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Contingent Negative Variation in Dementia

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Abstract

The Contingent Negative Variation (CNV) is a slow DC shift seen over the scalp during states of anticipation. The present investigation is an attempt to study the differences in the CNV between patients with dementia and the normal controls. The sample consisted of 8 patients with dementia, of which 4 had cortical atrophy and 4 had subcortical atrophy and 8 age and gender-matched normal subjects. CNV and auditory evoked potentials (AEP) were recorded on a Biologic Topographic Mapping System. Results indicated that in normals a typical topographic distribution of early and late components of CNV show greater amplitudes in the anterior and central electrodes. Of the 8 dementia patients, 4 patients with subcortical atrophy and 2 with cortical atrophy showed only early component. All the patients showed the NI component and there was no significant difference in the latency compared with the normal controls. However, significant amplitude reduction was noticed in the patients.

Key words -
Dementia,
Contingent negative variation,
Auditory evoked potentials

Contingent negative variation (CNV) is a slow surface negative electrical activity which was first reported by Walter [1]. The basic experimental paradigm for generating CNV is that of a constant preperiod reaction time task. It involves the presentation of a warning stimulus (S1), followed by an imperative stimulus (S22), to which a motor response by the subject is usually required. CNV appears within the S1-S2 interval as a negative DC shift rapidly appearing after the S1 and normalising after the S2.

Earlier workers considered CNV as a unitary phenomenon, while the two component hypotheses viewed a nearly component as the 'orienting response' and a second component as the 'terminal CNV, [2], [3], [4]. This hypothesis initiated studies of psychological constructs like attention, arousal, motivation, anticipated energy output, conation, orientation, expectancy, preparation for action and heightened state of attentiveness, using CNV. CNV has been found to be associated with a complex psychological process of anticipation or expectation which depend on factors as sensory registration and attentional arousal [5], [6], [7], [8]. These findings led to an array of research on brain lesion patients [9], [10], [11]. It was found that CNV was undetectable when thalamus was destroyed. Further, a significant difference

between normals and psychosurgery patients was found in the frontal and central regions and a near significant difference at the temporal regions [12]. It was, hypothesized that the first component was mediated by frontal cortex while the second component was associated with the central and parietal area. The frontal lobe lesion patients, might show inability to control the first component, but not the second [13]. In 30 alcohol dependent patients, 14 patients were found to produce significantly weaker CNV, the early component was found absent in 13 patients whereas the late component was not seen in 3 patients [14]. Studies on elderly subjects and dementia patients have revealed lower CNV amplitudes and this relationship was found stronger as the severity of dementia increased [15], [16], [17].

In dementia, the results of CNV was found capable of making an important contribution to the assessment and course of dementia [17]. The present study, therefore, was conducted to see what differences are present between the dementia patients and age matched normals and to understand the implications of differences in cortical and subcortical dementias. Other than CNV an Auditory Evoked Potential (AEP) was recorded to elicit the N1 component which is associated with arousal of attention [18], [19], [20]. The N1 component is found to represent a widespread activation of the frontal cortex during auditory stimulation.

Methodology

Sample:

The sample consisted of 8 dementia patients (ICD-10), 4 with cortical atrophy (Group 1) and 4 with subcortical atrophy (Group 2) on the basis of CT scan, detailed neurological examination and neuropsychological assessment. The severity ranged from mild to moderate degree in terms of activities of daily life. Patients suffering from psychiatric illnesses, particularly psychoses, head injury, epilepsy and those who had history of habitual alcohol consumption were not included. A normal group, numbering 8, matched for age and gender (6 male and 2 female subjects) were taken as the control. The age ranged from 25 to 70 years with a median age of 56.5 years for the patients and from 25 to 69 years with a median of 55.5 years for the control group. The difference between the age of the patients and the matched control subjects did not exceed by more than one year. The educational status ranged from uneducated to college education and the control subjects were individually matched for years of education and age with that of the patients.

Tools:

To screen the control group for psychiatric morbidity General Health Questionnaire [21] was used. After neurological examination and CT scan, a Neuropsychological Battery [22] and Dementia Scale [23] were administered to the dementia patients to assess the nature and severity of the illness.

Recording was carried out using a Biologic Brain Topography Mapping System. Nineteen electrodes with linked mastoids of the 10-20 system [24] were used for recording. An electro-cap was used for picking up bioelectric activity. The amplifiers were set to high pass filter of 0.01 Hz and low pass filter of 30 Hz. The Brain Atlas was set for recording the CNV by using the analysis length of 4090 ms of which 1000 ms was used as a negative delay. The gain of the amplifiers were set to reject epochs with amplitudes greater than 30 microvolt in any channel using the A/D artifact rejection programme. The Nihon Kohden stimulus generator SMP4100 auditory / visual generator was used to present the stimuli required to elicit the CNV and the AEP. The warning stimulus was a click at 80 dB and the imperative stimulus was LED flash at 10 Hz. The interval between the two stimuli was 2 sec and the subject was instructed to press to key with the preferred hand which switched off the LED flashes. The number of epochs collected were 50. The intertrial interval was 3 see with a random variation of 20%. the AEP

was recorded using a high pass filter of 0.1 Hz and low pass filter of 70 Hz. the auditory stimulus was a tone burst of 1000 Hz and of 50 ms duration with 10 ms rise and fall time. The tone intensity was 80 dB presented through a pair of earphones at intervals of 2 sec with 20% random variation to the subject who remained with eyes closed. Sixty epochs were collected which were averaged by the Brain Atlas using an analysis length of 1024 ms. The tests were carried out in a sound treated experimental room wherein the subject sat comfortably in a reclining chair.

Results

The neuropsychological assessment on the patients showed significant memory problem in the subcortical dementias whereas memory disturbance was relatively less acute in the cortical dementia patients. Memory impairment was reported by these patients as severe delayed recall impairment in neuropsychological tests. The latter group of patients had severe visuo-spatial, verbal and visual memory (immediate) and learning difficulties and working memory deficits. Their delayed recall performance was relatively better than that of the noncortical lesion patients. In the cortical lesion patients though memory impairment was present as reported by the informant the same was not reported by the patients. In terms of severity on the Dementia Rating scale, they were of mild to moderate nature and all patients could comprehend and respond to simple instructions.

The CNV components were identified as early and late and the amplitude was the maximum amplitude reached in the first half and the second half of the 2 sec interval between the two stimuli. All patients except two cortical dementia cases produced the early CNV component, whereas the late component was seen only in two subcortical dementia patients. thus for statistical analysis only the early component was considered (Table I). For AEP, the amplitude (Table II) and latency of N1 was analyzed. the mean latency of N1 of all the electrode leads taken together in the dementia and the normal groups were 96.5 ms (sd=12.7) and 105.6 ms (sd=14.6) indicating no significant differences between the mean values. The difference between mean amplitudes at the F3, FZ, F4, C3, CZ, C4, P3 PZ and P4 electrode positions were statistical compared using "t" test and is shown in Table II.

Table I - Mean amplitude (in microvolt) and SD of early component of CNV in subcortical damaged patient group and normal control group

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D: Dementia group
N: Normal group

Table II - Mean amplitude (in microvolt) and SD of N1 component of AEP in dementia patient group and normal control group

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.Grand average at CNV in - (a) subcortical - (b) cortical dementia and - (c) normal control groups

Discussion

The results show that patients with cortical dementia have shown poorly developed CNV and the early component could be detected only in two patients in whom the late component could not be identified. The other two patients did not have recognizable CNV components. The subcortical dementia patients produced a well formed CNV and the mean amplitude was comparable with that of the normal controls. The normal control subjects produced well formed CNV with the early and the late components prominently appearing. The AEP study showed a significant amplitude reduction of the N1 component in the patient group as a whole. there was no evidence of a latency difference of N1 in the patients compared to the controls.

The N1 has been identified as an attentional component and its amplitude reduction indicates reduced attentional allotment. But there is no significant difference between the N1 amplitudes between the group 1 and group 2 patients. That the Group 2 patients have produced early CNV components comparable to the normal controls show that the CNV is dissociated with the N1 or the passive attentional arousal indicated by it. The CNV appears to be related to a distinct state of anticipation or expectation involving directed attention, which is different from passively attending to a stimulus as in the case of the AEP paradigm. The wide spread neural activation of the early component of CNV in the frontal, central and parietal areas seen in normal subjects was absent in the Group 1 patients whereas it was evident in the Group 2 patients. With respect to the late component, in both the patient Groups, there is found to be significant abnormality. The group 1 patients have not produced the late component at all, where as highly reduced late components are seen in two of the Group 2 patients. The late component could be also influenced by the readiness potential because the task demand involved pressing a key to the presentation of the second stimulus. However the key was to be pressed only after the onset of the stimulus and the response terminated the stimulus. Thus though the subject could have remained prepared to receive the second stimulus, the actual need to respond has arisen only after the stimulus appeared. The readiness potential thus could have overlapped with the negative shift present prior to the onset of the second stimulus. The dementia patients also exhibited difficulty with the key press. the patients did not respond sharply to the occurrence of the flash stimulus and thus had a much greater response time compared to the controls. Though the response was delayed it was present on an average by 75%.the absence of the late component in most of the patients, though the response was present in them, shows that the readiness potential has not contaminated the CNV component. The absence of the late component of the CNV is an indication of a short lasting CNV phenomenon, indicating an inability to maintain a sustained anticipation in the patient group, though its arousal is disrupted mainly in the cortical patients.

The topography of the CNV in the normal subjects shows a uniform spread of amplitude around the precentral and central areas, which significantly reduces in the parietal area. This topography largely supports an anterior or frontal neurogenesis of the CNV. This is also supported by the findings in the dementia patients. Cortical lesion is found to destroy CNV whereas it has significantly lesser effect in noncortical lesion. The CNV may be considered to be a significant indicator of dementia more specifically in cortical dementia. It may also be a useful test to differentiate between cortical and subcortical dementia patients.

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