Disturbance of sensory filtering in dementia with Lewy bodies: comparison with Parkinson’s disease dementia and Alzheimer’s disease

M-P Perriol, K Dujardin, P Derambure, A Marcq, J-L Bourriez, E Laureau, F Pasquier, L Defebvre, A Destée

Introduction: Prepulse inhibition (PPI) is considered to mirror an organism’s ability to filter out irrelevant sensory or cognitive information. The disruption of PPI has never been studied in individuals suffering from dementia with Lewy bodies (DLB). As attention deficits largely contribute to cognitive impairment in DLB, an investigation with a PPI paradigm is useful for differential diagnosis of DLB versus Alzheimer’s disease (AD) and Parkinson’s disease dementia (PDD).

Objective and methods: PPI of the N1/P2 component of auditory evoked potentials was used to investigate the early stages of attention selectivity in 10 DLB, 10 AD, and 10 PDD patients, as well as in 10 healthy controls. The PPI paradigm consisted of the presentation of sound pulses (40 ms, 115 dB) preceded by a prepulse (40 ms, 80 dB). Sound stimuli were presented in a total of 80 trials in a pseudo-random order.

Results: Non-parametric analyses of variance revealed a significant group effect on the 120 ms lead interval. Retrospective analyses revealed that PPI was significantly reduced in DLB compared to healthy controls and AD. In the PDD group, the disturbance was of intermediate intensity.

Conclusion: The present study revealed a severe disturbance of PPI in DLB patients. The DLB patients displayed a specific disruption profile in terms of magnitude as well as time course.

The ‘startle response’ to an intense acoustic stimulus is attenuated when a weaker, non-startling stimulus or ‘prepulse’ precedes the startle eliciting stimulus. Prepulse inhibition (PPI) — is also observed for cortical responses, such as the N1/P2 component of the auditory evoked potential (AEP). PPI is considered to reflect an organism’s ability to ‘gate out’ or ‘filter out’ sensory or cognitive information, and is thought to reflect an automatic, pre-attentive inhibitory process whereby irrelevant stimuli are prevented from influencing ongoing behaviour.

It has been shown that PPI disruption is related to cognitive impairment in schizophrenia and in several basal ganglia disorders. Studies focusing specifically on neuro-psychological performance in dementia with Lewy bodies (DLB) have generally considered that attention deficits contribute significantly to fluctuating cognition and visual hallucinations, which are core criteria for clinical diagnosis of DLB along with extrapyramidal signs. These findings thus prompted us to investigate such deficits with the PPI paradigm, which does not require deliberate participation by the subject and thus rules out difficulties related to misunderstanding of the task instructions by demented patients. In contrast to numerous clinical tests, the PPI paradigm does not use visuospatial stimuli thereby preventing contamination of the results by the visuoperceptive disruption very commonly observed in these patients. Finally, the PPI paradigm enables study of the attention processes on which more elaborated cognitive processes are based.

It has been shown that the amplitude of the startle reflex decreases with age even though PPI remains constant; however, this can constitute a methodological limitation for the use of the PPI paradigm in aged subjects, because the lower the basal amplitude of the startle reflex the more difficult it is to detect further reductions. This age related amplitude reduction also concerns the AEP components, although here the signal to noise ratio remains high. Consequently, PPI of the AEP N1/P2 components can be considered as a better index for observations in elderly subjects.

Here, PPI of the AEP N1/P2 component was used to investigate the early stages of attention selectivity in DLB, Parkinson’s disease dementia (PDD), and Alzheimer’s disease (AD).

METHODS
Participants
Ten DLB, 10 PDD, and 10 AD patients participated in the study. The three groups were matched with respect to their score on the Mattis dementia rating scale (Mattis DRS) for assessing dementia severity. Ten healthy control subjects (matched to the patients with respect to age and educational level) also participated in the study. The characteristics of the four groups are presented in Table 1.

PPI paradigm
A typical PPI paradigm was used. Eighty sequences of sound stimuli (white noises gated to near instantaneous rise/fall time) were binaurally presented through headphones (Telephonics, TDH 39P). They consisted of 40 ms presentations of a 115 dB pulse (pulse alone trials) or 40 ms presentations of a 80 dB prepulse occurring 60, 120, or 300 ms prior to a 40 ms, 115 dB pulse (prepulse/pulse trials). All trial types were presented a total of 20 times but in a pseudo-random order. The inter-trial interval varied between 15 and 25 s (mean = 20 s). The stimulus sequence was

Abbreviations: AD, Alzheimer’s disease; AEP, auditory evoked potential; DLB, dementia with Lewy bodies; EEG, electroencephalogram; EOG, electro-oculogram; PDD, Parkinson’s disease dementia; PPI, prepulse inhibition
Disturbance of sensory filtering in DLB: comparison with PPD and AD

There was no significant group effect on the mean N1/P2 component measured at Cz, and the amplitude of the N1/P2 component was defined as the largest positive deviation from baseline in a 130–300 ms window following presentation of the pulse stimuli. The peak N100 and P200 values were measured at Cz, and the amplitude of the N1/P2 component was then computed.

The N100 component was defined as the largest negative deviation from baseline in a 80–200 ms window following presentation of the pulse stimuli, whereas the P200 component was defined as the largest positive deviation from baseline in a 130–300 ms window following presentation of the pulse stimuli. The peak N100 and P200 values were measured at Cz, and the amplitude of the N1/P2 component was then computed.

The percent PPI of the N1/P2 component was calculated using the following formula:

$$100 \times \left( \frac{\text{response amplitude in the pulse alone trials} - \text{response amplitude in the prepulse/pulse trials}}{\text{response amplitude in the pulse-alone trials}} \right)$$

### RESULTS

Kruskall-Wallis non-parametric analyses of variance revealed no significant group effect on the mean N1/P2 component amplitude ($H_{(3)} = 4.80$, $p = 0.187$) but a significant group effect on the %PPI at a 120 ms prepulse/pulse interval ($H_{(3)} = 12.57$, $p = 0.005$). There was no significant group effect on %PPI at the two other intervals (60 ms: $H_{(3)} = 3.23$, $p = 0.358$; 300 ms: $H_{(3)} = 5.41$, $p = 0.144$). At the 120 ms prepulse/pulse interval, retrospective analyses revealed that the %PPI was significantly reduced in DLB ($p = 0.002$) and PDD ($p = 0.017$) patients compared to healthy control subjects. In AD patients, there was a trend towards a significant reduction ($p = 0.058$). Comparison of the patient groups revealed a significantly reduced %PPI in DLB patients compared to AD patients ($p = 0.031$). The other comparisons were non-significant.

When plotting the mean %PPI for each group as a function of the prepulse/pulse interval (fig 1) the usually seen pattern (an inverted U curve) was observed: in every group, %PPI was the highest at the 120 ms interval and decreased at shorter and longer prepulse/pulse intervals. At the 120 ms interval, disruption of the PPI phenomenon varied among the three groups: AD patients showed a slightly reduced %PPI, this was more pronounced and reached the significance level in PDD patients, but the reduction was clearly most severe in DLB patients.

Even though there was no significant group effect at the other prepulse/pulse intervals, it is interesting to underline that at the 60 ms interval, the %PPI was reduced in the DLB patients compared to the three other groups (within which it was very similar). At very short intervals, DLB patients are thus the only group in which the phenomenon is already disturbed. With the 300 ms interval there was no observable PPI in the DLB and PDD groups, although AD patients showed a %PPI very close to that observed in the healthy controls.

### DISCUSSION

The present study uses a functional approach to show a severe disturbance of attention filtering in DLB patients. The usual attenuation of the cortical response to an intense sound when a ‘prepulse’ precedes this unexpected and intense
stimulus is no longer observed thus reflecting a loss of the ability to inhibit irrelevant information. This type of impairment was also observed in PDD patients but was less severe. In AD patients sensory gating appeared to be maintained (despite similar severity of cognitive degradation), because only a trend towards PPI reduction was observed at the 120 ms prepulse/pulse interval—that is, when the phenomenon is maximal in healthy controls. In fact, DBL patients displayed a specific PPI disruption profile in terms not only of magnitude but also time course, which suggests that several processes could be impaired. Indeed, according to Dawson et al., PPI is considered as an automatic involuntary phenomenon when prepulse/pulse intervals are shorter than 120 ms thus reflecting exogenous attention. When prepulse/pulse intervals are longer than 120 ms, PPI is considered as reflecting the involvement of attention processes. On this basis, both involuntary and attention-selective processes appear to be impaired in our DBL patients, although the impairment seemed only to concern attention-selective processes in PDD patients.

Using a similar paradigm, Golob et al. suggested that declines in cortico-cortical processing might cause cognitive impairment in patients with AD and mild cognitive impairment because sensory gating phenomenon was observed only when presenting stimulus pairs in different modalities (visual/auditory) and not for stimulus pairs having the same modality (auditory/auditory). In the present study (using auditory stimulus pairs), we reported PPI disruption in DBL and PDD patients although the phenomenon was relatively unchanged in AD patients. This suggests i) involvement of the dopaminergic subcortico-thalamo-cortical networks in PPI regulation and ii) more severe disruption of these networks in DBL than in PDD.

Because this study was an initial approach to gauging the utility of PPI for comparing attention disorders in DBL, PDD, and AD, we only included patients who met as many diagnosis criteria as possible. Consequently, the disease was already quite severe, which constitutes an important limitation because all patients received medication. Furthermore, for ethical reasons, treatments were not discontinued during the recording. It would be of great interest to investigate PPI disruption in newly diagnosed untreated patients in order to better assess the diagnostic value of the impairment observed here.

ACKNOWLEDGEMENTS

The authors thank N El Massioumi (NAMC, UMR 8620, CNRS, Orsay, France) for her help in setting up the PPI paradigm.

REFERENCES

Disturbance of sensory filtering in dementia with Lewy bodies: comparison with Parkinson's disease dementia and Alzheimer's disease

M-P Perriol, K Dujardin, P Derambure, A Marcq, J-L Bourriez, E Laureau, F Pasquier, L Defebvre and A Destée

J Neurol Neurosurg Psychiatry 2005 76: 106-108
doi: 10.1136/jnnp.2003.035022

Updated information and services can be found at:
http://jnnp.bmj.com/content/76/1/106

These include:

References
This article cites 17 articles, 7 of which you can access for free at:
http://jnnp.bmj.com/content/76/1/106#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

- Dementia (995)
- Memory disorders (psychiatry) (1360)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/