

Joseph Haydn's encephalopathy: new aspects

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Abstract

With increasing age, Joseph Haydn complained of progressive forgetfulness preventing him from composing for about the last 8 years of his life. He spent his days more and more inactive and immobilized, suffering from a disabling gait disturbance. Still, most biographers consider diffuse atherosclerosis and congestive heart failure to be reasons for Haydn's medical condition and physical decline during the last years of his life. A more sophisticated and detailed inspection of documents and sources, however, leads to the diagnosis of subcortical vascular encephalopathy (SVE), caused by progressive cerebral small vessel disease. Important features of the disease are mood changes, urinary symptoms, and in particular a characteristic gait disturbance, while dementia is only mild and occurs later in the course. Haydn was severely disabled by the symptoms of SVE for several years and often reported difficulties in the completion of his last oratorio "Die Jahreszeiten" (The Seasons). Subsequently, the disease prevented him from composing another large oratorio, "Das jüngste Gericht" (The last judgement), which had been already drafted. Finally, the progress of SVE stopped his long career as a composer and conductor at the age of 73 years.

Keywords

depression, dyspraxia, emotional lability, gait disorder, lacunar strokes, Haydn, small vessel disease, subcortical vascular encephalopathy, white matter lesions

1 INTRODUCTION

When in 1791 two of the major musical geniuses of all time, Haydn and Mozart, met in London, Haydn's biographers Griesinger and Dies both comment on the emotional moment of Haydn's departure when Mozart is reported to say: "we're going to say

Table 1 The clinical syndrome of subcortical vascular encephalopathy (SVE)

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1. Early presence of a gait disturbance (shuffling, small-stepped, “magnetic,” or apraxic–ataxic gait)
 2. History of unsteadiness and frequent, unprovoked falls with clinical signs of postural disturbance
 3. Behavioral and psychological symptoms such as depression, personality change, emotional lability, and psychomotor retardation
 4. Early urinary frequency, urgency, and other urinary symptoms not explained by urologic disease
 5. Dysarthria, dysphagia, and extrapyramidal signs (hypokinesia, rigidity)
 6. Cognitive syndrome interfering with complex (executive) social activities not due to physical effects of cerebrovascular disease alone
 - (a) Dysexecutive syndrome: Impairment in goal formulation, initiation, planning, organizing, sequencing, executing, set shifting and maintenance, abstracting
 - (b) Memory deficit (may be mild): Impaired recall, relative intact recognition, less severe forgetting, benefit from cues
 7. Distinct occurrence of lacunar syndromes often missing during the course of the disease
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farewell for the last time in our lives” (Dies, 1810; Griesinger, 1810, 1987; Landon, 1988). At that time, Mozart was 34 years old and might never have imagined that he was the one to die only a few months later. The 58-year-old Joseph Haydn, however, became a celebrated man in London and survived his younger colleague by more than 18 years.

Until today, it has been supposed that the 77-year-old Haydn died in 1809 of generalized atherosclerosis and congestive heart failure (CHF) (Carpani, 1812; Dies, 1810; Franken, 1976; Griesinger, 1810, 1987; Landon, 1980; Neumayr, 1989; Pohl, 1927). A careful and detailed review of the few original sources available and of Haydn's early biographies led us to create a more sophisticated description of Haydn's clinical syndrome, based on recent insights into the typical symptomatology of a common disorder of the elderly referred to as subcortical vascular encephalopathy (SVE, Table 1).

2 WHAT NEUROLOGICAL DISORDERS DID HAYDN SUFFER FROM? (TABLE 2)

2.1 GAIT DISTURBANCE

Haydn's gait disturbance already became evident at a relatively early stage of the disease. His last appearance as a conductor took place on December 26, 1803 in Vienna (Landon, 1980). On June 16, 1805, Pleyel noted: “we found him very weak, his face hasn't probably changed a lot, but he can hardly walk” (Landon, 1980). Dies reports from his visit on April 15, 1805: “After his usual nap he is getting completely dressed again, and climbs down the stairs with pain and misery.” On March 15, 1806, he noted: “Haydn just barely got up, tripped towards the writing table, took his

Table 2 Symptoms reported in Haydn's biographies

	Clinical syndrome	1799	1800	1801	1802	1803	1804^a	1805	1806	1807	1808	1809
1.	Gait disturbance					_{-b}		_{-b,c}		_{-c-g}	_{-b-f,h}	_{-b-e}
2.	Unsteadiness, dizziness						_{-i}				_{-b}	_{-b}
3.	Hand incoordination							_{-e,g,h}	_{-c,d}			_{-b,h}
4.	(a) Behavior		_{-i}					_{-b}				
	(b) Mood	_{-i}				_{-i}				_{-b}		
	(c) Lability of affect							_{-b}		_{-b}	_{-b-e}	_{-c}
5.	Urinary symptoms					None reported						
6.	Hypokinesia, rigidity										_{-b}	
7.	Memory, cognition							_{-b,d}	_{-d}		_{-b,d}	
8.	Rheumatic nerve fever		_{-i}			_{-g}		_{-d}	_{-d}			

^aStopped composing (Griesinger, 1987).

^bLandon (1980).

^cGriesinger (1810).

^dDies (1810).

^eCarpani (1812).

^fPohl (1927).

^gBartha (1965).

^hFranken (1976).

ⁱGriesinger (1987).

visiting card. . .,” and on August 17, 1806: “Haydn stood up, and we walked slowly back and forth in his room” (Dies, 1810). In 1807 and 1808, Haydn hoped to get some relief from his gait disturbance, when he had himself taken several times to the monastery of the Servites in a suburb of Vienna to visit the chapel of St. Peregrinus, the patron saint of patients with leg diseases (Franken, 1976; Pohl, 1927). The last public appearance of the composer took place at a performance of Haydn's oratorio “The Creation” in 1808 (Fig. 1): the Prince of Esterházy sent his entourage with a carriage and Haydn drove slowly to the old University of Vienna. Haydn was carried into the concert hall on an armchair and met Ludwig Van Beethoven and Maestro Antonio Salieri, who conducted the night's proceedings (Carpani, 1812; Dies, 1810; Griesinger, 1810). During the intermission, he felt exhausted and was overwhelmed by his emotions, so he decided to get carried back home.

Two strong men took the armchair he was sitting in and amidst the greetings, cheers and applause of the audience in the concert hall, the master of melodious music approached the steps.

Carpani (1812)



FIGURE 1

Aquarell by Balthasar Wigand (1808) displaying the scene in the concert hall of the old university in Vienna, on the occasion of Haydn's last public appearance for a concert of his oratorio “The Creation.” In the center of the painting Haydn is seated in an armchair with friends and admirers around him. On the left side, in a dark robe, Beethoven can be seen.

Copyright: Wien Museum.

On September 8, 1808, Iffland paid a visit to Haydn:

His house-maid said that Haydn was just coming back from the garden with his servant. However, his gait was somewhat slow, so that we had to be patient. (. . .) He made a movement as if he wanted to get up. His servant assisted him, and he approached, his hands held over his eyes, taking short steps and shuffling across the floor although willing to go fast.

Landon (1980)

Finally in November 1808, Reichardt describes Haydn on the occasion of his visit: “He was sitting very stiff and rigid, moved close to the table, both hands on the table, not dissimilar to a living waxwork” (Landon, 1980).

2.2 DYSPRAXIA AND COORDINATION DISTURBANCES

As a mediator between Joseph Haydn and his editors, Griesinger relieved Haydn, who started to have difficulties in writing letters. Indeed, his handwriting became more and more illegible (Fig. 2), so that he actually had to stop writing letters by his own hand in 1805 (Bartha, 1965; Franken, 1976). However, the last handwritten remark in his diary, although quite shaky is still legible, dating back to 1809, only a few months before his death. It says “Today I sold my beautiful pianoforte for 200

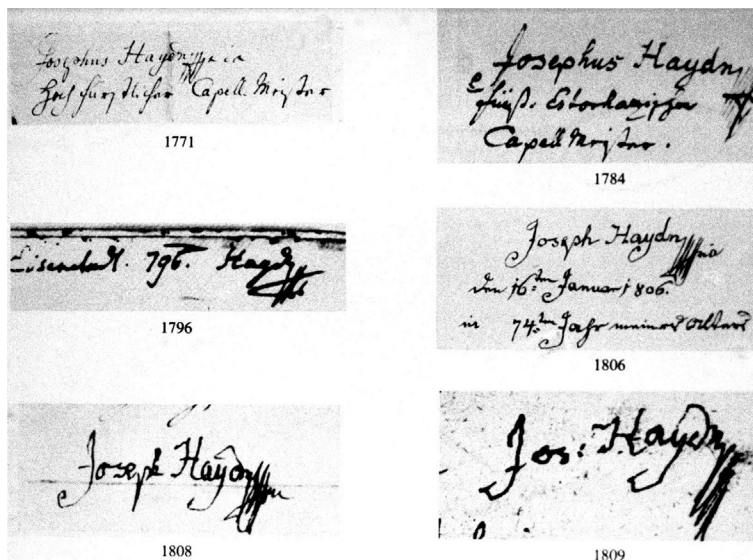


FIGURE 2

Haydn signatures from notes, receipts, and letters dating from 1771, 1796, 1808 (left), and from 1784, 1806, 1809 (right).

Courtesy Edition Roetzer, Wien-Eisenstadt.

Fl., Jos. Haydn in the 78th year of life" (Landon, 1980). Haydn's doctor already suggested in 1802 to buy a piano which was more suitable for his composition, because playing his old pianoforte became too stressful for him (Dies, 1810; Griesinger, 1810). This appears to be rather a precaution with regard to a potential source of frustration, since Haydn was still able to compose at that time. Griesinger wrote in a letter on January 8, 1804:

Haydn complained about the negative influence of the humid weather on his health: if he worked for only half an hour, he would become dizzy. He would have to take care of himself, if not he might suffer a stroke at the piano and so on.

Griesinger (1987)

During a conversation with Haydn on August 17, 1806, Dies recorded:

On my question: "How long haven't you touched your pianoforte?", he sat down, started to improvise slowly, missed the piano keys dilettantishly, looked at me meanwhile, corrected his mistakes and continued to fail in correcting. "Oh", he said after a minute (the performance didn't last longer than that), "you can see by yourself that it doesn't work anymore."

Dies (1810)

2.3 BEHAVIORAL CHANGES, EMOTIONAL LABILITY, AND DEPRESSION

Attempts to avoid the public as well as loss of interest, spontaneity, personality, and creativity can be found repeatedly in original sources. Griesinger wrote in a letter on November 11, 1800: "Haydn is not moving to the town this winter than earlier, but is staying in his house in one of the suburbs. There he can stay without being disturbed" (Griesinger, 1987). Camille Pleyel noted on June 16, 1805: "We found him sitting with a rosary in his hands and I believe he spends the whole day in pray" (Landon, 1980). As a farewell to the composer, Breitkopf and Härtel added the beginning of a late Haydn choral: "gone is all my strength, old and weak am I," to the printed scores of his incomplete last string quartet (Op. 103). Shortly before his death, Haydn said: "I'm no more useful for the world, I need care like a child, it might be time that god fetches me" (Schultheisz, 2007). Again Iffland added valuable information in 1808:

Haydn said: "I hold my prayers in the free today. I cannot do otherwise." There he squinted his eyes to start crying. (. . .) "I'm well, quite well!", he said. "But now I cannot do otherwise; whenever I am pleased about something, I feel like crying. I don't want to, but I cannot help it."

Landon (1980)

Furthermore, many guests attest Haydn's emotional lability during his final years, he burst into tears on every visitor (Franken, 1976).

2.4 COGNITIVE IMPAIRMENT: DYSEXECUTIVE SYNDROME, MEMORY DEFICITS—VASCULAR DEMENTIA

On July 12, 1799, Haydn wrote in a letter to his publisher:

...because of my impeding old age and my declining mental capacity, I can get only a small part of my work done. . .some days my weak memory and the deterioration of my nerves bring me down so much. . .and for many days afterwards I could not find any idea. . .

Griesinger (1987)

Remarkably, this is Haydn's very subjective impression, probably written in a state of depressive mood. Dies informs the reader of his biography in 1806 that Haydn "seems to take delight in presenting his own state of health worse than it actually is" (Dies, 1810). Objective remarks concerning a decline in his memory from his biographers are dated much later. Haydn himself attributed his decreasing productivity to the overwhelming burden he put on himself with the composition of his oratorio "Die Jahreszeiten" (The Seasons), which was his last important work published in 1801. Haydn himself was not completely satisfied with his composition, and in his own judgment with regard to musical quality, "The Seasons" ranked far behind "The Creation." In 1804, he retired from his position as Kapellmeister to the Prince of Esterházy. On February 28, 1804, he wrote to Esterházy: "I heartily regret that I cannot have the pleasure of conducting my little work for the last time" (Bartha, 1965). Meanwhile, it became impossible for Haydn to compose because it took him an enormous effort to capture ideas and write them down. Griesinger wrote to Breitkopf and Härtel on August 22, 1804:

Haydn has completely stopped working due to his health problems, and a quartet, of which two movements are already completed, is now his baby that he is caring for and, with big effort, he sometimes spend a quarter of an hour on.

Griesinger (1987)

Dies found on April 15, 1805: "He is aware of his weak spirit. He cannot think, not feel, not write, not listen to music" (Dies, 1810). On August 17, 1806 he wrote: "I found Haydn surprisingly weak. He looked jaundiced and complained of headache, deafness, forgetfulness, and other ailments" (Dies, 1810). Haydn complained on the same day: "Often people come to visit me, but talking, even giving only short answers leads to such a confusion that in the end, I don't know where I am and I'm longing to rest" (Dies, 1810). On September 3, 1807, Haydn said to Griesinger: "I never thought that a human being could sink down like I feel myself now. My memory is gone, sometimes I still have some good ideas on the piano, but I could cry because I am no longer capable of repeating them or writing them down" (Griesinger, 1810). Only in 1808, from Iffland's report, one can deduce an obvious memory problem with perseveration in his words and thoughts. Haydn's words spoken in the context of Iffland's visit in 1808 have been recorded as follows:

“‘The Seasons’ exhausted me completely. . . For whole days I struggled with one single idea and then, then - no, you just won’t believe how much trouble I had. . . My ‘Creation’ has brought in more than 2000 Taler for the poor in Berlin.” At this point he was lying back in his chair and burst into tears of joy. “For the poor! My work has brought a good day to the poor! This is marvelous, this is consolatory!” After a while he sat up again and spoke somewhat gloomily: “It is over now! I’m not working any more. But,” gazing friendly at everybody in the room, “it went quite well, didn’t it? How much did ‘The Creation’ bring in to the poor again? Take note of it!”

Landon (1980)

Finally, Dies added on April, 1808:

Haydn’s extraordinary exhaustion doesn’t allow him to think of the past. Even the present was not clear to him. His memory was blunted, but not going as far to describe his weakness childish.

Dies (1810)

2.5 STROKE EPISODES?

It cannot be proven whether Haydn suffered a stroke event, nor a clear lacunar syndrome can be derived from biographical data. However, there is a mention of “rheumatic head fever” in the year 1800 (a common and unspecific diagnosis at that time), preventing Haydn from attending a performance of his oratorio “The creation” (Dies, 1810). In 1801, at the age of 69, he decided to make his will. In a letter to his brother Michael on January 22, 1803, Haydn mentioned: “I have lost my previous good health for such a long time. . . due to a continuing nerve weakness, I have been totally incapable to undertake anything for 5 months” (Bartha, 1965). On August 20, 1803, Haydn replied to a letter: “Härtel (Haydn’s editor) is wealthy and my illness costs me a lot, since the doctor comes to see me twice a day” (Griesinger, 1987). Indeed, the Prince of Esterházy, Haydn’s former employer for many years, was responsible for payment of the doctors’ bills and the costs for medication in his last years of life. It remains fairly unclear, which specific symptoms Haydn suffered during these episode of “rheumatic head fever,” which recurred in 1805 and 1806. Maybe these episodes reflect a complicated headache, but “continuing nerve weakness” may either be interpreted in terms of a paresis or may well be Haydn’s name for a depressive episode. Griesinger reports on June 18, 1803:

Haydn was totally inactive for some months and didn’t feel like doing anything (which could be interpreted as a symptom of depression); now he is strengthened by the good season and the use of the baths (at that time this has been a common medical treatment for sequelae of stroke), and he admitted to be able to “improvise a little again.”

Griesinger (1987)

2.6 HAYDN'S FINAL DAYS

On May 10, 1809, when the French army approached the borders of Vienna, Haydn's servants came into his bedroom to get him up and ready for the day, when four canister shots exploded very close to the building. According to Dies, Haydn was absolutely horrified by the first detonation, and a heavy trembling and shaking took over his body. Without the help of his servants standing by he would have collapsed beyond doubt, and with the following three detonations his convulsive trembling got even worse. However, Haydn then gathered all his courage together and screamed in an unnatural and horrendous sounding voice: "Children, don't be afraid. Where Haydn is, nothing can happen to you!" (Dies, 1810). He was taken back to bed, and his physical weakness deteriorated from this moment on. On May 26, he made his servants carry him to the small piano in his living room, where he was able to play his beloved "Kaiserlied" (Emperor's song) for the last time. In the evening he complained of headache and chills. His doctors were called, but they couldn't help any more. Haydn died on the early morning of May 31, 1809.

2.7 WHAT MEDICAL EVIDENCE SUPPORTS THE DIAGNOSIS OF SVE?

During his last 10 years of life, Joseph Haydn suffered from an illness that included a progressive gait disturbance resulting in an inability to walk but, apart from moderate upper limb dyspraxia, preserved motor function of the arms. Additional symptoms were lability of affect, depression, and finally dementia, all representing cardinal features of SVE. This clinical entity emerges as a result of a severe cerebral small vessel disease, which affects the small cerebral arteries and arterioles and leads to two main pathological manifestations with predominance of either one or a combination: (1) recurrent lacunar strokes that can finally result in the so-called lacunar state, and (2) a more diffuse and widespread degeneration of cerebral white matter on the basis of chronic hypoperfusion and incomplete ischemia, mostly in arteriolar watershed zones close to the lateral ventricles (Fig. 3). Following the original description of

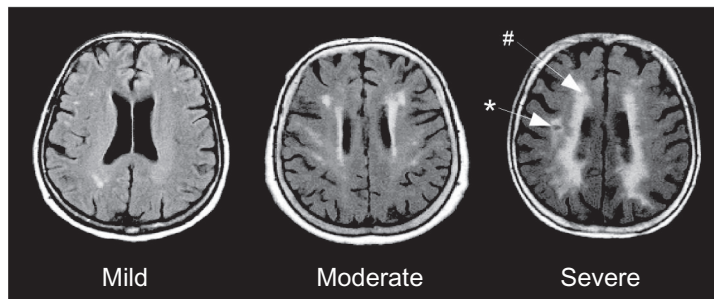


FIGURE 3

White matter changes: the three severity degrees (mild, moderate, and severe) according to the modified Fazekas scale. *Lacunar ischemic lesion. #Diffuse white matter changes.

Pierre Marie (Marie, 1901), many reports since have stressed the particular manifestation of small vessel disease in frontal lobe territories in SVE, leading to a probable critical involvement of parallel circuits from the prefrontal cortex to the basal ganglia and corresponding thalamocortical connections (Cummings, 1994; Fisher, 1965; Román et al., 2002; Tullberg et al., 2004). The disease often starts with postural imbalance and progressive disturbance of locomotion (Fig. 4) (Baezner et al., 2000, 2008; Blahak et al., 2009) and mood, mostly in the absence of distinct lacunar syndromes, when white matter lesions become evident on magnetic resonance imaging (Gass et al., 1998). The motor disturbances in SVE are in contrast to Parkinson's disease, where hypokinesia and coordination deficits affect the arms to a greater degree and are frequently asymmetric.

Several publications proposed sets of clinical criteria as a basis for clinical and pharmacological studies (Erkinjuntti et al., 2000; Pantoni et al., 2005), although still some used the misleading term of "subcortical vascular dementia," a term rather unsuitable for the complex clinical syndrome. This is of importance, because serious dementia frequently becomes evident only at a later stage of the disease, whereas features like mild personality changes with lack of initiative, fatigue, and psychomotor slowing as well as gait and postural disturbance are present in early stages and

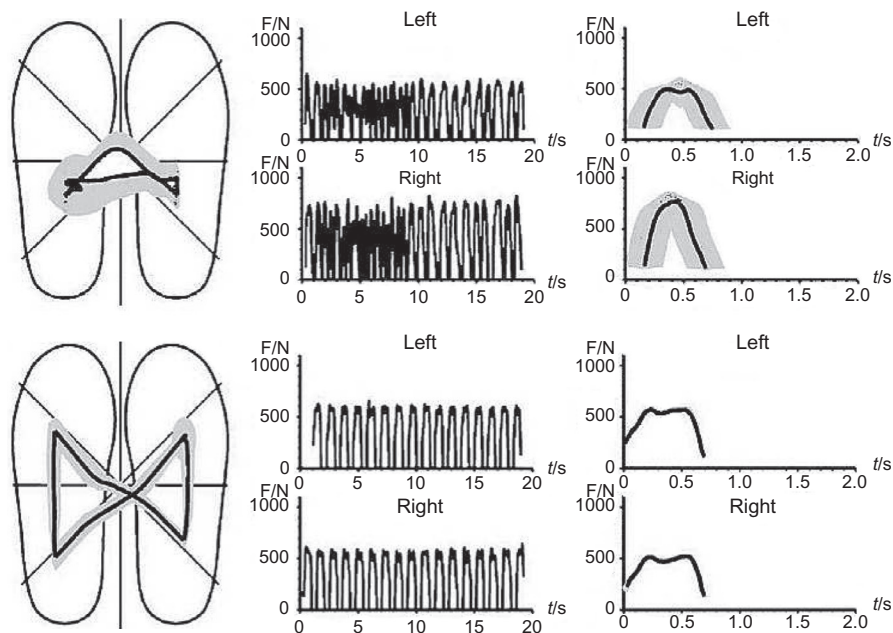


FIGURE 4

Gait disorder in a patient with subcortical vascular encephalopathy (upper row) and gait pattern of a healthy person (lower row), measured with the Computer Dyno-Graphy gait analysis system.

even predict the occurrence of non-Alzheimer dementia (Baezner et al., 2000; Inzitari et al., 2009; Verghese et al., 2002).

Haydn is an excellent example of the classical course of SVE: his gait disturbance with small shuffling steps, the need of assistance to transfer from bed to chair, and his lack of postural control with acoustic stimuli reflects the typical gait and balance disorder in SVE. He had to be carried to his small piano but was still able to play. Later, he stopped writing letters, but was still able to make short handwritten notes during the last year of his life. His inability to improvise or to compose on the piano may be explained by a progressive dysexecutive syndrome and changes in personality. In addition, a tendency to perseveration and a marked lability of affect can be found. He also reportedly suffered from short episodes of depressed mood.

Haydn's medical history is particularly interesting also because of another aspect, that fits well with the common clinical course of SVE: Until 1799, Haydn was 67 years old at that time, his creativeness and productivity had hardly been troubled by any illness of note (Franken, 1976). In the following 2 years during the composition of "The Seasons," however, Haydn's state of health deteriorated substantially. He had great difficulty in finding themes and motifs and repeatedly complained, even in later years, the extraordinary hard work and effort the completion of "The Seasons" had cost him. As mentioned above, during that time (1800) an episode of "rheumatic head fever" as a possible correlate of a stroke has been described (Griesinger, 1987). It has been proven that cerebral small vessel disease is a predictor of poor outcome and recovery in patients with an acute stroke, independent of age or comorbidity (Grips et al., 2005; Held et al., 2012). The pathophysiological concept behind this is that the occurrence of strategic ischemic lesions results in a decompensation of an already damaged, but still largely functioning widespread network of brain regions connected by anatomical tracts and functional associations. Haydn's creative strength declined rapidly around 1800–1801 whereupon he was virtually unable to compose any more after he had finished "The Seasons," and it is to be assumed whether a small lacunar stroke in combination with cerebral small vessel disease could have triggered this.

With regard to Haydn's risk factors, frequent leg swelling and shortness of breath point to CHF. CHF is a frequent complication of long-lasting arterial hypertension and concomitant small vessel disease of the heart. Also his frequent headaches and dizziness and the mentioned brownish-reddish face skin (Dies, 1810) might be caused by high blood pressure. However, medical procedures to diagnose risk factors like hypertension were not generally available at Haydn's time, and treatment of risk factors for vascular disease was not available. This is in contrast with today's situation, where the early symptoms of SVE should already result in a close monitoring and early therapeutic intervention. Although the spectrum of therapeutics is gradually growing with the introduction of NMDA antagonists (Baezner et al., 2001; Orgogozo et al., 2002) and cholinesterase inhibitors (Erkinjuntti et al., 2002; Kumar et al., 2000; Pratt and Perdomo, 2002), they are mainly being tested for the dementia aspect and gait disturbances, but interventional studies for other key features of the disease are still lacking.

REFERENCES

- Baezner, H., Oster, M., Daffertshofer, M., Hennerici, M.G., 2000. Assessment of gait in subcortical vascular encephalopathy by computerized analysis: a cross-sectional and longitudinal study. *J. Neurol.* 247, 841–849.
- Baezner, H., Oster, M., Henning, O., Cohen, S., Hennerici, M.G., 2001. Amantadine increases gait steadiness in frontal gait disorder due to subcortical vascular encephalopathy: a double-blind randomized placebo-controlled trial based on quantitative gait analysis. *Cerebrovasc. Dis.* 11, 235–244.
- Baezner, H., Blahak, C., Poggesi, A., Pantoni, L., Inzitari, D., Chabriat, H., et al., 2008. Association of gait and balance disorders with age-related white matter changes: the LADIS study. *Neurology* 70, 935–942.
- Bartha, D., 1965. Joseph Haydn—Gesammelte Briefe und Aufzeichnungen. Bärenreiter, Kassel.
- Blahak, C., Baezner, H., Pantoni, L., Poggesi, A., Chabriat, H., Erkinjuntti, T., et al., 2009. Deep frontal and periventricular age related white matter changes but not basal ganglia and infratentorial hyperintensities are associated with falls: cross sectional results from the LADIS study. *J. Neurol. Neurosurg. Psychiatry* 80, 608–613.
- Carpani, G., 1812. Le Haydine, overo Lettere su la vita e le opere del celebre maestro Giuseppe Haydn. Candido Boccinelli, Milano.
- Cummings, J.L., 1994. Vascular subcortical dementias: clinical aspects. *Dementia* 5, 177–180.
- Dies, A.C., 1810. Biographische Nachrichten von Joseph Haydn. Camesinäische Buchhandlung, Wien.
- Erkinjuntti, T., Inzitari, D., Pantoni, L., Wallinm, A., Scheltens, P., Rockwood, K., et al., 2000. Research criteria for subcortical vascular dementia in clinical trials. *J. Neural. Transm. Suppl.* 59, 23–30.
- Erkinjuntti, T., Kurz, A., Gauthier, S., Bullock, R., Lilienfeld, S., Damaraju, C.V., 2002. Efficacy of galantamine in probable vascular dementia and Alzheimer's disease combined with cerebrovascular disease: a randomised trial. *Lancet* 359, 1283–1290.
- Fisher, C.M., 1965. Lacunes: small deep infarcts. *Neurology* 15, 774–784.
- Franken, F.H., 1976. Joseph Haydn's Leben aus medizinischer Sicht. *Wien Klin. Wochenschr.* 88, 429–432.
- Gass, A., Oster, M., Cohen, S., Daffertshofer, M., Schwartz, A., Hennerici, M.G., 1998. Assessment of T2- and T1-weighted MRI brain lesion load in patients with subcortical vascular encephalopathy. *Neuroradiology* 40, 503–506.
- Griesinger, G.A., 1810. Biographische Notizen über Joseph Haydn. Breitkopf & Härtel, Leipzig.
- Griesinger, G.A., 1987. Eben komme ich von Haydn. Korrespondenz mit Breitkopf und Härtel. Atlantis, Zürich.
- Grips, E., Sedlaczek, O., Baezner, H., Fritzing, M., Daffertshofer, M., Hennerici, M.G., 2005. Supratentorial age-related white matter changes predict outcome in cerebellar stroke. *Stroke* 36, 1988–1993.
- Held, V., Szabo, K., Baezner, H., Hennerici, M.G., 2012. Chronic small vessel disease affects clinical outcome in patients with acute striatocapsular stroke. *Cerebrovasc. Dis.* 33, 86–91.
- Inzitari, D., Pracucci, G., Poggesi, A., Carlucci, G., Barkhof, F., Chabriat, H., et al., 2009. Changes in white matter as determinant of global functional decline in older independent

- outpatients: three year follow-up of LADIS (leukoaraiosis and disability) study cohort. *Br. Med. J.* 339, b2477.
- Kumar, V., Anand, R., Messina, J., Hartman, R., Veach, J., 2000. An efficacy and safety analysis of Exelon in Alzheimer's disease patients with concurrent vascular risk factors. *Eur. J. Neurol.* 7, 159–169.
- Landon, H.C.R., 1980. Haydn: Chronicle and Works. vols. I–V. Thames and Hudson, London.
- Landon, H.C.R., 1988. 1791: Mozart's Last Year. Thames & Hudson, London.
- Marie, P., 1901. Des foyers lacunaires de désintégration et de différents autres états cavitaires du cerveau. *Rev. Med.* 21, 281–298.
- Neumayr, A., 1989. Joseph Haydn. In: Musik und Medizin. Am Beispiel der Wiener Klassik. Edition Wien, Wien.
- Orgogozo, J.M., Rigaud, A.S., Stoffler, A., Mobius, H.J., Forette, F., 2002. Efficacy and safety of memantine in patients with mild to moderate vascular dementia: a randomized, placebo-controlled trial (MMM 300). *Stroke* 33, 1834–1839.
- Pantoni, L., Basile, A.M., Pracucci, G., Asplund, K., Bogousslavsky, J., Chabriat, H., 2005. Impact of age-related cerebral white matter changes on the transition to disability—the LADIS study: rationale, design and methodology. *Neuroepidemiology* 24, 51–62.
- Pohl, C.F., 1927. Joseph Haydn. Breitkopf & Härtel, Berlin/Leipzig.
- Pratt, R.D., Perdomo, C.A., 2002. Donepezil-treated patients with probable vascular dementia demonstrate cognitive benefits. *Ann. N. Y. Acad. Sci.* 977, 513–522.
- Román, G.C., Erkinjuntti, T., Wallin, A., Pantoni, L., Chui, H.C., 2002. Subcortical ischaemic vascular dementia. *Lancet Neurol.* 1, 426–432.
- Schultheisz, E., 2007. “All my strength is gone . . .” Medical history of Haydn. *Orvostort. Kozl.* 52, 79–82.
- Tullberg, M., Fletcher, E., DeCarli, C., et al., 2004. White matter lesions impair frontal lobe function regardless of their location. *Neurology* 63, 246–253.
- Vergheze, J., Lipton, R.B., Hall, C.B., Kuslansky, G., Katz, M.J., Buschke, H., 2002. Abnormality of gait as a predictor of non-Alzheimer's dementia. *N. Engl. J. Med.* 347, 1761–1768.