Basal ganglia and the limbic system - role in stuttering and other movement disorders

Henny-Annie Bijleveld
Neurolinguist, Université Libre de Bruxelles, Belgium
e-mail hbijleve@ulb.ac.be

In this paper I will develop three parts:

A. Research evidence from subcortical implication in Stuttering
B. Research evidence from basal ganglia implication in Gilles de la Tourette and other movement Disorders (Huntington Disease, Parkinson, Sydenham's chorea)
C. Research evidence from fMRI showing the relationship between the limbic system and the basal ganglia and neocortical structures (SMA) in anxiety, memory (feed forward loop) and learning.

A. Research evidences for subcortical implication in Stuttering

This research is not new. Indeed, already in 1934 Seeman thought that a dysfunction of the basal ganglia could play a role in stuttering and that the autonomous system (expression of emotions), through the striato-pallidal pathway could disrupt the motor activity of speech and Gracco (1991) supposed the intervention of the basal ganglia and the SMA for the production of speech.
Studies on stereo tactic stimulation of the left posterior and ventrolateral thalamic nucleus by Schaltenbrand (1965, 1975), Andy and Bathnagar (1989,1991, 1992), Ojemann and Ward (1971), Ojemann (1975, 1976, 1989) showed elicited perseverations and stutter like speech (repetitions of parts of words, as well as blocks) as a result of thalamic stimulation.

The stereo tactic stimulation studies confirmed the importance of the left thalamus in speech production, also from a negative point of view. Bell (1968) studied some patients who developed speech disturbances (dysphasia, diminished voice volume, difficulty in initiating speech, pitch changes and impaired speech rhythm or dysarthria) after having received thalamic stimulation for epilepsy.
On the other side, Andy and Bhatnagar (1991) noticed relieve of stuttering and epileptic attacks through electrical stimulation of the frontal thalamus. They conclude that "*chronic pain and stuttering may be implicated … in reticular networks extending from the brainstem to the thalamus, and that acquired stuttering may be recruited as one component of a larger syndrome complex"* (Andy and Bhatnagar, 1992).

Studies on acquired stuttering after subcortical lesions, notably after basal ganglia lesions, have provide further information about the impact of basal ganglia on speech and speech disturbances. Marshall and Neuburger (1987), Meyers et al. (1990), Wallesch (1990), Ludlov (1987) observed acquired stuttering after left or bilateral basal ganglia lesions. Moreover, they noticed disturbances in finger movements and in timing of sequences and delayed reaction time, which again shows the role of these subcortical nuclei in the organization of coordination of volitional movements. It persuaded Ludlov et al. (1987) of the fact that:

"Acquired stuttering is a motor control disorder that can occur with unilateral right- or left sided lesions involving the basal ganglia and white matter tracts, as identified on CT scans".

The breakdown in timing sequences was also observed by Ciabarra et al. (2000) in a patient with a left basal ganglia infarction, as well as by this author in one of my patients.

Kent (1984), Cipolotti et al. (1988), Marsden (1982) , Caruso (1991) also observed acquired stuttering in spontaneous speech and reading, impairment in the motor programming sequences and impaired rhythm of speech in patients with basal ganglia lesions. That is why Cipolotti called acquired stuttering with basal ganglia involvement "*a general disturbance of motor programming and a central inability to mentally plan the program"* (1988). The thalamus could function as a central relay station. Van Borsel et al. (2003) raised the question if acquired thalamic stuttering could be considered as a clinical entity.

B. Research evidence from basal ganglia implication in Gilles de la Tourette and other movement Disorders

(Parkinson, Sydenham's chorea, Huntington disease)

Gilles de la Tourette syndrome (TS) s a developmental neurological disorder, characterized by motor and vocal tics, rapid and involuntary stereotyped movements, with occasionally coprolalia and stuttering. TS can be accompanied by OCB and Attention Deficit and Hyperactivity. Kurlan (1994, 1997) Marcus and Kurlan (2001) consider TS as a part of a "*clinical spectrum that includes a range of increasing functional impairment, indicating various degrees of abnormality in basal ganglia development*. Groenewegen et al ((2003) suppose an imbalance between dorsal and ventral striato-pallidal systems to play a role in TS. Through dopaminergic pathways (from substantia nigra to dorsal striatum) limbic information can influence the expression of motor and behavioral processes. For Yoshiko Nomura and Masaya Segawa (2003), TS is a developmental dopamine disorder. They also stress the dopaminergic abnormality in the basal ganglia and the strong relation between the basal ganglia and the limbic system. Stern et al. (2000) observed the relation between (abnormal) brain activity in the anterior cingulate cortex (limbic cortex), AMS, as well as in the putamen and caudate (which are part of the basal ganglia).

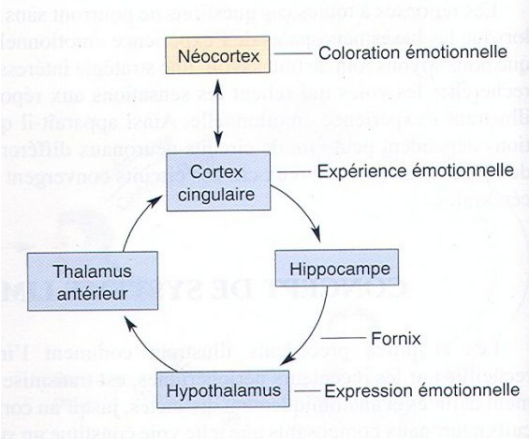
Parkinson Disease is an acquired degenerative neurological disorder showing akinesia, hypertonia, resting tremor with possibly psychiatric disorders like depression; PD is known to be the result of a decrease in dopaminergic levels due to a degeneration of melanin containing neurons in the substantia nigra (pars compacta), which are responsible for production of this neurotransmitter. These neurons project to the striatum (caudate and putamen). Hardie et al. (1984) observed in some patients that treatment with levadopa to decrease hypertonia gave rise to stereotyped movements and OCB, which suggests the impact of dopamine on the striatum (caudate) nucleus of the basal ganglia. Bonneville et al. (2005) and Phil Hyu Lee et al. (2004) observed basal ganglia hyperfusion and abnormal volume of the subthalamic nucleus in Parkinson patients. Lebrun et al. (1986) and Koller (1982) observed acquired stuttering with Parkinson Disease.

Basal ganglia are involved in movement disorders like Huntington disease. Fennema et al. (2004), in their study of patients with HD, observe that: "*basal ganglia and cerebral cortical grey matter volumes were significantly smaller in HD patients"*. The loss of cerebral cortical grey and white matter was "*related to caudate atrophy"*. In their study, the putamen and the globus pallidus were also affected. Aylward et al. (2004) noticed striatal atrophy in patients with preclinical HD.

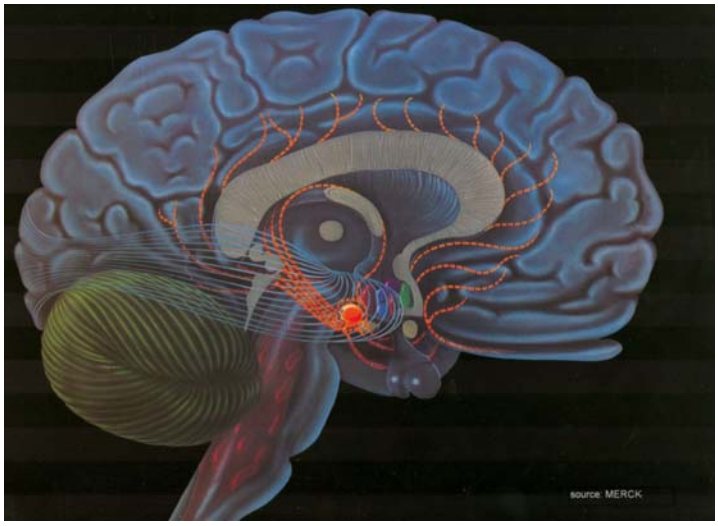
Sydenham's chorea is a developmental disorder affecting the basal ganglia and is characterized by involuntary movements, hypotonia and occasionally by emotional instability. Grimshaw (1964), Swedo et al. (1993), Pauls and Leckman (1986) observed obsessive compulsive behavior and psychopathological vulnerability as well as hyperactivity in patients with Sydenham's chorea.

C. Relation between basal ganglia, limbic system in anxiety, learning and stuttering

Since the beginning of the last century, speculations were made about the role of the limbic system in emotion and learning. As a matter of fact, in 1934 already Seeman proposed a theory of stuttering implicating the basal ganglia (by the striato-pallidal pathway) and the autonomous system. In the same year, 1934 Kleist published the hypothesis that the limbic system (cingulated cortex) was responsible for the emotional behavior. He considered the hypothalamus the relay-station and the central regulation of the system. In 1937 Papez proposed a hypothesis for the expression of emotion in human language, which remained under the name of "*Circuit de Papez*".



It includes the cingulated cortex, the basal ganglia (putamen caudate nucleus) globus pallidus, the hypothalamus and the anterior thalamic nucleus. The circuit works as follows: the cingulated cortex projects to the hippocampus, from the hippocampus to the hypothalamus (through the fornix pathway). From the hypothalamus to the anterior thalamus (implicated in involuntary movements), and from there back to the cortex (see slide). Referring to Lamendella (1976): "*Papez circuit gave emotion a testable physiological basis"*. Through research he came to the conclusion that emotional language was processed through the limbic system.



Freire et al. (1999), Baxter et al. (1987, 1992) showed with their RMI studies the relationship between basal ganglia and the limbic system. Baxter et al proposed the hypothesis that the cortico-striato-thalamic circuit which should function as a filter or inhibitor looses its control due to a dysfunction of the striatum. The input and role of the substantia nigra (pars compacta, through the production of dopamine), and its projection to the striatum seems to be of major importance in the balance/imbalance of the circuit. The consequence of this imbalance/dysfunction would be that the inhibitory function of the globus pallidus to the thalamus is defective, what would liberate the thalamus from the inhibitory control. This then would give raise to uncontrolled and involuntary movements.

Abwender et al. (1998) and Larry Molt (1999) analyzed the similarities between stuttering, TS and other neurological disorders and the probable involvement of the basal ganglia and limbic system in the onset of the disease.

The PET scan studies of Wu et al. (1997) have shown higher blood flow in the striatum (caudate nucleus) during stuttered words that during non stuttered words. They have noticed a decrease in stuttering severity after medication normally given to TS patients, like haloperidol or risperidone. To the authors several neurological disorders of movement control would be the result of a dysfunction in the dopamine transport or of a dysfunction of the dopamine neurotransmitters.

Marsden (1982) and Mink (1996) put forward the following hypothesis: basal ganglia would have a control function and a facilitator function in motor and cognitive processes (language and movement). Shah et al. (2003) think that stuttering sometimes might be badly diagnosed as stuttering in stead of a form of TS.

Conclusion

The multiple connections between the limbic system and the basal ganglia are very interesting. To resume:

- the role of the limbic system in the expression of emotion/anxiety;
- the role of the hippocampus in the limbic system intervening in learning (in the feed forward loop: anticipation of anxiety provokes anxiety);

- the role of the basal ganglia in the control of movements

The interconnectivity and the fine balance of this complex network bring me to the following hypothesis.

> Could it be that anxiety in a stutterer (limbic system) through the intervention of the hippocampus (feed forward loop and learning) provokes a temporary dysfunction in the dopamine transmitter from the substantia nigra, which provokes a temporary imbalance in the basal ganglia which result in a temporary loss of inhibitory control which provokes stuttering and other involuntary movements. In other words, **is it possible to integrate these three elements and thus relate anxiety to the physiologic factors in Stuttering?**

Similarities between stuttering and other movement disorders linked to a dysfunction of the limbic system and the basal ganglia.

1. Developmental disorders in the young child
2. Boys are more affected than girls (3x)
3. Genetic transmission is a known factor
4. Multi-causal disorders
5. The basal ganglia dysfunction can be the result of genetic factors, metabolic factors, illness, transmitter dysfunction, intoxication
6. Manifestation of the disorder is not constant but intermittent
7. Symptoms often decrease in condition without stress and increase with stress (low tolerance in front of stress)
8. Body scheme is often uncertain (clumsiness)
9. Anxiety as trait character
10. Hyperactivity is often present

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