

rCBF SPECT evaluation of dementia

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Introduction

Dementia is an acquired impairment of intellectual function, affecting at least three out of six spheres of mental activity: language, memory, visuospatial skills, emotion, personality and cognition. Dementia may be divided into global dementia, when all intellectual functions are more or less randomly impaired and lacunar dementia with more selective functional impairment. The aetiology of dementia is complex. Dementia may be of neurodegenerative origin, vascular origin or may be so called reversible dementia, due to the factors like vitamin deficiency, chronic subdural hematoma, circulatory insufficiency and others.

The crucial factor in the diagnosis and management of dementia is the correct identification of underlying cause. In Alzheimer's disease (AD) early diagnosis is important not only for the purpose of prognostication and family counselling, but also it may provide medication of AD patient with some, more or less promising experimental drug trials. Additionally, establishing or excluding diagnosis of AD will stabilise the position of family members, who will be not left for prolonged financial and emotional draining. Certain other disorders, accompanying and/or mimicking signs of dementia like major depression or cerebrovascular diseases may be treated for stopping, slowing down or sometimes reversing the course of dementia.

An important aid in the differential diagnosis of dementia is cerebral blood flow brain (CBF) SPECT scanning. Although the sole use of neuroimaging methods should not allow to establish the final diagnosis, CBF SPECT scanning may improve diagnostic precision and may help to diagnose dementias of different types — above all — AD. The widely available brain SPECT examination

versus the more limited availability of PET may have a key role in diagnosis and staging of dementia severity.

The aim of this paper is to overview cerebral blood flow changes in particular types of dementia and the applications of brain SPECT in this group of diseases.

Alzheimer's disease

Alzheimer' disease (AD) is considered the most common neurodegenerative disorder, about 30–60% of dementia cases, although in common practice the diagnosis of AD happens to be overutilised. For example, a vascular infarct of temporal lobe may produce signs resembling AD. The onset of AD is insidious, the first symptoms are the difficulties in remembering names and recent memory problems. The course of disease is characterised by steadily progressive cognitive impairment with lack of motor and neurologic signs (1). Neurofibrillary tangles and neuritic plaques are typical pathological finding in AD. In early stage of AD neurodegenerative changes are found in the limbic system, particularly in hippocampus, a structure playing an important role in recent memory processing (2). In later stages of disease those changes are found mostly in temporoparietal lobes, which is consistent with CBF changes.

The main SPECT finding is a symmetric drop of rCBF starting in the mesial part of temporal lobe, then spreading on the rest of temporal lobe and parietal lobes. Temporo-parietal hypoperfusion is considered to be the most outstanding feature of CBF alterations in AD. Cerebellum, motor and visual cortex is spared (3).

There are two difficulties with radionuclide evaluating of AD:

- temporoparietal perfusion deficit is not entirely specific for AD; it may be found in dementia with Lewy bodies — DLB (4), in mitochondria encephalopathy (5) and monoxide poisoning (6); two latter situations, however, may be confirmed or excluded on a basis of case history and clinical data;
- secondly, AD is heterogenous disease and this heterogeneity is reflected in SPECT studies (7); temporoparietal deficit is not found in all patients with AD and this is suggested that this neuroimaging finding may be helpful in differentiating subtypes of AD (8); furthermore, reduced frontal glucose metabolism and blood flow impairment has been reported in some studies (9, 10); those findings may however reflect unrecognised LBD and not AD.

The crucial problem of rCBF SPECT scanning in AD is fact that although its sensitivity in advanced disease is about 70–80%,

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in early stages SPECT's sensitivity is lower. This may be solved by careful evaluation of early hippocampal changes or by image analysis standardisation, for example as proposed by Imran et al. (11).

Another use of rCBF SPECT may be its use as a marker of the effects of pharmacotherapy (12).

Dementia with Lewy bodies

Dementia with Lewy bodies (DLB) is considered to be the second most common senile degenerative dementia after AD (13). The central clinical feature of DLB is a progressive and fluctuating cognitive decline with recurrent visual hallucinations, systematised delusions and spontaneous parkinsonian symptom. Repeated falls, syncope, transient loss of consciousness and neuroleptic sensitivity are also useful clinical characteristics (14). When the initial presentation of DLB is characterised by impaired cognition it can mimic AD (15). Furthermore, neuropsychological evaluation can disclose severe but similar degrees of impaired performances concerning attention, frontal lobe function and motor function sequencing in both DLB and AD (16). Pathological study remains the only way to confirm the diagnosis of DLB, when evidence of Lewy bodies is found in the cortex, the subcortical regions and the brain stem (*substantia nigra* and *locus coeruleus*) (17). The precise nosological relationship of DLB and AD is still a matter of debate. On one hand common clinical and pathological features of DLB and AD are observed, so some authors consider DLB to be a variant of AD; on the other hand some authors consider the two diseases independent, with DLB seen as a more extended form of idiopathic Parkinson's disease — IDB (18).

Early diagnosis is an important problem in DLB. Cholinergic deficit in DLB is more extensive when compared with AD. This explains the beneficial effect of therapy with cholinesterase inhibitors, with improvement of cognitive function (19).

In DLB SPECT scanning reveals a global decrease of cerebral blood flow in all cortical regions except posterior part of frontal lobes and occipital regions (4, 20). This could be a marker of disease, distinguishing DLB from AD where a posterior half of the brain is affected by CBF alterations and FTLT where the anterior half is affected. The diffuse decrease of blood flow observed in DLB suggests widespread lesions in the cortex, which is consistent with pathological studies. Lewy bodies are observed in many cortical structures: especially in frontal, insular and temporal cortex and in anterior cingulate (15). Some authors underline the occurrence of occipital hypoperfusion and/or hypometabolism and recommend it as the marker of DLB (21). The crucial point in DLB SPECT studies is that definite diagnosis of DLB can be established at post-mortem studies, so most of papers refer to patients with probable, but not fully established diagnosis of DLB.

Frontotemporal lobar degeneration

The term „frontotemporal lobar degeneration (FTD)” is a concept delineated independently by Neary (22) and Gustafson (23). It is a group of neurodegenerative disorders characterised by progressive changes of social conduct, poor insight, poor hygiene and disinhibition. Spontaneous speech becomes increasingly economical with disease progression, culminating in mutism in some patients. By contrast, visuospatial and motor functions are preserved

and neurological examination is usually normal. Sometimes this examination may reveal frontal lobe release phenomena. The criteria for diagnosis of FTD were summarised in 1994 by Brun et al. (24). In contrast to AD in which memory loss is early, FTD may lack this feature. FTD accounts for 10–15% of all dementias with Pick's disease as a subtype of FTD accounting only for 1% of dementias.

In FTD brain SPECT is an established diagnostic criterion. CBF changes are most pronounced in anterior half of the brain in contrast to AD, where a posterior half is involved (22, 23, 24). Frontal hypoperfusion may be however an unspecific finding as it can be met in schizophrenia (25), chronic alcohol abuse (26) or as parallel to multiple cerebral infarctions (27).

Progressive aphasia

In progressive aphasia patients present with progressive disorder of speech. Spontaneous speech is non-fluent and effortful, containing literal paraphasias. Word finding difficulty is one of most considerable phenomenons. Comprehension, although usually may be preserved, is eventually affected late in the disease progression. Visuospatial and motor function is usually preserved and neurological examination normal, sometimes showing frontal release phenomena. Brain CT is either normal or shows cortical atrophy of diverse degree (28).

SPECT findings in progressive aphasia are not entirely specific. Unilateral, left-sided posterior CBF decrease is considered to be the most frequent finding and significantly increases the odds of patient having progressive aphasia as opposed to other forms of dementia (29, 30).

Vascular dementias

Vascular diseases that may cause dementia include multiple cortical infarcts, single cortical infarct in strategic location (e.g. hippocampus) and small vessels disease (31). Those patients usually exhibit deficits in at least two cognitive domains indicative of cortical or subcortical dysfunctions (32). This may be accompanied by focal neurological signs suggestive of cerebrovascular disease such as hemianopia, dysarthria, hemisensory deficit, hemiparesis or Babinski sign. Brain CT shows multiple large vessels infarcts or multiple cortical infarcts and/or periventricular lucency.

The typical SPECT feature of multi-infarct dementia (MID) are asymmetrically distributed multifocal CBF deficits, also called „patchy” changes (30, 33). On one hand CT and MRI should play an essential role in identifying cortical infarcts because of better spatial resolution, on the other SPECT may prove superior in depicting multifocal cerebrovascular insufficiency, which was seen in patients with collagen tissue diseases (34), terminal renal lesion (35) and head trauma (36). MRI scanning may moreover detect white unspecific matter hyperintensities also in asymptomatic, healthy elderly people (37). For the differential diagnosis of neurodegenerative disease vs. vascular insufficiency may be useful stress test with acetazolamide, revealing areas of hypoperfusion not seen in baseline study and augmenting ones little visible in baseline study (38). In vascular dementia acetazolamide test reveals three-fold decreased reserve blood flow capacity in comparison with AD (39).

The crucial point in diagnosing multi-vascular lesion using SPECT scanning is the possibility of co-existence of cortical infarcts and neurodegenerative diseases, especially in older patients. Here fusion of SPECT/CT/MRI data may be a compromise leading to the correct diagnosis.

Reversible dementias

Reversible dementias is a group of disorders usually secondary to the other diseases either directly affecting the brain or with its extra-CNS localisation. This includes brain tumours, chronic subdural hematoma, communicating hydrocephalus, hepatic encephalopathy, chronic alcoholism, hypothyroidism, insulinoma, vitamin deficiencies, sarcoidosis, syphilis, giant-cells arteritis, chronic intoxications, adverse drug reactions. Some of those changes are hardly reversible, therefore „potentially reversible dementias” seems to be the more correct description. Also primary depressions may mimic dementia.

For most of those disorders frontal hypoperfusion is a marker. In primary depression also paralimbic hypoperfusion is a typical finding (40). In contrast to FTD CBF changes in depression may improve in course of therapy, whereas that of FTD worsens in time.

Follow-up CBF SPECT scanning in dementia

Follow up SPECT scanning may prove valuable in two situations: differentiation of neurodegenerative and vascular disorders, where SPECT changes usually are progressive (41) and cognitive disorders secondary to depression, where the treatment leads to perfusion improvement.

Synthesis

Perhaps the best neurologists’ point of view synthesis of the above was given by Talbot and co-workers in 1998 (30). They proposed the following approach: ^{99m}Tc-HMPAO SPECT is most useful in distinguishing Alzheimer’s disease from vascular dementia and fronto-temporal dementia; least useful in differentiating between Alzheimer’s disease and Lewy body disease; also least useful in differentiating between vascular dementia, fronto-temporal dementia and progressive aphasia. Therefore, in those authors opinion CBF SPECT should be used selectively and as adjunct to clinical evaluation and CT. As a summary of considerations given above the most typical CBF changes in dementia of diverse origin are showed in a table below (Table 1).

Conclusions

CBF SPECT provides a valuable contribution in the clinical differentiation of dementia. It provides information that is useful for the clinician in the interpretation of individual tests. CBF abnormalities are not specific to a single disease, so its role is an adjunct to clinical evaluation. However, due to its functional character CBF SPECT scanning usually provides more valuable information than CT and MRI and SPECT’s application in dementia is one of the most important aims in a routine work of nuclear medicine department.

Table 1. The most typical CBF changes in dementia of diverse origin

Type of dementia	CBF changes	Remarks
Alzheimer’s disease (AD)	hippocampal and temporo-parietal CBF deficit	changes may be vary in AD subtypes
Dementia with Lewy bodies (DLB)	global CBF decrease except posterior part of frontal lobes and occipital regions	may be difficult in differentiating with AD
Frontotemporal lobar degeneration (FTLD)	frontal and sometimes left temporal CBF decrease	frontal CBF decrease is not entirely specific for FTLD
Progressive aphasia	unilateral, left-sided posterior CBF decrease	some forms of AD may have similar CBF changes
Multi-infarct dementia (MID)	asymmetrically distributed multifocal CBF deficits	MID may coexist with the other forms of dementia

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