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ORIGINAL COMMUNICATION

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Gait abnormalities induced by acquired bilateral pallidal lesions

A motion analysis study

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Abstract *Background* Bilateral pallidal lesions induce a range of cognitive and motor disorders, principally a parkinsonian syndrome in which severe disturbances of gait and gait initiation are frequently reported. However, the precise clinical features of these disorders (and the role of the pallidum therein) remain to be established. *Objectives* The goal of this study was to characterise gait and gait initiation disorders within the context of a parkinsonian syndrome in patients with acquired, bilateral, pallidal lesions (PAL patients), to compare these disorders to those seen in Parkinson's disease (PD), and to assess the corresponding physiopathological implications. *Patients and methods* By using a video motion analysis system (VICON), we studied gait kinematic parameters in two patients presenting with bilateral, pallidal lesions. Kinematic and kinetic parameters were also determined during gait initiation. The two patients were compared with a group of 17 PD patients and to 20 healthy controls. *Results* In both PAL and PD patients, kinematic parameters (gait and gait initiation) and kinetic parameters (gait initiation) were similarly impaired, evidenced by akinesia (difficulty in initiating gait characterized by impairment of anticipatory postural adjustments). Hypokinesia and bradykinesia (respectively reduced stride length and reduced speed during gait) were also noted. *Conclusion* The gait and gait initiation disorders seen in cases of bilateral pallidal lesions (namely akinesia, hypokinesia and bradykinesia) are similar to those observed in PD. Subject to confirmation in more extensive studies, we hypothesize that bipallidal patients may present higher level gait disorders, with potential mediation by cognitive impairment.

Key words gait · gait initiation · pallidum · basal ganglia

Introduction

Acquired bilateral, pallidal lesions in otherwise healthy subjects are responsible for a number of motor disorders (principally a parkinsonian syndrome) and cognitive disorders as initially described by Jellinger et al. [1]. The clinical presentation is relatively homogeneous, as long as one only considers individuals where the lesions are strictly limited to the pallidum, which, in fact, is not often the case. Furthermore, it is evident that a simple computed tomography (CT) scan is not sufficient for establishing the exact topography of the lesion. Only cases involving a precise clinical description, with a brain magnetic resonance imaging (MRI) assessment and, ideally, the results of an anatomopathological analysis are worthy of interest. Hence, only 10 primary observations can be identified in the literature [2–8].

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In terms of motor function, it is interesting to note that this "pallidal" parkinsonian syndrome is frequently characterised by axial symptoms (hypomimia, dysarthria, falls) in general and severe postural, gait, and gait initiation disorders (freezing, postural instability, gait initiation failure) in particular.

Severe apathy is another frequently reported consequence of acquired, bilateral, pallidal lesions. It leads to "psychic akinesia", a disturbance of psychic self-activation [9–11] characterised by a dramatic decrease in spontaneous behaviour of any kind (motor, thought, language). However, this behavioural aspontaneity contrasts with relatively normal reactions to external stimuli and commands [12].

The gait and gait initiation disorders induced by bilateral, pallidal lesions have never yet been the subject of specific studies. The pathophysiology of these conditions remains largely unexplored, and we do not know whether their nature is identical to the gait and gait initiation disorders observed in Parkinson's disease (PD). Given the difficulties in treating them (medically and surgically), these latter disorders have been extensively analysed via biomechanical studies and are principally characterised by reduced speed, stride and step length, increased duration of the double limb support phase, increased trunk flexion and decreased arm swing [13–18]. A deficit in stride length control would be the fundamental deficit and we have previously emphasized the possible role of the subthalamic nucleus (STN) in stride length regulation [18].

The goal of this video motion analysis study was firstly to precisely characterize the gait and gait initiation disorders in two patients with acquired bilateral, pallidal lesions (PAL) and secondly to compare these disorders with those seen in PD, with a view to assessing the corresponding pathophysiological implications.

Subjects and methods

Subjects

Case 1

Patient 1 (male, 71 years of age) consulted for gait disorders which had progressively appeared 4 years previously but which had been stable over the last 2 years. He presented with a history of arterial hypertension (well controlled by medical treatment). His gait initiation was particularly perturbed; these symptoms were accompanied by freezing and postural instability, leading to frequent falls and forming part of a predominantly axial parkinsonian syndrome which also included amimia, marked hypokinetic dysarthria with severe palilalia, whereas segmental akinesia was moderate and hypertonia was minimal. Tremor was absent. The subject's dopa-sensitivity was mediocre, with his UPDRS III (Unified Parkinson's Disease Rating Scale) motor score [19] decreasing from 34 to 28 following acute administration of 200 mg of levodopa. Gait and axial symptoms were not dopa-sensitive.

The subject displayed an impairment in overall cognitive performance, with an MMS (Mini Mental Status) score [20] of 23 out of 30 (cut-off = 24) and a Mattis Dementia Rating Scale score of 122 out of 144 [21]. There was a general cognitive slowing and a reduction in attention abilities. All the tasks assessing executive functions revealed a severe dysexecutive syndrome. The FAB (Frontal Assessment Battery) score [22] was 10 out of 18 (cut-off = 16). Despite severe apathy, the patient was not depressed, with a score at the Montgomery and Asberg Depression Rating Scale of 8 (MADRS) [23].

Brain CT (Computed Tomography) revealed discrete, pallidal calcifications. Brain MRI (Magnetic Resonance Imaging) (1.5 T) showed bilateral, pallidal lesions (of unknown aetiology) affecting both the external (GPe) and internal (GPi) segments of the pallidum and which could not be explained by the pallidal calcifications alone (Fig. 1). The periventricular white matter was spared. 99m-Tc-hexamethylpropyleneamineoxime (HMPAo) single photon emission computed tomography (SPECT) showed bilateral hypoperfusion in the prefrontal, superior frontal and fronto-orbital cortex. The patient underwent neurophysiological gait analysis described later and then received levodopa treatment (1 g per day for 3 months), without success. Amantadine (300 mg per day) improved the freezing slightly. All symptoms remained stable over the next year.

Case 2

Patient 2 (male, 74 years of age) consulted in our department for gait disorders which had first appeared 3 years previously but which had been stable over the last 2 years. He presented with a history of arterial hypertension (well controlled by medical treatment). Gait initiation was severely perturbed, postural instability was notable, and freezing regularly provoked falls. The symptoms were set against a predominantly axial parkinsonian syndrome, characterised by hypomimia and slight hypokinetic dysarthria; segmental rigidity and akinesia were not pronounced and there was slight asymmetry at the expense of the right side. Tremor was absent. The subject's dopa-sensitivity was mediocre, the UPDRS III motor score going from 30 to 28 following acute administration of 200 mg of levodopa. Gait and axial symptoms were not dopa-sensitive.

The subject recorded an MMS score of 23 out of 30 and a Mattis score of 114 out of 144, indicating a clear decline in overall cognitive performance. Attention was impaired, and assessment of executive functions revealed a severe dysexecutive syndrome. The FAB score was 14 out of 18. Signs of disinhibition, logorrhoea and occasional, inappropriate speech suggested a frontal dysfunction. The patient was not depressed (score at the MADRS of 4).

A brain CT scan revealed only moderate cortical and subcortical

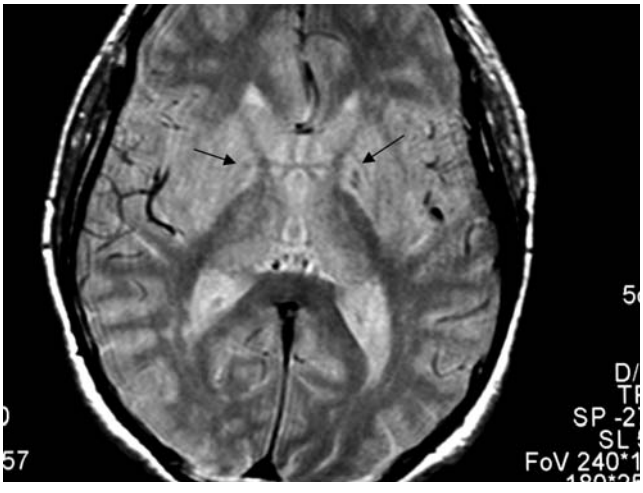

Fig. 1 T2-weighted MRI sequence: axial slice showing the bilateral pallidal lesions (arrows)

atrophy. However, brain MRI (1.5 T) detected bilateral, focal, T2-hyperintense lesions (unknown aetiology) affecting both the GPe and the GPi (Fig. 2). The periventricular white matter was spared. An HMPAo SPECT detected bilateral hypoperfusion in the prefrontal cortex and frontal laterodorsal cortex. The patient received levodopa treatment (1 g per day for 3 months), without success. Amantadine (300 mg per day) improved the freezing slightly. All the symptoms remained stable over the next year.

Parkinsonian controls (PD controls)

Data from the PAL patients were compared with those from 17 parkinsonian controls (mean age ± standard deviation (SD), 58 ± 7 years; mean disease duration ± SD, 14 ± 5 years; mean UPDRS III motor score in the Off Drug condition (see below) ± SD, 55 ± 13 out of 108) presenting with idiopathic PD according to the criteria proposed by Gibb and Lees [24]. Dopa-sensitivity was 52 % for the UPDRS III, and 35 % for the gait scores. There was no subpopulation of PD controls that had dopa-resistant gait scores.

Healthy controls

Healthy control data was obtained from normative gait and gait initiation measurements in our gait analysis department (20 elderly subjects; mean age ± SD, 64 ± 9 years).

Methods

Clinical evaluation

We assessed the parkinsonian syndromes in the PAL patients and in the PD controls on the UPDRS III scale (optimal score, 0; maximal score, 128). Subscores from the UPDRS were also determined: gait disorders (items 29 and 30; optimal score, 0; maximal score, 8), tremor (items 20 and 21; optimal score, 0; maximal score, 28), rigidity (item 22; optimal score, 0; maximal score, 20) and akinesia (items 23, 24, 25, 26 and 31; optimal score, 0; maximal score, 36) were also evaluated. PD controls did not take any antiparkinsonian drugs after the evening before the assessment (12 hours previously) (i. e. the *Off Drug* condition). For PAL patients, evaluation was always performed prior to the instigation of treatment. Clinical assessment was carried out before each gait recording session.

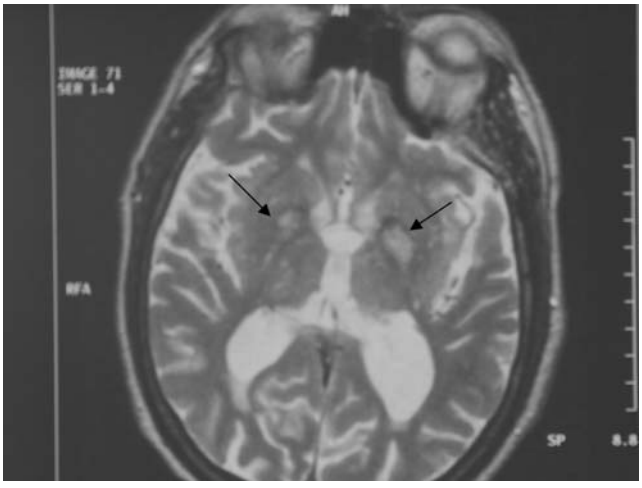

Fig. 2 T2-weighted MRI sequence: axial slice showing the bilateral pallidal lesions (arrows)

Neurophysiological analysis of gait and gait initiation

Data collection

Kinematic spatial and temporal gait and gait initiation measurements were made automatically with a VICON video motion analysis system (Oxford Metrics, Oxford, England), using 5 infrared cameras with a 50 Hz sampling frequency. Fifteen spherical, retroreflective markers placed bilaterally on anatomically well-defined points were used to define different segments of the pelvis and legs [18]. The 3-dimensional trajectories in the frontal, sagittal and axial planes were recorded by the cameras.

Two force platforms (AMTI, OR6) were used to assess kinetic gait initiation parameters. The signal was sampled at 250 Hz. Each platform enabled us to obtain the 3 components of the resulting ground reaction force (the point of application of which corresponds to the centre of pressure, (CoP)) in three-dimensional space (Fx, Fy, Fz).

Assessment of gait

The procedure has been previously described in detail [18]. The subjects walked at their normal speed and passed through the recording area, thus defining a trial which was composed of one or two gait cycles. We used the VICON Clinical Manager (VCM) software for data analysis. Spatial (stride length) and temporal (cadence, speed, and stride duration) gait kinematic parameters were determined for each cycle. Single limb support duration is also a temporal parameter and corresponds to the swing phase duration. However, we analysed the single limb support duration/double limb support duration ratio, which is more relevant: the higher the ratio, the more normal the gait. Ten gait cycles (corresponding to about 6 trials) were taken into account for each patient or control subject.

Assessment of gait initiation

The patient was instructed to initiate gait (always with the same foot) as soon as possible after hearing a sound trigger. We first used a computer programme to reconstruct the three-dimensional trajectory of the various markers: this procedure was necessary in order to identify each marker during acquisition. Next, on the basis of a biomechanical model (which notably took into account the anthropometric parameters), we used the dedicated VCM software to reconstruct the three-dimensional trajectory of internal points of articulation, thus enabling kinematic analysis. We then identified the initiating step (first step) and the second step by measuring the moment of "foot off" (i. e. when the sole or heel or toe leaves the ground) and "foot contact" (when the sole or heel or toe touches the ground). Finally, the software calculated the following spatiotemporal, kinematic parameters: gait speed, length and duration.

An additional analysis took into account the kinematic initiation parameters by monitoring 8 signals, all sampled at 250 Hertz: 1) a starting beep sound (controlled by the investigator and produced by a buzzer placed axially and in front of the subject); 2) the vertical coordinates of the heel and toe markets on the initiating side (but not the points of articulation); 3) the trajectory of the centre of pressure (CoP); 4) the three components of the ground reaction force (Fx, Fy, Fz) measured by the 2 force platforms; and 5) the two components of the CoP as pre-calculated by a computer programme on the basis of the classical equation: $x = My/Fz$, $y = Mx/Fz$.

We next used a MathCad program to automatically determine the moment of the sound beep. The investigator visually identified and recorded the times tA and tC, corresponding to the start and end of the swing phase ("foot off" – i. e. when the sole or heel or toe leaves the ground – and "foot contact" – when the sole or heel or toe touches the ground – for the initiating step) by studying the trajectory on sagittal plane of heels and toes markers. The signal was sampled at 50 Hz. The software determined the recentred CoP trajectory from the start of the sound until the subject had fully cleared the platform, and automatically marked the end of the swing phase (tC). The investiga-

tor next used this trajectory to visually identify and record the coordinates corresponding to heel (point tA) and toe (point tB) lift-off for the initiating side. The following parameters were then calculated: the anteroposterior position of the CoP (CoP-AP) at tA and the lateral balance of the CoP (CoP-BAL) between tA and tB (Fig. 3).

The horizontal trajectory of the centre of gravity (CoG) was calculated by integrating the anteroposterior and lateral components of the ground reaction forces (according to the equation $xG = \iint Fx/m$ and $yG = \iint Fy/m$) between the moment of the sound beep and tC (foot contact). The posteroanterior and lateral displacement of CoG achieved at tC could thus be calculated. The CoG's speed in the sagittal plane was calculated at the moment of heel lift-off (tA). The maximum amplitudes of vertical (Rz) and anteroposterior (Rx) ground reaction forces (in Newton) were also analysed for all patients (Rz max = Fz max – mg, m = mass of the subject, g = 9.81 ms^{-2}; Rx max = Fx max) and normalized to the subject's weight (Pz = 100 * Rz max/mg, Px = 100 * Rx max/mg).

Results

Clinical results

The clinical results are summarised in Table 1. On the whole, the PAL patients' UPDRS III scores were lower than those of the PD patients. However, the gait subscore was similar in both groups. In contrast, the patients' tremor, rigidity and akinesia subscores were either lower than (rigidity for subject 1, akinesia for the patient 2) or very close to the minimum values observed for the PD patients.

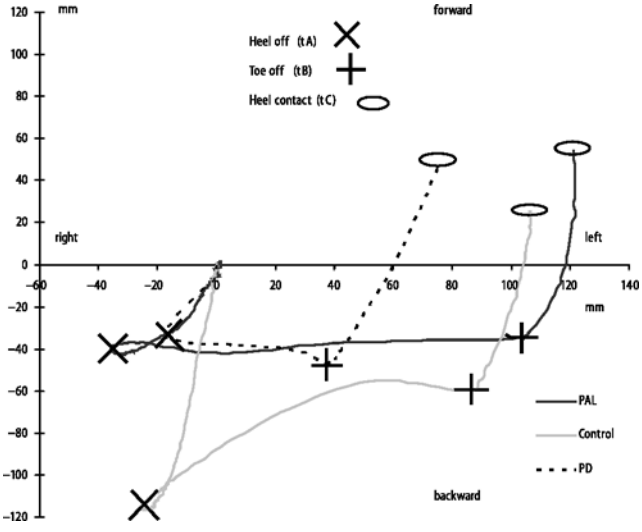

Fig. 3 Trajectory of the CoP (centre of pressure) when gait is initiated by right foot in a PAL patient (PAL), a PD patient (PD), and a healthy control (control). Heel off (point tA) and toe off (point tB) were noticed. Other parameters were the anteroposterior displacement of the CoP (CoP-AP) at tA and the lateral balance of the CoP (CoP-BAL) between tA and tB; *mm* millimeters

Table 1 Clinical features

	Patient 1	Patient 2	Parkinsonian controls (mean ± SD)
UPDRS III/108	34	30	55 ± 13
Gait/8	5	5	4.6 ± 1.6
Tremor/28	0	0	6.05 ± 6.4
Rigidity/20	2	6	11.2 ± 4.3
Akinesia/36	14	10	23 ± 6

Gait results

The kinematic parameters for gait did not differ when comparing the PAL patients with the PD controls (Table 2). The values were nevertheless lower than for healthy controls. So, we observed a clear decrease in gait speed and stride length in PAL patients. Cadence seems to be similar in PAL patients, as well as in PD and controls.

Gait initiation results

Kinematic, spatiotemporal parameters

The kinematic gait initiation parameters did not differ when comparing the PAL patients with the PD controls, especially for first speed and cycle length (Table 2). The spatial values (speed and cycle length) were, however, lower than for healthy controls. We did not observe an increase in temporal parameters such as first step duration in PAL patients.

Kinetic parameters (Fig. 3)

The kinetic gait initiation parameters did not differ when comparing the PAL patients with the PD controls (except for the CoP-BAL which was lower in the PD group) (Table 2). The values were however lower than for healthy controls (except for CoP-BAL).

Discussion

For the two cases presented here, the lesions visible on MRI concern both the GPe and the GPi and do not extend into adjacent structures (notably the putamen). A predominantly axial parkinsonian syndrome was indeed present: the UPDRS III and the tremor and segmental rigidity and akinesia were less severe than for parkinsonian controls whereas gait subscore was similar. Furthermore, the cognitive and behavioural disorders were compatible with the previous description of psychic akinesia. The motor and cognitive presentations

Table 2 Spatial and temporal kinematic and kinetic parameters

	Patient 1	Patient 2	Parkinsonian controls (mean ± SD)	Healthy subjects (mean ± SD)
Spatial and temporal kinematic parameters (gait)				
Cadence (step/mn)	108	98	100±25	112±8
Speed (m/s)	0.81	0.67	0.60±0.32	1.23±0.15
Stride duration (s)	1.10	1.20	1.29±0.37	1.04±0.06
Stride length (m)	0.90	0.81	0.70±0.28	1.29±0.12
Single support/Double support	1.03	0.95	1.00±0.57	1.78±0.26
Spatial and temporal kinematic parameters (gait initiation)				
1st step speed (m/s)	0.62	0.71	0.69±0.27	2.2±0.44
1st step length (m)	0.35	0.30	0.36±0.10	1.34±0.21
1st step duration (s)	0.58	0.41	0.57±0.17	0.61±0.08
Kinetic parameters (gait initiation)				
CoP-AP (mm)	24	46	33±18	74±12
CoP-BAL (mm)	137	112	70±17	96±16
CoG speed (cm/s)	3.23	6.18	4.31±2.67	6.26±1.71
CoG-PA (cm)	13.55	12.99	9.83±5.31	18.4±5.1
CoG-Lateral (cm)	1.95	1.72	1.60±1.42	3.4±1.22
Px	10.82	12.45	10.5±3.16	31.16±9.5
Pz	3.88	3.52	6.01±3.37	15.73±4.34

m meter; *mn* minute; *s* second; *CoP-AP* anteroposterior displacement of the centre of pressure; *CoP-BAL* lateral balance of the centre of pressure; *CoG speed* centre of gravity's speed in the sagittal plane at tA (heel lift-off); *CoG-PA* posteroanterior displacement of the centre of gravity achieved at tC (foot contact); *CoG-Lateral* lateral displacement of the centre of gravity achieved at tC (foot contact); *Px* maximum amplitude of anteroposterior ground reaction forces normalized to the subject's weight; *Pz* maximum amplitude of vertical ground reaction forces normalized to the subject's weight

were thus comparable with those seen in other cases of bilateral, pallidal lesions described in the literature [1]. One can thus legitimately seek to establish a cause and effect relationship between the clinical picture and our two patients' radiological lesions.

Gait disorder analysis in PAL patients indicated that the spatiotemporal gait and gait initiation parameters were comparable with those observed in PD subjects with far longer disease histories. The spatiotemporal gait parameters were impaired: we observed a reduced stride length in PAL patients compared with controls, which is a main feature of hypokinetic gait of PD patients. The kinetic gait initiation parameters were, in general, also comparable with parkinsonian results suggesting impairment of the anticipatory postural adjustements phase. Indeed, those patients presented a dramatically reduced antero-posterior CoP displacement as do PD patients, which was responsible for reduced first step speed, although lateral CoP displacement (CoP-BAL) was increased. Increase in lateral CoP displacement (CoP-BAL) may be explained by an increase of the basis of support in PAL patients such as in older subjects [25]. In summary, gait and initiation of gait disorders in PAL patients were characterized by akinesia (difficulty in initiating gait), hypokinesia and bradykinesia (respectively reduced stride length and reduced gait speed).

The very moderate degree of limbs akinesia and rigidity in the PAL group compared with the parkinsonian group (whilst gait disorders were similar) suggests that akinetic-rigid symptoms in limbs are barely (if at all) involved in gait disorders. In contrast, this observation could suggest the involvement of a structure specialising in the physiology of gait and on which the pallidum exerts an influence: the pedunculopontine nucleus (PPN) could fill this role. Certain data support this hypothesis: we know that a deficit in gait cycle length regulation is probably the fundamental impediment in parkinsonian gait [18]. We have furthermore shown that GPi stimulation has only a limited effect on cycle length control [17]. This parameter may depend on a structure other than that the GPi but which nevertheless forms part of the basal ganglia system: stimulation data show that the STN may play such a role [18], possibly via its links with the PPN (whose role in stable gait, gait initiation and its modulation is well known) [26–28]. Hence, neurophysiological studies have shown that the PPN receives afferents from the GPi: these GABAergic afferents inhibit locomotion, whereas the glutaminergic afferents from the STN stimulate locomotion [28].

However, another hypothesis can be put forward: the gait disorders presented by the PAL patients could be explained via a disturbed output of the basal ganglia to

cortical areas (supplementary motor area, motor cortex and frontal lobes). Thus, the PAL patients could present with "higher level gait disorders", as introduced by Nutt et al. [29], and this could be mediated by cognitive impairment: Nakamura et al. [30] found similar gait disturbances in patients with Alzheimer disease, and this was correlated with reduced regional cerebral blood flow in the frontal lobe (as described in our PAL patients). Indeed, it is possible that the motor inertia seen in our PAL patients results from the psychic emptiness which they experience [10]. Hence, an inclusive relationship between the pallidal motor and cognitive syndromes can be proposed. However, another hypothesis may also be put forward: that of segregation between the 2 types of symptoms but with some partial overlap, explained by the preceding hypothesis. Indeed, even though there are distinct sensorimotor, associative and limbic territories within the pallidum [31], they probably function in close correlation, as suggested by Joël and Weiner [32] via their interconnected model of basal ganglia-thalamocortical circuitry.

In conclusion, the gait and gait initiation disorders seen in cases of bilateral pallidal lesions (namely akinesia, hypokinesia and bradykinesia) are similar to those observed in PD. In light of our present results and subject to confirmation in more extensive studies, we hypothesize that patients with bipallidal lesions may present with "higher level gait disorders" (a notion introduced by Nutt et al. [29]). Furthermore, one can reasonably suggest that the said disorders could be mediated by cognitive impairment.

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