT scan reveals bilateral calcifications of the basal ganglia. In fact, it is believed that 32% of those with IBGC may be asymptomatic (Merlini, Peruzzotti-Jametti, Bacigaluppi, Mantovani, Spada, et al 2012).

For those with mild symptoms, headaches are an often reported symptom (Kotan & Aygul, 2009). Aggwarwal and colleagues (2012) report the case of a 34-year-old man with headaches and a low grade fever for approximately 4 weeks, as well as several generalized tonic clonic seizures while hospitalized. A CT scan revealed the presence of bilateral symmetrical calcification of the basal ganglia as well as the cerebellum and subcortical white matter. The patient’s brother also experienced seizures and a CT scan showed calcification as well, but of the three structures that compose the basal ganglia as well as the thalamus. The original patient was prescribed antitubercular drugs, and antiepileptic medications. His sibling was also treated with
antiepileptic medication. After six months, both brothers were symptom free, both of seizures and other neurological symptoms.

Paraslevas and colleagues (2012) report an 80-year-old woman presenting with hemiballism and hemichorea, both movement disorders. This woman possessed many risk factors, such as advanced age and hyperglycemia, but it was the Fahr’s disease that was determined to be the predisposing factor to the other presenting symptoms. Though the hyperkinetic disorders were not resolved with clonazepam, symptoms improved with haloperidol (0.5mg, tid).

In another case of mild symptomology, an 18-year-old woman was diagnosed twisting and abnormal movements of the neck, in addition to depression. Her IBGC was confirmed, and was also noted in her father’s brain. Other than the dystonic neck movements and depression, there were no other symptoms present (Maeda, Idehara, Nakamura, & Hirai, 2012).

Sudden onset of seizure activity and resolution with treatment and observation have been reported in some mild cases of IBGC (Sogüt, Kaya, Gökdemir, Solduk, & Sayhan, 2010; Menon & Harinarayan, 2009), while other long-term cases of seizure disorders secondary to IBGC, controlled with anti-epileptic medication (Sinha, Sodhi, John, & Singh, 2010).

Severe:

In a severe case affecting a 23-year-old woman, Fahr’s disease presented in conjunction with the congenital absence of all permanent teeth, stunted growth and missed milestones beginning at 4 or 5 years of age, and severe intellectual disability (Aditya, Lele, & Aditya, 2012).

Tsuchiya and colleagues report the death of a 32-year-old Japanese woman, diagnosed with both IBGC as well as membranoproliferative glomerulonephritis. Though proteinuria had been diagnosed since the age of 12, the years leading up to the patient’s death were significantly affected by degeneration distressing her gait, bradykinesia, drop attacks, soft palate paralysis, swallowing and articulation issues, cerebellar ataxia, bilateral pyramidal symptoms as well as extrapyramidal symptoms, and a deterioration on her intelligence quotient from a baseline rate of normal. This period of decline lasted from the age of 27 to her death at age 32. The patient ultimately died from aspiration pneumonia (Tsuchiya et al., 2011). In another case, ultimately resulting in death, a 76-year-old man with IBGC presented with a 50-year history of movement disturbance. At fifty years of age and over the next decade, the symptoms began worsening and included cognitive disturbance, memory issues, and behavioral escalation. After losing the ability to stand, chew, and verbalize, and following significant weight loss over two years, this patient died at the age of 85 (Wider, Dickson, Schweitzer, Broderick, & Wszolek, 2009).

In another case, a 56-year-old man presented with a history positive for polio and acute anterior spine disease at the age of seven years old. This patient lived a normal and productive life until the age of 46 years, when aphasic syndrome and motor syndrome affecting his right side began a slow progression. A CT scan revealed worsening basal ganglia calcification from the baseline scan 15 years prior. As a result of these symptoms, this patient was no longer able to engage in substantial gainful employment and also needed assistance with household matters. This patient also has clinically asymptomatic monozygotic twin children (26 years of age) with calcifications of the brain (Mendes de Oliveira & Fernandes de Oliveira, 2012; Mendes de Oliveira, Filho, & Zatz, 2008).

Neuropsychiatric symptoms may affect up to half of those with IBGC. These symptoms may include both auditory and visual hallucinations, psychosis, and delusions. For those with
early-onset Fahr’s disease, in the 20 to 40 year range, psychosis is a common symptom (Gülsün, Baykiz, Kabataş, & Belli, 2006). Many researchers have supported the hypothesis that defects in the basal ganglia are implicated in the development of psychosis and/or schizophrenia symptoms (Chabot, Roulland, & Dollfus, 2001).

In one case a 30-year-old woman with paranoid schizophrenia developed Capgras syndrome, a condition in which a person misidentifies someone they are emotionally close to as an imposter with persecutory intentions. It was hypothesized that IBGC, disrupting the cortico-subcortical circuits, led to a worsening of her schizophrenia symptoms, such that Capgras syndrome symptoms appeared. These symptoms were alleviated with an increase of the patient’s medication, olanzapine (Mishra, Prakash, Mishra, Praharaj, & Sinha, 2009). Ideas of persecution have been reported in other cases (Nicolas, Guillín, Borden, Bioux, Lefaucheur, et al., 2013), as well as passive hoarding, especially of food, suggesting an organic basis of these neuropsychiatric issues (Slama, Amrani, Leboyer, & Houenou, 2012). In a unique case, a 23-year-old woman diagnosed with IBGC presented with auditory hallucinations, ideas of persecution, and intellectual disability. The unique feature of this case was the woman’s arrest for two alleged instances of arson (Shirahama, Akiyoshi, Ishitobi, Tanaka, Tsuru, et al., 2010). In one case a 52-year-old male had experienced deteriorating physical and mental faculties over the past 5 years, including memory issues and sleep disturbance. In addition, his mood fluctuated, his behavior was aggressive at times and he attempted to strangle his wife at one point (Mittal, Agrawal, Mittal, Gupta, & Jain, 2010). In another case, a 34-year-old woman presented to the hospital with “acting-out attacks,” issues with concentration, and violence toward others with little to no known antecedents. Memory issues were also detected during neuropsychological testing. A CT scan confirmed the presence of bilateral calcification, and was further evidenced by a PET scan. Doctors hypothesized that reduced glucose reuptake due to calcification of the basal ganglia may be implicated in these neuropsychiatric symptoms (Yulug, Bakaar, Karapolat, Güzel, Schäbitz, 2007).

In addition to aggression toward others, suicide attempts and/or ideation have accompanied mania and delusions (Johnson, Legesse, Camprodon, Murray, & Price, 2013), dementia (Konupčíková, Masopust, Vališ, & Horáček, 2008), and mood disorders with psychotic symptoms (Saito, Nakamura, Shimizu, Oda, Ishiwata, Ishii, & Isse, 2010; Gülsün, Baykiz, Kabataş, & Belli, 2006).

Sudden onset of symptoms occurred for a 39-year-old schoolteacher, who had no medical issues until auditory hallucinations and ideas of persecution began. A CT scan showed bilenticular calcifications. Interesting no causative mutation was discovered and this patient’s 64-year-old parents had only faint indications of calcification (Nicolas, Guillín, Borden, Bioux, Lefaucheur, et al., 2013). In a particularly severe case, a 31-year-old obese man with schizophrenia, developed a sudden onset of paranoid hallucinations, refused anything by mouth and experienced psychomotor retardation. Catatonic features were also present and after three days the patient was transferred to the intensive care unit as the catatonic features had progressed into a pulmonary embolism. The pulmonary embolism was secondary to the catatonia, which was secondary the IBGC (Woo, 2007). A second report of catatonia, paranoid delusions, and hallucinations secondary to IBGC in a 60-year-old man was reported by Maley and Hebert (2013) recently. Though rare, there have been several reports of severe, life-threatening cases of anorexia nervosa secondary and likely causally related to IBGC (de Jager, Hoekstra, Nijsten, Lansink, & Ismael, 2011).
In the familial form of idiopathic basal ganglia calcification, several genotypes exist. In a particularly severe example, within an affected family, the age of onset was around 30 years old and symptoms included schizophrenia or schizophrenia-like psychotic symptoms, delusions, and eventual movement disorders and dementia symptoms. Several members of the family had been institutionalized for varying lengths of time (Le Ber, Marié, Chabot, Lalevée, & Defer, 2007).

It appears that some patients are asymptomatic aside from neuropsychiatric symptoms, until they enter their fifth decade of life, when symptoms akin to movement disorders begin to appear exacerbating previous neuropsychiatric symptoms (Nicolas, Pottier, Maltête, Coutant, Rovelet-Lecrux, et al., 2013). For some, the onset of symptoms in IBGC may occur much earlier in life. Paroxysmal kinesigenic dyskinesia was diagnosed in two 16-year-old males and IBGC was not found to be the cause until the second and third decades of life, respectively (Diaz, Wirrell, Matsumoto, & Krecke, 2010; Chung, Cho, & Kim, 2012). In other cases, psychiatric symptoms are absent and the fifth decade of life with IBGC is marked with a decline in mental deterioration, subsequently affecting reasoning, calculations, and sequential activities. This decline is dementia-like and further deterioration results in an inability to perform activities of daily living (Modrego, Mojonero, Serrano, & Fayed, 2005). In some cases, stroke may accompany dementia and extrapyramidal issues (Cavalcanti-Mendes, Carvalho, Christo, Malloy-Diniz, & Sousa, 2009). Seizures have been reported to accompany cognitive decline and Parkinson-like symptoms in some cases of IBGC (Amin, 2013; Hasan, Bajpai, & Varshney, 2007). Of particular interest for this project is the fact that whether the symptoms of IBGC include movement disorders, neuropsychiatric symptoms, dementia, or some combination, the progressive deterioration leads to an inability for a person to care for him or herself and to rely on others for their care (Ozdilek, Uluc, & Gunal, 2012). In one severe case, a 50-year-old man rapidly deteriorated over the course of 14 months. In addition to IBGC and dementia, the man, who was asymptomatic and presumably healthy 6 months prior, experienced severe neurological impairment, motor disturbances and psychiatric symptoms (Benke, Karner, Seppi, Delazer, Marksteiner, & Donnemiller, 2004). Though asymptomatic patients are mostly classified as mild in this report, it is important to highlight a report by Unkrig and colleagues (2011) in which the cause of sudden death for a 42-year old woman was Fahr’s disease. The woman’s history was positive for a prior suicide attempt, depressed mood, and unspecified skin issues but her death was sudden and occurred while cooking a meal.

Comparison with SSA criteria:

In relation to the first research question, it was determined that IBGC and all presentations of this condition do not invariably meet the Compassionate Allowance List criteria. All levels of severity, including those who are asymptomatic, meet the first disability criteria specifying that the condition must last for a continuous period of at least 12 months. While IBGC may be asymptomatic for a period of a patient’s life, there is no treatment or cure. This condition will last a lifetime. When IBGC becomes symptomatic, the condition impacts the quality of a person’s life, such that they are unable to work, participate in their normal domestic routines and hobbies, or continue on with school. Treatment may lead to or necessitate inpatient care in a psychiatric or medical facility. In some severe cases, this condition and symptoms or conditions secondary to IBGC have led to death (Wider et al., 2009). Most medical literature does not report on the extent to which a condition interferes with substantial gainful employment. A number of cases have been reported regarding situations where the condition becomes disabling such that
substantial gainful employment is no longer possible (for instance: Lam, Fong, Yiu, & Wing, 2007; Benke, Karner, Seppi, Delazer, Marksteiner, & Donnemiller, 2004) and in other cases it would appear to be impossible to maintain substantial gainful employment, given the interruptions in a person’s life to hospitalizations, level of cognitive/affective impairment present, and/or movement disturbances.

In relation to the second research question, it would appear from the literature that those cases that are symptomatic are often severe, given the progressive deterioration of cognitive and neurological faculties, and myriad symptoms affecting a variety of different bodily systems. As a result, it is recommended that consideration extend to symptomatic idiopathic basal ganglia calcification for inclusion in the Compassionate Allowance List. Given that differentiating between those who are symptomatic and those who are not, among all those diagnosed with IBGC, may include citation of medical evidence, the Quick Disability Determination process may be a more applicable expedited review procedure.

**Discussion/ Implications:**

The Compassionate Allowances List provides a benefit to both the Social Security Administration and its respective claimants. By identifying diagnoses that will invariably meet the criterion for disability, claimants may experience an expedited review time and the Social Security Administration can expect to see a decrease in their backlog of applications. This systematic review provided one example of a system to identify those diagnoses that may be considered for inclusion in this initiative. This review originally included both progressive bulbar palsy as well as idiopathic basal ganglia calcification. During the course of this project, progressive bulbar palsy was added to the Compassionate Allowance List, thereby resolving the need to investigate that specific condition.

Limitations to this review exist. The time frame for exploration of databases was from 2000 to early 2014. Pertinent literature may be available prior to this timeframe, and this limiter may have excluded evidence. Only available full-text articles written in English were included to provide sufficient review, though steps were taken to procure unavailable manuscripts from two different institutions of higher learning. This systematic review did not utilize meta-analysis techniques, and opted instead for interpretive synthesis (Dixon-Woods, et al, 2005). A future study of this kind utilizing meta-analysis may yield more detailed quantitative results, though this may exclude the single case studies which provided in-depth information on the severity, intensity and course of these conditions.

This systematic review provided an in-depth examination of the extent to which IBGC invariably met or failed to meet the definition of disability provided by the Social Security Administration. As a result, it is strongly recommended that symptomatic idiopathic basal ganglia calcification receive consideration for inclusion in the Compassionate Allowances List.
References:


