Morphological aspects and symptomatology of fronto-basal injury

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Fronto-basal injuries in humans are known to produce very special disturbances of mood and behaviour with depression, anxiety or aggression (Busch and Alpern 1998, Anderson and Silver 1998). The lasting clinical symptoms may hinder social integration during lifetime. In cases where motor disturbances and other usual traumatic sequelae are missing, we are dealing with an obviously "healthy patient" who is a burden to himself, his family and his doctors. It should be considered that patients with chronic alcoholism or drug addicts exhibit an increased percentage of orbito-frontal or temporal traumatic scars_at autopsy. Mostly these lesions have not been recognized during lifetime, thus their contribution to the clinical picture remains unknown in many cases. This paper undertakes to approach fronto-basal injury from the pathological point of view to attempt to understand the combination of processes and their possible symptoms.

The first important point is the topography of the injury and additional anatomical structures involved. **Figure 1** demonstrates the types of possible lesions to the basal frontal lobes, which are correlated to different clinical symptoms. We have to mention that there have been recent reports which may point to specific functions of the right and the left basal frontal lobes. This would be in accordance with other functional differences between the right and the left hemispheres. The suggestion of divergent functions of right and left basal frontal lobes is based on experimental and clinical observations (Robinson and Szetela 1981,

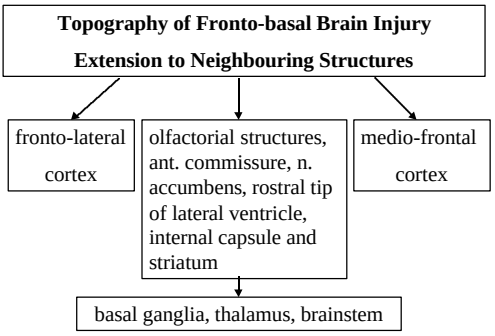

Fig. 1.

Grafman et al 1986, Robinson et al 1988, Davidson 1992, Meyers et al 1992).

The topography includes important extensions of traumatic damage to brain structures in the immediate neighbourhood of the frontal basal lobes **(Figure 2)**. There may be an additional involvement of the medio-frontal or fronto-lateral cortex. Frequently the tip of the anterior horn is involved

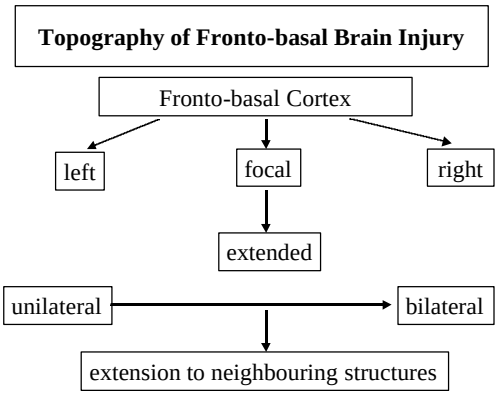

Fig. 2.

in a fronto-basal injury, extending to the limbic cortex, nucleus accumbens, anterior commissure and the most frontal tip of the striatum and the internal capsule. This may or may not include additional clinical symptoms to the basal frontal lobe syndrome.

Finally, it has been considered that the frontal cortex is functionally involved in neuroanatomical circuits which reach subcortical structures such as the basal ganglia, the thalamus, the mesencephalon and the caudal brainstem. These connections are important in understanding clinical symptoms in frontal lobe injuries and will be mentioned later. The possible pathological main mechanisms which may influence the brain in trauma are listed in **Table 1**.

First, cortical contusion destroys brain tissue and vessels of the cortex as well as vessels of the arachnoidea. The contusion hits the surface of the cortex at the tops of the gyri. Sometimes the depths of the sulcus are protected or less damaged. The degree of involvement of the underlying white matter depends on the extent of the contusion. This picture is demonstrated in **Figure 3-5**. In its quality it can be compared to experimental ablations of the cortex in animals. If this is not influenced by other mechanisms, it can be called a circumscribed lesion and focal. The stretching and tearing of vessels has been mentioned already. This may hurt not only the smaller vessels but larger vessels inside the white matter. This involves especially larger venous vessels producing haematomas of different size. They may even be space occupying. The size and duration of the haemorrhage decide the lasting damage to axons, which include many directions of frontal lobe connections. The functional result may be a "diffuse" damage of the whole frontal lobe depending on the localisation and size of the haemorrhage.

The second important pathomechanism involved is damage to axons by tearing and stretching. First mentioned by Strich (1956), this finding has recently become important. It is more frequent than estimated in earlier investigations. The functional result depends on the direction of

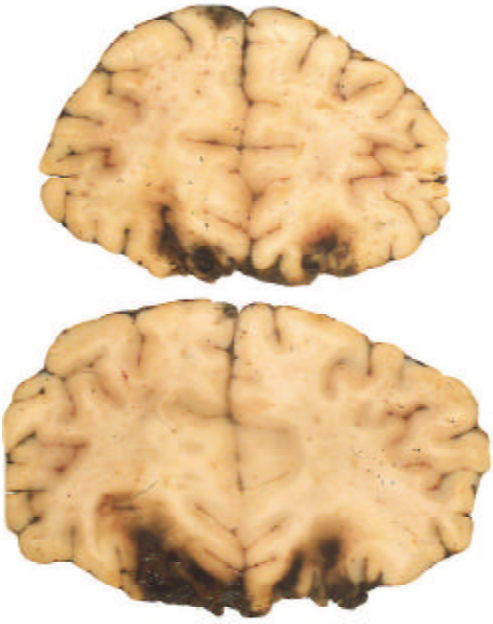

Fig. 3: 4 –day- old hemorrhagic contusion of both frontal lobes. Additional circumscribed lesions in the dorsal and lateral cortex of the frontal lobe. No visible involvement of the central white matter. Male, 32 yrs., 0,5x

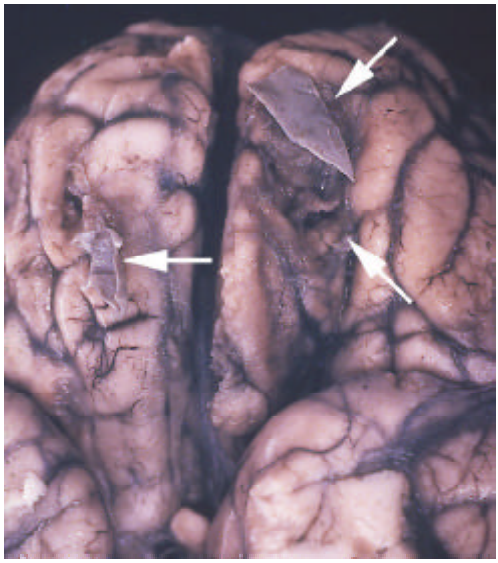

Fig. 4: Surface of the frontal lobes some weeks after injury. Circumscribed lesions of the right, more extensive contusions on the left side. Adhesions of dura to the cortical lesions on both sides (←). Male, 40 yrs., 1x

Mechanism	Pathology	Symptomatology
Contusion	Cortical lesions mainly in the gyral tips	Circumscribed cortical deficits
Hemorrhage	Diffuse hemorrhages Mass bleedings in the deep white matter	Diffuse, depending on size and duration
Axonal lesion	Direction-depending preferation of tracts	Focal to multifocal
Brain edema	Increased permeability of vessels Increased intracranial pressure	Diffuse
Hypoxy	Depending on pronouncement	Symmetric-focal Diffuse
Penetrating injury	Circumscribed lesion of cortex and white matter	Focal

Table 1. Pathomechanism and symptomatology of fronto-basal brain injury

tearing and the direction of the involved fibre tracts. The result is multifocal damage which should not be called "global". This is similar to the situation caused by bleedings in the white matter, where axons of different origin are involved. This could be called diffuse only with regard to the clinical picture.

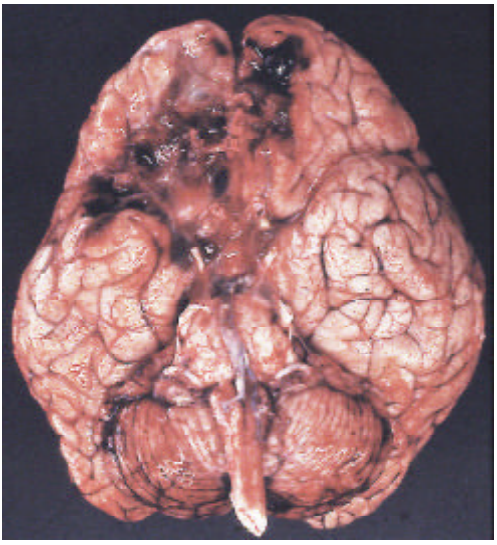

Fig. 5: Scars of both frontal lobes 25 years after gun shell injury. Between lesion and neighbouring_cortex the border is deeply sunken in. Prior to death hemorrhagic abscess. Male, 56 y., 0,2x

Brain edema is a third event which may influence brain damage and symptomatology. However, it is rarely concentrated in the frontal lobes only. Thus, the correlation to the functional loss is quite diffuse (increased intracranial pressure) and may involve even the brainstem. Finally, hypoxia and hypoxic events may be mentioned. The localized lesion in the contusion can be accompanied by very local hypoxic effects but generalized hypoxic events similar to brain edema may affect more or less the whole brain. For the correlation with clinical symptoms it should be important to consider the highly different vulnerability of neurones in the brain. Frequently only the most susceptible structures are involved selectively (Hippocampus, Purkinje cells, Pallidum etc.) This may add to the clinical picture special features besides the frontal cortical damage.

As mentioned above, the prefrontal cortex is involved in the fronto-subcortical circuits shown in **Figure 6**. These circuits are mainly characterized by inclusion of different anatomical parts of the PFC which account for different clinical and behavioural functions (Masterman and Cummings 1997). Fronto-basal injuries will mostly affect the orbito-frontal cortex, which is frequently associated with a phenomenology of disinhibited behaviour,

since this part of the PFC is involved in behavioural inhibition. There is some evidence that serotonergic systems play a role in these functions (Moeller et al 1996, Olausson et al 1999) and alterations in serotonin receptor subtypes have been localized in the PFC in suicidal and aggressive behaviour (Arango et al 1992). Disinhibition will greatly increase the difficulties in treating these patients and will mainly hinder the patient's social and professional rehabilitation. Moreover, lesions of the orbito-frontal cortex may result in mood disturbances such as dysphoria and in depressive and compulsive cognition and behaviour.

More extensive injuries of the frontal lobe will include lateral and medial parts of the PFC. Executive functions such as problem solving, monitoring performance, allocating resources, organizing behaviour in a time domain to attain goals (Levin HS 1998) will be dysregulated mainly by lesions or functional alterations of the dorso-lateral PFC. Signs of apathy with lack of initiative, cognitive ability and emotional responsitivity predominantly belong to the psychological disturbances resulting from changes in the medial PFC.

Additionally, the PFC is modulated by monaminergic afferents deriving from brainstem neurones which produce these monoamines. In particular serotonergic, noradrenergic and dopaminergic systems have been shown to be involved in a variety of psychological and behavioural functions such as mood, motivation, sleep, food intake, psychomotor activity and social integration. Disruption of these systems by frontal lesions results in dysregulation of intracellular signal transduction systems and can finally be transformed into morphological changes of dendrites and synapses, which may form a biological basis for a wide range of psychosocial disturbances.

Summarizing the different possible pathological mechanisms involved and the complex anatomical connectivity of the fronto-basal cortex, the individual clinical picture of the single patient may

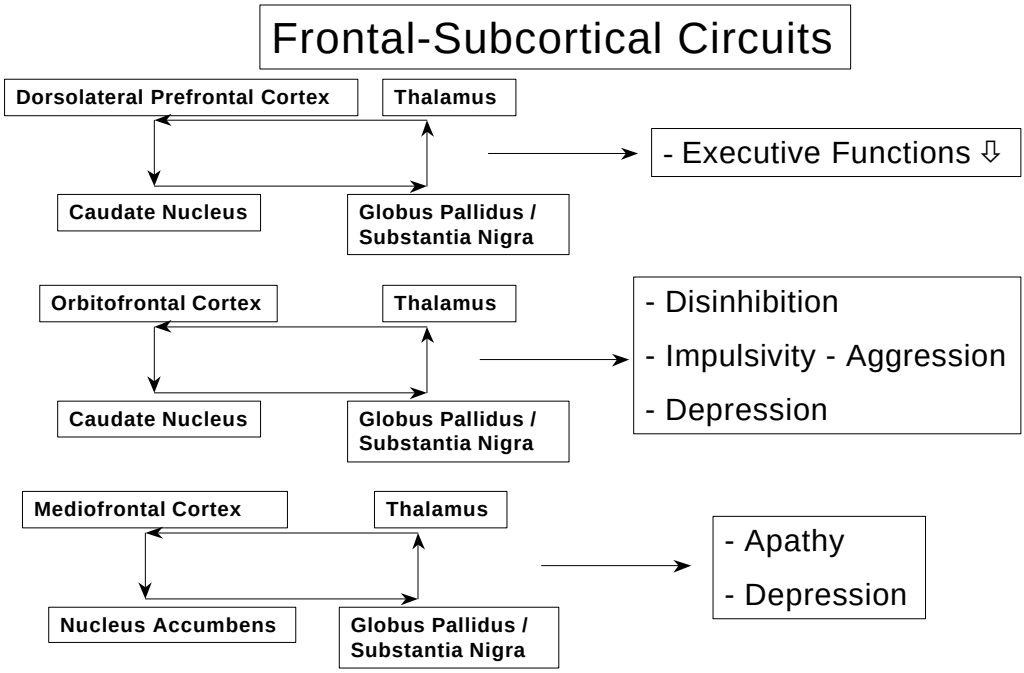

Fig. 6.

Modified from Masterman and Cummings 1997

be very variable. Basically, however, it is due to the special disturbances of mood and behaviour which appear as a result of disrupted neurocircuits including the fronto-basal cortex. Post-acute treatment strategies targeting compensation for such structural lesions remain a matter of concern and will have great impact on the final functional outcome of patients with frontal damage.

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