Article *NIMHANS Journal*

Contingent Negative Variation in Patients with Cortical Lesions

Volume: 04 Issue: 01 January 1986 Page: 25-32

Jaswinder Singh, C R Mukundan, - *Clinical Neuro-Psychology Laboratory, Department of Clinical Psychology, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*
B S Das, - *Department of Neurosurgery, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*
B Y T Arya, - *Department of Neuro radiology, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

Abstract

The present investigation aims at understanding the nature of early and late components of Contingent Negative Variation (CNV) in patients with cortical lesion. C. T. Scan was used for determining the site of lesions. 12 space occupying lesion (SOL) patients matched with equal number of normal controls were studied. CNV was recorded with the conventional paradigm in which first stimulus was a click followed by a flash after a preset interval of 3 secs; the inter-trial interval was 4 secs. Cz and Fz electrode sites with linked ear-lobe reference electrodes were used. On line analysis was carried out with the help of a signal analyser. Results are indicative of deficits in the amplitudes of CNV measures in the patient group with respect to early and late components. An attempt was made to examine the effect of the caudality of lesion on the CNV components. Patients with anterior SOL showed more impairment as compared to the patients with posterior SOL, with respect to the early and late component of CNV. Results are discussed in the light of frontal lobe functions.

Key words -
Slow potentials,
Expectancy wave,
Anticipation,
Attentional processes,
Frontal lobes

Contingent Negative Variation (CNV) is one of the event-related slow potentials and is an important electrophysiological measure of the psychological phenomenon generally termed 'anticipation', 'conation' or 'intention to act' or 'expectancy' [1], [2], [3], [4], [5], [6], [7], [8], [10]. CNV can be recorded by simple foreperiod reaction time experiment in which a warning stimulus is followed by an imperative stimulus after a preset interval, to which the subject makes a motor response. It has been reported to be maximal in amplitude at the vertex and minimally attenuated in the frontal areas of the brain [4].

Some workers have demonstrated the aymmetrical distribution of CNV over two cerebral hemispheres [9], [11]. In split-brain study on human subjects CNV has been found to be normal and symmetrical over the hemispheres [12]. Following the pioneer work of Grey Walter [1], others studied the various aspects of the potential and later the emphasis

shifted to the study of psychopathological and pathophysiological groups. CNV has been viewed as one of the most useful and objective measures of brain functions of pathophysiological clinical population which is likely to show impairment of higher cortical functions. In the earliest study in this direction, Winter recorded CNV in a single epileptic patient and emphasised the utility of this potential as an electrophysiological measure of transient disturbances of attentiveness [13]. As a first systematic attempt to study the nature of this potential in brain lesioned cases, McCallum et al. and McCallum and Cummins [14], [15] compared CNV of normals and brain lesion cases which included patients diagnosed as cases of Parkinson's diseases, cerebrovascular accidents, haemotomas resulting from head injury and tumours, thus including cortical as well as subcortical lesions. They reported reduced CNV amplitudes and, asymmetry with respect to amplitude in a large number of cases, and also a positive relationship between asymmetry and the site of lesion. CNV asymmetry was more pronounced in case of localized lesions, though reduced CNV amplitudes were seen in both conditions. Cohen [16] supported the findings of MacCallum and Cummins by reporting diminished CNV in patients with hemispheric vascular lesions. Zappoli et al. [17] found decrement in CNV amplitudes in unilateral as well as bilateral frontal lesion cases, and attributed these findings to the dysfunction of attentional processes. CNV could not be detected in atleast 10 of their patients and they stressed that it was related more to "mental disturbances" rather than to the site or extent of lesion. In another study, the same group of workers [18] studied the vertex CNVs in 8 patients who had undergone unilateral and bilateral prefrontal lobotomy and who had dorsomedial thalamo-frontal pathways severed. With the classical CNV paradigm, it was possible to obtain CNV with normal morphology and uniform latencies. The authors suggested that the prefrontal region has meagre role in generating CNV. They emphasised the role of non-specific ascending reticular activating system in the genesis of CNV and conjectured that CNV might be widely distributed in the central nervous system. Rizzo et al. [19] observed a striking decrease in CNV amplitudes in head injury patients and attributed this decrement to a primary or secondary impairment of cortical or subcortical structures. Tecce et al. [20] studied CNV in patients who had been subjected to bimedial prefrontal leucotomy and reported, "augmented disruption of CNV development produced by short term memory task". Curry [21] recorded CNV in head injury patients and reported abnormalities in the form of large early components. Low [22] reported the absence of CNV in 13 patients of intracranial lesions. The absence was more pronounced in cases where lesion was in the thalamus. The unique finding of the study was that some patients with mass lesions produced normal CNV. Lutzenberger et al. [23] studied patients of frontal lesion of traumatic origin with respect to self regulation of slow cortical potentials and reported the absence of first negative component in these cases. Both normals and patients showed no difference in self control of slow cortical potential with feedback.

The review of literature thus indicates the limited number of studies on the nature of CNV in patients with cortical lesions. The results of these studies are equivocal and warrant a fresh look into the understanding of the role of various cortical structures in the germination of CNV. The major limitation of these studies is that the nature of lesion has not been controlled adequately and hence the findings cannot contribute much to the understanding of the precise effect of lesion on CNV. The anatomical locus of underlying process cannot be elucidated unless patients are selected with specific lesions, because greater the understanding of the specificity of lesion better will be our understanding of the possible neurogenerators of this cortical potential.

The present paper is a preliminary report of a study carried out on patients with space occupying lesion (SOL). The main aim of the study was to explore the nature of vertex and frontal CNV in patients with cortical SOL.

Methods

Twelve right handed inpatients (age range : 25-45) selected from the Department of Neurosurgery, NIMHANS, without previous history of psychiatric and / or organic illness, and with intact visual and auditory acuity constituted the patient group. Only patients with space occupying lesions were included in the sample. The nature of lesion was determined by C. T. scan and neurological findings. The types of lesions determined by the histopathological findings of these patients are shown in Table I. All the patients had bilateral papilloedema. The other clinical features included, headache and

vomiting; 4 patients had mild hemiparesis. One patient had nominal aphasia and another had global dysphasia. All the patients were either on steroids, analgesics, or anti-convulsant drugs at the time of recording. Only cooperative patients were selected. CNV was recorded prior to any surgical intervention. Equal number of normal volunteers (Age range : 25-45) comprised the normal control group. All the patients were administered a short battery of neuropsychological tests prior to the recording of CNV. The battery consisted of tests of attention and mental set, visual scanning, delayed response learning and test of ideational fluency.

Recording of CNV

Recording was carried out in the Clinical Neuropsychology Laboratory in a dimly lit sound proof room with the subject seated comfortably in a reclining chair. As CNV is found to be maximum at the vertex and the frontal area of the brain, Cz and Fz electrode sites of the 10-20 electrode system with linked ear-lobe reference electrodes were used. Electrodes were standard 7mm Ag/AgCl disc electrodes and they were affixed with kaolin paste. The subject was instructed to attend a click which was delivered through a speaker placed in front of the subject at a distance of one and half meter. The click was followed by a 2 joules stroboscopic flash. On seeing the flash, the subject was required to simultaneously press two micro switches fixed on the arm rests of the chair with each hand. The responses were monitored by a digital counter. The two stimuli with an inter-stimulus interval of 3 secs and with inter-trial interval of 4 secs were delivered using a microprocessor. On line EEG recording was done by Nihon Kohden Bio-Amplifier system with a time constant of 14 seconds. The EEG was averaged by SM2100B Signal Analyser of Iwatzu Electric Company. Analysis length was 5 secs and a negative delay of 1 second was used to record the base line activity. Forty-nine averagings were carried out. The trigger which was time locked with the click, started the analysis. EEG was monitored separately and artefact free sweeps were captured by using artifact rejection programme and on line editing.

Results

The amplitudes of early and late components of CNV were measured and compared between groups for the Cz and Fz leads separately. The amplitude of early component was measured 200 milliseconds after the onset of the first stimulus. This elicited the DC shift after recovery from the middle latency peaks. The amplitude of the late component was the maximum negativity reached before the second stimulus was presented. The median test and t test were employed as per data requirements for the group comparisons. The results of median analysis of early component of patients and controls are shown in Table no. II (for Cz and Fz respectively). The two groups significantly differed on the median values of the early component at both the electrode sites, indicating that a significantly larger proportion of patients have less than median amplitude. The late component comparison at the Cz leads also showed a statistically significant difference between the control and experimental groups. However the median analysis of Fz leads did not reach the level of statistical significance as is shown in Table III. An attempt was made to compare the amplitudes of CNV at the Cz and Fz leads with

respect to the caudality of the lesion. Of the 12 cases, 8 had SOL in the anterior part (mainly frontal lobes) of the brain (Rolandic Fissure as the centre), whereas 4 cases were with posterior SOL (mainly parietal lobes). Though a statistical analysis could not be carried out because of the small sample size, the mean values of both these sub-groups show that the anterior lesion patients have markedly smaller CNV amplitudes as compared to the posterior lesion patients as is shown in the Table IV. Typical CNVs of the normal control group, anterior and posterior lesion patients are shown in figures I and II

Table 1 - Distribution of the type of lesions of the SOL patients based upon histopathology findings

Table 1 - Distribution of the type of lesions of the SOL patients based upon histopathology findings

Table II - CNV : Median Analysis of Early Components

Table II - CNV : Median Analysis of Early Components

Table III - CNV : T values of Late Component

Table III - CNV : T values of Late Component

Table IIIa - CNV : T values of Late Component

Table IIIa - CNV : T values of Late Component

Table IV - CNV: Mean and SD of Early and Late Components (μ V) of Anterior and Posterior SOL cases

Table IV - CNV: Mean and SD of Early and Late Components (μ V) of Anterior and Posterior SOL cases

- ***CNV of normals (a: Cz - A1-2) and SOL (b: Cz - A1-2) patients***
- ***CNV of normals (c: Fz - A1-2) and SOL (d: Fz - A1-2) patients***

The ideometric interpretation of the neuropsychological test reveals that all the patients generally performed poorly on these tests. However, it was interesting to note that the patients with anterior SOL failed in all the tests as compared to the posterior SOL patients, who showed better performance on tests of attention and of delayed response learning. Both the groups performed poorly on the test of ideational fluency.

Discussion

As CNV is closely related to the most primary psychological functions such as attention, anticipation and expectancy, the present study was designed to examine the nature of it's disintegration in patients with cortical SOL. Since the diffused and localized lesions can differentially affect it's nature, only patients with localized lesions were studied. The first interesting finding of the study was that no significant difference was observed with respect to the topographical distribution of this potential in neurologically normal subjects. The patients with SOL generally showed a marked impairment of both early and late components of CNV. This impairment was observed in all the patients irrespective of the caudality of lesion. A statistically significant difference was found with respect to both the

components. The sole exception was the Fz values of the late component. Thus, the results generally point out the possible role of the anterior and posterior cortical substrates in the genesis of CNV. The results of the present study are consonant with the findings of the earlier workers [14], [15], [16], [19]. The results are in disagreement with findings of Zappoli et al [18] Curry [21], and Low [22]. Curry recorded larger early component in head injured patients. Low could record normal CNV in 13 patients with mass lesions. Zappoli et al. recorded normal CNV in frontal lobotomized patients. The findings of the present study seem to suggest that CNV components are impaired irrespective of the site of lesion. This is tantamount to saying that attention might be a physiologically widely distributed function and gets adversely affected by lesion in any portion of the cortex. Zappoli also emphasised a similar notion. Another aspect which needs further comment is related to the topographical distribution of CNV in patient group. The patient group as in case of normals did not exhibit a clear cut topographical difference between frontal and vertex leads. Also, our results failed to ascribe to the hypothesis that the first component of CNV is primarily mediated by the frontal lobes, and the late component by the retrorolandic brain structures [24]. The results of the present study did not show such a pattern because both the components were equally affected by both the anterior and posterior cortical lesions.

An attempt to establish a relationship between the type of lesion and the nature of deficit did not yield any positive results. Though the patients in the present study were cooperative and could carry out the required task, certain degree of cognitive and behavioural fluctuations cannot be totally ruled out. On the neuropsychological tests all the patients in general showed deficits, however the deficits were more striking in patients with anterior SOL. It might be stated that it may not be the site or extent of the lesion that directly affect CNV. It is the psychophysiological state of anticipation in the individual that is electrically manifested as CNV. If an individual is not able to achieve or maintain this psychophysiological state because of a pathophysiological condition, CNV is obviously affected.

In the present study of 12 patients, 4 had posterior, and 8 had anterior SOL. It was interesting to note that the posterior SOL group obtained comparatively higher amplitudes as compared to the anterior SOL group, particularly with respect to the late component. The variance of both the groups was high. The anterior structures of the brain are occupied by the frontal lobes. The relatively greater impairment of CNV in anterior SOL group might imply the significant role of frontal lobes in the mediation of the attentional processes. Our results are in conflict with the findings of Zappoli et al. who recorded normal CNV in patients who had been subjected to the prefrontal lobotomy. On the other hand, clinical neuropsychological results have documented the primary role of the frontal cortex in various higher cortical functions namely, attention, anticipation, judgement, comprehension and regulation of psychomotor acts [25], [26]. A considerable impairment of CNV in the anterior lesion group is self explanatory. The frontal lobe is richly connected with cortical and subcortical areas of the brain; it receives extensive sensory input from various posterior structures of the brain and it is only the final programming with respect to selective or directed attention which is performed by anterior part of the brain. The attenuated CNV in posterior lesion cases might be due to the involvement of posterior structures causing sensory inhibition at various input levels. The reduced amplitudes and changes in morphology of the CNV in anterior lesions of the brain gives this slow potential a marked scope to be used as a measure of attentional processes in various organic and functional diseases which affect higher cortical functions.

1.Walter W G, The contingent negative variation : an electrocortical sign of significant association in the human brain

Science Page: 146: 434, 1964
2.Tecce J J, Contingent negative variation and psychological processes in man
Psychological Bulletin Page: 77 (2) 73-108, 1972
3.Tecce J J & Scheff N M, Attention reduction and suppressed direct-current potentials in the human brain
Science Page: 164: 331-333, 1969
4.Walter W G, Slow potential changes in human brain associated with expectancy, decision and intention. In Cobb W & Morocutti C (Eds)
*The Evoked Potentials. Amsterdam, Elsevier*1967
5.Tecce J J, Attention and evoked potentials in man
*In D I Mostofsky (Ed) Attention :contemporary Theory and analysis. New York :Appleton Century Crofts*1970
6.Walter W G, Aldridge V J, McCallum W C & Winter A L, CNV : an electric sign of sensory-motor association and expectancy in human brain
Nature (London) Page: 303: 380-384, 1967
7.Cohen J, Very slow potentials relating to expectancy : The CNV
In E Donchin and d B Lindsley (Eds) Average Evoked Potentials : Methods, results and Evaluation NA Page: 143-198, 1969
8.Low M D, Borda R P, Frost J D & Kellaway, Surface negative slow potential shift associated with conditioning in man
Neurology (Minneap.) Page: 16: 771-782, 1966
9.Marsh G R & Thomson L W, Effect of verbal and non-verbal psychological set on hemispheric asymmetries in the CNV. In McCallum W C & Knott J R (Eds) event related slow potentials of the brain: their relation to behaviour
Electroencephalography & Clinical Neurophysiology Suppl Page: 33: 195-200, 1973
10.Otto D A & Leifer L J, The effect of modifying response and performance feed back parameters on the CNV in humans. In McCallum W C & Knott J R (Eds) Event related slow potentials of the brain : their relation to behaviour
Electroencephalography & Clinical Neurophysiology Suppl Page: 33: 195-200, 1973
11.Buttler S R & Glass A, Inter-hemispheric asymmetry of CNV during numerical operations
Electroencephalography & Clinical Neurophysiology Page: 30: 66, 1971
12.Gazzaniga M S & Hillyard S A, Attention mechanisms following brain bisections. In : S Kornblum (Ed) Attention and performance Vol. IV
Academic Press, New York Page: 221-238, 1972
13.Winter A, The Contingent Negative Variation (CNV) in a patient with spike wave discharges evoked by photic stimulation
Electroencephalography & Clinical Neurophysiology Page: 23: 489, 1967
14.McCallum W C, Walter W G, Winter A, Scotton L & Cummins B, The CNV in case of known brain lesions
Electroencephalography & Clinical Neurophysiology Page: 28: 210 Abstract, 1970
15.McCallum W C & Cummins B, The effects of brain lesions on the Contingent Negative Variations in neurosurgical patients
Electroencephalography & Clinical Neurophysiology Page: 35: 449-456, 1973
16.Cohen J, The CNV in cases of hemispheric vascular lesions
Electroencephalography & Clinical Neurophysiology Page: 38: 542, 1975
17.Zappoli R, Papini M, Briani S, Benvenutti P & Pasquinelli, A, CNV in patients with frontal lobe lesions and mental disturbances
In :The Responsive Brain McCallum W C & Knott J R (Eds) Wright and Sons, Bristol Page:

158-163, 1976
18.Zappoli R, Papini M, Denoth F, Pasquinelli A, Rossi L, Martinelli M G & Guerri S, CNV in patients after psychosurgery affecting thalamocortical pathways to prefrontal cortex
In Multidisciplinary Perspectives in Event Related Brain Potential Research Otto D A (Ed), U S Gover
Page: 376-382, 1978
19.Rizzo P A, Amabile G, Caporoli M, Spodaro M, Zanasi M & Morocutti C, CNV study in a group of patients with traumatic head injuries
Electroencephalography & Clinical Neurophysiology Page: 45: 281-285, 1978
20.Tecce J J, Orzack M H & Mirsky A F, Psychosurgery outcome and CNV asymmetry
In Progress in Brain Research. Kornhuber & Deecke (Eds) Page: 54: 790-797, 1978
21.Curry S H, Event-related potentials as indicants of structural and functional damage in closed head injury
In Progress in Brain Research, Kornhuber & Deecke (Eds) Page: 505-515, 1978
22.Low M D, Event related potentials and the electroencephalogram in patients with proven brain lesions
In Desmedt J E (eds) Progress in Clinical Neurophysiology Cognitive components in cerebral event-re
Page: 258-264, 1979
23.Lutzenberger W, Birabaumer N, Elbert T, Rockstroh B, Bippus W & Breidt R, Self regulation of slow cortical potentials in normal subjects and patients with frontal lobe lesion
In Progress in Brain Research. Kornhuber & Deecke (Eds) Page: 54: 427-434, 1978
24.Rohrbaugh J W, Syndulko K & Lindsley D B, Brain wave components of the contingent negative variation in humans
Science Page: 191: 1055-1057, 1976
25.Luria A R, *Higher Cortical Functions in Man Basic Books New York*1969
26.Teuber H L, The riddle of frontal lobe functions in man
*In The Frontal Granular Cortex and Behaviour (Eds) Warren J M & Akert K, McGraw Hill New York*1964