Imagerie cérébrale des pathologies psychiatriques vieillissantes

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Enjeux

• **Applications** de l’imagerie cérébrale dans l’évaluation des **cognitions** ?

• Applications de l’imagerie cérébrale dans l’évaluation des **comportements** ?

• Applications de l’imagerie cérébrale en **routine clinique** ?

• Applications de l’imagerie cérébrale en dehors des **théories localisatrices** ?
Schizophrénie

from the cellular to the systems levels. We will not discuss all of these connections, but rather focus on most salient circuits in the text and a series of simplified figures (Figs. 2–10) and their legends.

2.1. Prefrontal cortex anatomy

The prefrontal cortex is the region rostral to the motor and premotor cortices, receiving the cortical projection of the mediodorsal thalamic nucleus (MD), and is distinguished by a granular layer IV\(^51\). It is divided into 'limbic' and 'non-limbic' components, based on function, cytoarchitecture, limbic (e.g. amygdala) and MD connections\(^51–55\). As illustrated in Fig. 2, the 'dorsal' cortex is generally used with reference to Brodmann's areas (BA) 8, 9 and 10; the 'dorsolateral prefrontal cortex' generally refers to BA 46 and ventral part of BA 9, the lateral prefrontal cortex is dominated by the premotor and motor language cortices (BA 44, 45, 47), and the 'orbitofrontal' or 'orbital prefrontal cortex' (BA 11, 12) refers to the ventral region. The cortex on the medial surface includes the medial prefrontal cortex (BA 32) and the anterior cingulate region (BA 24 and 25).

MRI imaging studies have shown reduced gray matter volumes in the prefrontal cortex \(^56,57\), while cortical white matter defects have also been identified\(^56\). Using diffusion tensor imaging, Buchsbaum et al. \(^58\) found a significantly lower diffusion anisotropy in the frontal lobe white matter of schizophrenics, which coincided with a lower correlation coefficient for metabolic rates in frontal lobe and striatum, indicating fronto-striatal dysfunction. Such evidence suggests that events producing changes in cortical gray matter may also cause significant white matter morphological changes, and a functional disconnection or...
Graphical visualization of multimodal network hierarchy in healthy volunteers and people with schizophrenia. Nodes are ordered according to their degree (y-axis). Size of nodes indicates greater than (large) or less than (small) average clustering. Color of the nodes indicates lobe location: frontal (blue), temporal (green), parietal (black), or occipital (red). Lettering indicates approximate Brodmann area and the apostrophe ' denotes left sided regions.

Note that highly clustered nodes are concentrated at the bottom of the normal hierarchy which is dominated by highly connected nodes (many of them frontal) with low clustering; whereas in people with schizophrenia, highly clustered nodes are more evenly distributed in terms of their degree and frontal hubs are less prominent.
Symptômes négatifs

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Am J Psychiatry 161:1, January 2004

Brief Reports

http://ajp.psychiatryonline.org

and 15 men, three women), or chlorpromazine equiva-
lents (mean=496.3 [SD=351.7] and 421.6 mg [SD=293.5]).

They also had similar BPRS total scores (mean=44.5 [SD=
11.2] and 47.2 [SD=6.6]) and BPRS depression scores
(mean=1.9 [SD=1.3] and 1.8 [SD=1.3]). The high apathy
group had higher scores than did the low apathy group on
the SAPS (mean=10.5 [SD=3.3] versus 7.0 [SD=4.6]; t=2.69,
df=36, p=0.01) and SANS (mean=12.3 [SD=3.0] versus 5.8
[SD=3.3]; t=6.38, df=36, p=0.001). Healthy subjects were
comparable in age (mean=31.7, SD=8.7), WRAT reading
score (mean=102.4, SD=12.5), handedness (all were right-
handed) and sex (11 men, one woman).

A MANOVA that included all neuropsychological test
scores was significant (F=1.80, df=24, 72, p=0.03). Further
analyses revealed that the high apathy group scored lower
than comparison subjects on Trail Making Test Part A (F=
4.10, df=2, 47, p=0.02) and Part B (F=3.97, df=2, 47, p=0.03)
as well as the California Verbal Learning Test measures of
learning (F=5.95, df=2, 47, p=0.005) and delayed recall (F=
3.59, df=2, 47, p=0.04). The high apathy group also had
a lower performance IQ score than the low apathy and com-
parison groups (F=3.26, df=2, 47, p=0.04).

The high but not low apathy group showed significantly
reduced adjusted volumes relative to the healthy compar-
sion subjects in the right frontal lobe (high apathy group:
mean=195.7 [SD=19.6]; comparison subjects: mean=215.8
[SD=17.8]) (F=5.53, df=2, 47, p=0.007) and left frontal lobe
(high apathy group: mean=184.8 [SD=19.9]; comparison
subjects: mean=200.4 [SD=16.2]) (F=3.48, df=2, 47, p=0.04)
(Figure 1). The high apathy and low apathy schizophrenia
patient groups both had significantly smaller adjusted vol-
umes than did the comparison subjects in the right tem-
poral lobe (mean=107.5 [SD=6.0] and 111.7 [SD=6.2] ver-
sus 118.5 [SD=6.5], respectively; F=11.71, df=2, 47, p=
0.001) and left temporal lobe (mean=107.2 [SD=5.6] and
109.2 [SD=8.3] versus 118.8 [SD=8.0]; F=10.20, df=2, 47, p=
0.001). A similar but nonsignificant difference was noted
for adjusted left and right parietal lobe volumes. SAPS
score did not correlate with any of the dependent mea-
sures in the combined patient group.

Discussion

In this study, schizophrenia patients with high levels of
apathy had poorer visuomotor sequencing and verbal
learning and memory, lower performance IQ, and bilateral
frontal lobe volume reductions. In contrast, both patient
groups performed more poorly than comparison subjects
on psychomotor speed and naming, had lower verbal and
full-scale IQ scores, and showed bilateral temporal lobe
volume reduction, consistent with other studies of schizo-
phrenia (13). Lack of effort during testing is unlikely to ac-
count for these findings, since a generalized cognitive defi-
cit was not found in the high relative to low apathy group.

Findings were unrelated to level of depression or overall se-
vior of psychopathology. However, we cannot rule out the
possibility that differences in overall negative and positive

FIGURE 1. Adjusted Right and Left Frontal Lobe Volumes of Schizophrenia Patients With Low Versus High Levels of Apathy

and Healthy Comparison Subjectsa

a Apathy level classified by score on the SANS apathy subscale (low: score of 0 or 1; high: score ≥ 2).

Roth 2004
Vieillissement accéléré

Loss to specific brain regions. Figure 2A presents regions of significantly reduced gray matter volume in schizophrenia relative to comparison subjects (p < 0.05, family-wise error corrected). Brain regions with significant gray matter volume loss were evident in schizophrenia relative to comparison subjects at all ages. This loss was primarily circumscribed to frontal and temporal brain regions in early adulthood, gradually progressing to most cortical and subcortical areas with advancing age (Figure 2A). Areas most severely affected were the medial prefrontal cortex, hippocampus, and thalamus (see Movie 1 in the online edition of this article).

Figure 2B presents regions with a significantly faster rate of gray matter volume loss in schizophrenia relative to comparison subjects (p < 0.05, family-wise error corrected). The rate of gray matter volume loss was significantly faster in schizophrenia at ages 30–45 within the frontal, cingulate, temporal, occipital, and cerebellar cortices, as well as in the caudate nucleus and thalamus. Consistent with total gray matter volume, the rate of regional gray matter volume loss slowed beyond age 45 (Figure 2C) to levels that were not significantly different from those associated with healthy aging.

Fractional Anisotropy Total fractional anisotropy. The explanatory variables involving the square of age were not significant predictors of age-related changes in total fractional anisotropy.
FIGURE 2. Areas of Age-Related Gray Matter Volume Loss and Faster Rates of Loss in Schizophrenia Patients Relative to Healthy Comparison Subjects

Panel A presents cortical renderings of clusters of significantly reduced gray matter volume in schizophrenia patients relative to comparison subjects (p < 0.05, family-wise error corrected). Cortical renderings for seven different ages are shown, ranging from 25 to 55 years in increments of 5 years. Reduced gray matter volume was found in schizophrenia at all ages. Gray matter volume loss was primarily circumscribed to frontal and temporal regions in early adulthood, including the bilateral frontal pole, the superior and inferior frontal gyrus, the anterior cingulate gyrus, the left superior and inferior temporal gyrus, and the right middle temporal gyrus. The area of significant gray matter volume reduction expanded to the medial prefrontal cortex, all cortical regions of the temporal lobe, subcortical structures, and the inferior parietal cortex by middle age (30–40 years). In older age (40–60 years), gray matter volume loss progressed to encompass the cerebellum, and the magnitude of loss was increased across the cortex. At no age was there significantly increased gray matter volume in schizophrenia patients relative to comparison subjects.

Panel B presents areas where the rate of gray matter volume loss was significantly faster in schizophrenia relative to comparison subjects (p < 0.05, family-wise error corrected). The rate of gray matter volume loss was significantly faster in schizophrenia at ages 30–45 years. At age 30, this faster loss was focally localized to the right medial superior frontal gyrus, posterior cingulate gyrus, and lateral occipital cortex; it extended to include dorsal aspects of the right superior frontal gyrus and the right precuneus; and there was a bilateral extension to the head of the caudate, thalamus, gyrus rectus, inferior frontal gyrus, medial occipital, temporal, and cerebellar cortices by ages 35 and 40. Regions with significantly slower rates of gray matter volume loss in schizophrenia were not found.

To show regional variation in effect sizes, the color scale used to represent significant clusters is proportional to the voxel-specific t statistic for the between-group difference in gray matter volume ($\beta_2$) and the between-group difference in the rate of gray matter volume loss ($\beta_4$).
Montreal Neurological Institute used a small volume correction with a volume of interest sphere of 10 mm. A complementary analysis was performed using a routine that carries out a proportional scaling. The SPM (T) maps were smoothed by a Gaussian filter (full width at half maximum 12 mm). The schizophrenia and control groups were compared using the 'comparison' routine, which determines which areas were affected by the decreasing regional blood flow.

Decreased blood flow was observed in the bilateral frontal lobes (the right inferior frontal gyrus, the left inferior frontal gyrus, the right sublobar extranuclear white matter) in controls. Moreover, step-wise multiple regression analysis was used to determine which areas were affected by the decreasing regional blood flow (rCBF) in schizophrenia. The correlation between age and rCBF change in the bilateral temporal lobes, which are related to age, was investigated using a step-wise multiple regression analysis. The results showed that age was correlated with rCBF change in the bilateral temporal lobes.

Statistics were performed using Matlab or SPSS. The graphs in Figure 3 showed adjusted response changes in perfusion of bilateral temporal lobes, which were related to age. The correlation between age and rCBF change in the bilateral temporal lobes was investigated using step-wise multiple regression analysis. The correlation between age and rCBF change in the bilateral temporal lobes was investigated using step-wise multiple regression analysis.
Effet de l’âge

N=100 (n=49 schizophrènes)
Âge moyen = 49 ans (SD=18)

Hippocampe droit et gauche
Troubles bipolaires

ORIGINAL ARTICLE
Cortical abnormalities in bipolar disorder: an MRI analysis of 6503 individuals from the ENIGMA Bipolar Disorder Working Group
We examined the effects of five major drug families (lithium, antiepileptics, antidepressants, atypical and typical antipsychotics) on cortical thickness and surface area in BD patients. Our statistical model accounted for different drug combinations across individuals. In adults and adolescents/young adults, treatment with lithium or antiepileptics showed significant evidence of effect on cortical thickness (whereas lithium was positively associated with cortical thickness, antipsychotics showed a negative relationship). Prior studies of these medication types found a similar pattern of effects on surface area and thickness throughout the brain.9–13 The increased cortical thickness associated with lithium treatment is hypothesized to be driven by a neurotrophic effect of lithium on the brain.
Troubles bipolaires et DFT

Hippocampal and amygdala volumes in an older bipolar disorder sample

Table 1. Demographic and clinical characteristics of bipolar disorder and healthy control groups

<table>
<thead>
<tr>
<th>BIPOLAR DISORDER GROUP (N = 18)</th>
<th>CONTROL GROUP (N = 21)</th>
<th>STATISTICS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>57.0 (9.9)</td>
<td>t = 1.21</td>
<td>0.232</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>6 (33%)</td>
<td>χ² = 3.17</td>
<td>0.075</td>
</tr>
<tr>
<td>Education (years)*</td>
<td>13.1 (3.9)</td>
<td>t = 0.67</td>
<td>0.509</td>
</tr>
</tbody>
</table>

Table 3. Hippocampal and amygdala volumes of bipolar disorder and healthy control groups, according to time since onset and duration of mood episodes

<table>
<thead>
<tr>
<th>REGION OF INTEREST</th>
<th>TIME SINCE FIRST EPISODE DEPRESSION</th>
<th>TIME SINCE FIRST EPISODE MANIA</th>
<th>DURATION OF ALL DEPRESSIVE EPISODES</th>
<th>DURATION OF ALL MANIC EPISODES</th>
<th>DURATION OF ALL MOOD EPISODES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
<td>p</td>
<td>R</td>
<td>p</td>
<td>R</td>
</tr>
<tr>
<td>Hippocampus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>−0.240</td>
<td>0.477</td>
<td>−0.509</td>
<td>0.110</td>
<td>−0.664</td>
</tr>
<tr>
<td>Right</td>
<td>−0.253</td>
<td>0.453</td>
<td>−0.557</td>
<td>0.075</td>
<td>−0.493</td>
</tr>
<tr>
<td>Total</td>
<td>−0.269</td>
<td>0.424</td>
<td>−0.581</td>
<td>0.061</td>
<td>−0.636</td>
</tr>
<tr>
<td>Amygdala</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>−0.268</td>
<td>0.426</td>
<td>0.135</td>
<td>0.693</td>
<td>0.178</td>
</tr>
<tr>
<td>Right</td>
<td>0.217</td>
<td>0.521</td>
<td>0.348</td>
<td>0.294</td>
<td>0.417</td>
</tr>
<tr>
<td>Total</td>
<td>−0.064</td>
<td>0.853</td>
<td>0.250</td>
<td>0.458</td>
<td>0.310</td>
</tr>
</tbody>
</table>

Hippocampal and amygdala volumes are measured in mm³; values are mean (SD).
Combined analysis of grey matter voxel-based morphometry and white matter tract-based spatial statistics in late-life bipolar disorder

Table 1: Demographic and clinical characteristics of patients with bipolar disorder and healthy controls

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group; mean (SD)*</th>
<th>Z/χ²</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bipolar disorder, n = 19</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control, n = 47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>68.53 (5.89)</td>
<td>–0.60</td>
<td>0.55</td>
</tr>
<tr>
<td>Sex, % women</td>
<td>74</td>
<td>4.47</td>
<td>0.034</td>
</tr>
<tr>
<td>Education, no. yr</td>
<td>15.00 (3.99)</td>
<td>–0.58</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>13.23 (3.52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GDS score (max 15)</td>
<td>1.53 (1.65)</td>
<td>–0.01</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>1.40 (1.42)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>YMRS score (max 44)</td>
<td>0.95 (1.43)</td>
<td>–3.89</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>0.06 (0.32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCI score (max 19)</td>
<td>0.79 (0.71)</td>
<td>–1.50</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>0.55 (0.85)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at onset of illness, yr</td>
<td>39.37 (15.26)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Unless otherwise indicated.

Table 2: Neuropsychologic test results of patients with bipolar disorder and healthy controls

<table>
<thead>
<tr>
<th>Neuropsychologic measure; test</th>
<th>Group; mean (SD)*</th>
<th>t/Z</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control, n = 47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Processing speed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple reaction time latencies, msec²</td>
<td>339.92 (73.67)</td>
<td>–2.26</td>
<td>0.027</td>
</tr>
<tr>
<td>Working memory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letter–Number Sequence score²</td>
<td>7.89 (2.69)</td>
<td>3.89</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Episodic memory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48-item cued recall score⁴</td>
<td>22.95 (5.958)</td>
<td>3.06</td>
<td>0.003</td>
</tr>
<tr>
<td>CERAD 10-word total recall score⁶</td>
<td>18.84 (4.729)</td>
<td>3.75</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Executive function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flexibility</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colour Trail Making Test relative ratio score</td>
<td>1.04 (0.58)</td>
<td>–0.23</td>
<td>0.82</td>
</tr>
<tr>
<td>Inhibition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroop Colour relative ratio score</td>
<td>0.27 (0.09)</td>
<td>–0.59</td>
<td>0.56</td>
</tr>
<tr>
<td>Updating</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consonant updating</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 updating cost</td>
<td>–0.22 (0.22)</td>
<td>1.82</td>
<td>0.07</td>
</tr>
<tr>
<td>4 updating cost</td>
<td>–0.15 (0.28)</td>
<td>0.48</td>
<td>0.63</td>
</tr>
</tbody>
</table>

CERAD = Consortium to Establish a Registry for Alzheimer’s Disease; SD = standard deviation.
Combined analysis of grey matter voxel-based morphometry and white matter tract-based spatial statistics in late-life bipolar disorder

Table 1: Demographic and clinical characteristics of patients with bipolar disorder and healthy controls

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<td>0.55</td>
</tr>
<tr>
<td>Sex, % women</td>
<td>74</td>
<td>χ² = 4.47</td>
<td>0.034</td>
</tr>
</tbody>
</table>

Group: bipolar disorder, n = 19; Control, n = 47

<table>
<thead>
<tr>
<th>Education, no. yr</th>
<th>13.00 (3.59)</th>
<th>13.23 (3.32)</th>
<th>0.95 (1.43)</th>
<th>0.06 (0.32)</th>
</tr>
</thead>
</table>
| CCI = Charlson Comorbidity Index | 41 score between patients with bipolar disorder.6–13 However, results show that in elderly patients, this involvement mainly concerns the ventrolateral prefrontal, anterior cingulate, temporal and ventral striatum.3–7 Voxel-based morphometry (VBM), a fully automated image analysis of the whole brain that is free from the observer’s viewpoint by reusing the spatial transformation parameters that were estimated in the initial fractional anisotropy analysis.

White matter TBSS analysis of DTI data

- Longitudinal (also known as axial diffusion and mean diffusivity values between groups using non-parametric statistics in late-life bipolar disorder.

- The TBSS analysis of the DTI data was also performed with White matter TBSS analysis of DTI data.

- The additional ROI analyses reusing the spatial transformation parameters that were estimated in the initial fractional anisotropy analysis.

- These differences persisted after controlling for medication effect (data not shown).

- The MRI involvement of the white matter is pronounced in the right inferior frontal gyrus and, to a lesser degree, in the right precentral gyrus, left medial frontal gyrus and ventrolateral prefrontal, anterior cingulate, temporal and ventral striatum.3–7 Voxel-based morphometry (VBM), a fully automated image analysis of the whole brain that is free from the observer’s viewpoint by reusing the spatial transformation parameters that were estimated in the initial fractional anisotropy analysis.

- Severe white matter abnormalities in patients with bipolar disorder and either VBM or DTI data.

- Regarding medication, 79% of patients received mood stabilizers, 26% received antidepressants, 37% received benzodiazepines and 26% received neuroleptics. In 15% of patients, reported a reduced grey matter co-activation of brain networks containing the anterior cingulate, amygdala, thalamus and ventral striatum.3–7 Voxel-based morphometry (VBM), a fully automated image analysis of the whole brain that is free from the observer’s viewpoint by reusing the spatial transformation parameters that were estimated in the initial fractional anisotropy analysis.

- Severe white matter abnormalities in patients with bipolar disorder and either VBM or DTI data.

- Previous magnetic resonance imaging (MRI) studies in young patients with bipolar disorder indicated the presence of grey matter changes that affect the anterior limbic network, including the prefrontal cortex, subgenual anterior cingulate cortex, anterior hippocampus, amygdala, thalamus and ventral striatum.3–7 Voxel-based morphometry (VBM), a fully automated image analysis of the whole brain that is free from the observer’s viewpoint by reusing the spatial transformation parameters that were estimated in the initial fractional anisotropy analysis.

- In contrast to traditional ROI analyses, our ROIs were not derived parameters — longitudinal (also known as axial diffusion and mean diffusivity).
Atesci Figen Culha · Ozdel Osman · Yuksel Dogangün · Karadag Filiz · Kırac Suna Öguzhanoglu Nalan Kalkan · Varma Gulfizar · Akdağ Beyza

Changes in regional cerebral blood flow demonstrated by $^{99m}$Tc-HMPAO SPECT in euthymic bipolar patients

Abstract Single photon emission computed tomography (SPECT) with $^{99m}$Tc-HMPAO was used to compare regional cerebral blood flow (rCBF) in patients with bipolar disorder and in healthy controls. The sample of this study consisted of 16 euthymic bipolar patients who met the DSM-IV criteria and 10 healthy control subjects. The mean regional cerebral blood flow values of the bipolar euthymic patients were significantly lower than those of the controls in the bilateral medial-basal temporal, occipital; medial frontal; parietal regions and in the cingulate gyrus; the hypoperfusion in the cingulate had the highest significant $P$ value (.001, Bonferroni correction). No significant differences in rCBF emerged between right and left-brain regions. The most important findings of

10 patients Vs 16 VS
Age moyen = 32 ans !!!
Neuroimaging Findings in Late-Onset Schizophrenia and Bipolar Disorder

Changtae Hahn, MD, PhD¹, Hyun Kook Lim, MD, PhD²,³, and Chang Uk Lee, MD, PhD¹

10 études Late-Onset Vs Early-Onset Scz
• Atrophie hippocampus
• Atrophie de l’amygdale
• Pas de différences
• +WMH
• ➔ Perfusion lobe frontal et temporal

10 études Late-Onset Vs Early-Onset BP
• Atrophie générale
• + WMH
• + AVC inaperçu

Pas de spécificités robustes
Dépression & Démence

Da Silva 2013; Diniz 2014

Fig. 6 Forest plot of studies that evaluated bipolar disorder as a risk factor for dementia or Alzheimer’s disease.
Depression as a prodromal state of AD

Geriatric depression

MCI + BPSD/ "Mild Behavioural Impairment" MBI?

ASAP Study: ongoing
ClinTrials NCT01962753

Perspective

Neuropsychiatric symptoms as early manifestations of emergent dementia: Provisional diagnostic criteria for mild behavioral impairment

Zahinoor Ismaiel, Eric E. Smith, Yonas Geda, David Sultzer, Henry Brodaty, Gwenn Smith, Luis Agüera-Ortiz, Rob Sweet, David Miller, Constantine G. Lyketsos.
PET imaging of Amyloid in depression

- Traceur : FDDNP
- Effectif:
  - 20 MDD 67.5 ± 8 years
  - 19 HC 66.5 ± 6 years

Kumar: Arch Gen Psych 2011 (68): 1143-1150
PET imaging of Amyloid in depression

- Tatano *Int J Ger Psych* 2015;30 (7)720-728

- Wu *JNNMI* 2016; 43: 1067-1076
Dépressions récurrentes

FIGURE 1. Relationship Between Hippocampal Volume and Days of Untreated Depression in 38 Female Outpatients With Recurrent Depression in Remission

FIGURE 1. Model of Treatment Response in Late-Life Depression

- Genetics
- Stress
- Resiliency

Vascular risk factors
White matter hyperintensities

Late-Life Depression

Cognitive Processing Speed
- Episodic Memory
- Executive Function
- Language Processing

Depression severity
- Slow
- Fast

Time

In this model, the predictor variables for late-life depression are shown as stress and genetics, with resilience as a protective factor, modified by Framingham vascular risk factors and white matter hyperintensity severity. This is not meant to be an exclusive list; other factors, such as baseline depression severity, clearly influence antidepressant response. Furthermore, in some samples, late-life depression can be confounded by dementia. Not shown are the covariates in the model—age, age at onset, education, gender, depression severity, and race.

Late-life depression is associated with smaller hippocampal volumes and slower cognitive processing speed. Within cognitive processing speed are subsumed executive function, episodic memory, and language processing. Together, smaller hippocampal volume and slower cognitive processing speed predict a slower rate of response to antidepressant treatment.

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Sheline 98, 03 & 12
Increased levels of glucocorticoids → Hippocampal atrophy

Increased levels of amyloid plaques

Depression

Proinflammatory changes

Vascular disease

Alterations in nerve growth factors

Frontostriatal abnormalities

Dementia

Increased levels of glucocorticoids → Depression

Vascular disease → Depression

Depression → Proinflammatory changes

Proinflammatory changes → Dementia

Depression → Increased levels of amyloid plaques

Increased levels of amyloid plaques → Dementia

Depression → Alterations in nerve growth factors

Alterations in nerve growth factors → Dementia

Depression → Frontostriatal abnormalities

Frontostriatal abnormalities → Dementia
RESULTS

Group Differences in Hippocampal Volume and Amyloid Pathology

Hippocampal volume was normally distributed, whereas SUVRcomp values (Figure 3).

To examine an association with APOE genotype, we applied such that p values for multiple comparisons, a Bonferroni correction was applied.

Secondary analyses in patients.

There was no association between total hippocampal volume and white matter hyperintensity volume in either patients or comparison subjects.

The hippocampal volume difference could be attributed to a group difference in the distribution or median amyloid load.

Association between amyloid binding, hippocampal volume, and white matter hyperintensities, hippocampal volume, and amyloid binding.

To examine potential associations between clinically relevant factors, hippocampal volume, and amyloid binding, we performed a series of exploratory MANCOVA analyses and partial correlations controlling for age. To control for multiple comparisons, p values for multiple comparisons, a Bonferroni correction was applied.

Tables and figures summarize characteristics, APOE genotype, cognitive and clinical characteristics, and imaging data.

Association between APOE genotype, amyloid binding, and hippocampal volume.

To investigate any associations relevant to patients or comparison subjects.

Secondary analyses in patients.

There were no statistically significant associations between

- APOE genotype
- Amyloid binding
- Hippocampal volume

Characteristics, APOE genotype, cognitive and clinical characteristics, and imaging data are summarized in Table 1.

Association between white matter hyperintensities, hippocampal volume, and amyloid binding.

Toward amyloid-negative patients.

There were no statistically significant associations between

- APOE genotype
- Amyloid binding
- Hippocampal volume

Characteristics, APOE genotype, cognitive and clinical characteristics, and imaging data are summarized in Table 1.

Association between white matter hyperintensities, hippocampal volume, and amyloid binding.

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Association between white matter hyperintensities, hippocampal volume, and amyloid binding.
Conclusion

• Imagerie de la PPA = Imagerie des troubles psycho-comportementaux = Imagerie en psychiatrie=.....

• .... Pas d’application en routine clinique à visée diagnostique

• Perspectives
  – Apprentissage par machine : converters Vs non converters.
  – Réponse thérapeutique.
Neuro-imagerie des pathologies psychiatriques vieillissantes

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