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CONTINGENT NEGATIVE VARIATION AND EVOKED RESPONSES RECORDED BY RADIO-TELEMETRY IN FREE-RANGING SUBJECTS

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The Contingent Negative Variation (CNV), first described by Walter *et al.* (1964a, b), is a sustained potential change, involving mainly the frontal cortex, during which the surface of the brain becomes electro-negative by about 20 μV with respect to deeper structures or a remote reference electrode. This effect develops during the time interval between a conditional and an unconditional or "imperative" stimulus, provided that the two are significantly related from the standpoint of the subject. The shortest interval between the signals for complete development of the CNV is about 0.5 sec and the longest that has been studied is 20 sec (Walter 1964). The appearance and maintenance of this effect is contingent on the significance of an association, and its amplitude reflects the degree of "subjective probability" felt by normal subjects. The amplitude of the CNV is also related to the extent of engagement of the subject in relation to the imperative stimulus. In the early experiments the subjects were instructed to press a button as quickly as they could so as to terminate the imperative stimulus, and the CNV was found to increase from trial to trial as they mastered this task and to terminate abruptly from a high level at the instant that the operant response was performed. This was thought at first to indicate specific involvement of the effect with motor activity but it was discovered later that a similar pattern of evolution could be observed when the subject performed a purely mental task such as recognizing a picture or deciding when a specified time interval had elapsed (Walter 1964, 1965; Walter *et al.* 1964a, b; Cohen *et al.* 1965).

Recent reports by Irwin *et al.* (1966) and McAdam *et al.* (1966) have emphasized the importance of motivational factors in the production of the CNV; both these experimenters and Low *et al.* (1966a) have suggested that the initials be considered as an abbreviation of "Conative" Negative Variation since it is a "cerebral electric sign of a specific mental state, that of conation, which denotes a conscious drive to perform apparently volitional acts". Kornhuber and Deecke (1965), using opisthochronic averaging from tape records, described a similar slow negative variation *preceding* spontaneous voluntary movements, which they designated "Bereitschaftspotential" or readiness potential. This would seem to support the suggestion that the CNV is related to conation, but experiments in which spontaneous voluntary movements were used to initiate pictorial exposures after fixed delays have shown that the "readiness" wave preceding the voluntary movement merges into an "expectancy" wave (Walter 1966). This persists through and after the phase of motor action until the appearance and recognition of the semantic presentation, even when this is delayed by several seconds after the completion of the voluntary act.

In standard conditions and with moderate intervals between stimuli the appearance of the CNV is remarkably constant. In a survey of over 100 normal subjects aged 18 to 88 it has been the most consistent feature of the EEG, reaching a mean potential of 20 μV between vertex and common mastoid after 1 sec, with a standard

deviation of $\pm$ 6 μV in this population. Contamination by various extracerebral sources has been suspected, ocular potentials being the most likely source of variations with such a time course. This possibility has been eliminated by control experiments with circum-ocular electrodes and by recording directly from the cortex in patients with implanted electrodes (Walter 1964, 1966). The amplitude of the CNV is not greatly attenuated by the integuments of the brain because it arises almost synchronously from patches of cortex over a wide area (Cooper *et al.* 1965).

Effects similar to the human CNV have been observed during conditioning in rabbits by Shvets (1958) and by Rowland and Goldstone (1963) in cats, while Caspers (1961) has demonstrated slow potential changes in cortex during arousal from sleep. Sakhiulina and Merzhanova (1966) observed slow surface negative waves in the operant motor zone following establishment of a conditional reflex to low frequency stimulation of midline thalamic nuclei in cats, and Wurtz (1966) has reported similar effects in self-stimulation experiments with rats. Low *et al.* (1966a, b) have demonstrated surface negative slow potential shifts during operant conditioning in rhesus monkeys and regard these as identical with the human CNV.

These various observations suggest that there may be no single conventional designation of mental state that corresponds specifically and uniquely with the development of the CNV. Conditions such as attention, intention, expectancy and conation favour its appearance and the potential falls abruptly at the moment when a decision is made or a motor act is completed. A serious difficulty arises from the most interesting property of the CNV — its sensitivity to changes in the mental and emotional state of the subject. Distraction, anxiety, a sense of constraint or surveillance and uncertainty tend to attenuate the CNV, while concentration, reassurance, exhortation, and in some people competition, will augment it. In the usual conditions of an experimental laboratory these factors are difficult to estimate or control. Even if there is no actual discomfort or direct restraint the sense of being tethered to the machinery by the electrode leads can be a disturbing factor. Observation of EEG patterns in free-ranging dogs by telemetry has shown considerable differences from those when they are linked to the apparatus even by long cables (Storm van Leeuwen, personal communication).

The experiments to be described here were planned in order to ascertain whether the development and maintenance of the CNV were significantly altered when the subjects were free to move, indoors and out, while they performed various tasks and engaged in normal everyday activities such as reading, walking, playing ball, riding in a car and riding a bicycle. The development of light multi-channel radio transmitters for EEG telemetry provides a simple and effective means for liberating subjects from all material involvement with the recording apparatus (Kamp 1963a, b).

METHODS

Studies were made on four normal adults and one child with scalp electrode derivations, and three psychiatric patients with both scalp and intracerebral electrodes. All the subjects were familiar with the procedure.

In order to provide controlled stimuli the subjects were provided with the receiver of a small commercial radio-control set (designed to fit into a model aeroplane) working on 27 Mc/sec which was modified so that the modulated carrier tone could be heard in a hearing-aid and cut off by pressing a button in the pocket. In this way the subject could perform a simple operant response. The antenna for this receiver was a short length of wire. The transmitter of this set was connected to the central programmer so that a conditional, warning stimulus in the form of a brief tone pip could be transmitted to the subject, followed after a fixed time interval by the continuous modulated carrier. With this code the subject could be instructed to perform a variety of actions and the combinations of stimulus associations used in the laboratory could be reproduced as the subject moved around freely. The only difference was that instead of the usual visuo-auditory or auditory-visual association the radio link was limited to two types of auditory stimulus. This arrangement was tested beforehand with conventional direct connections; the signals evoked responses indistinguishable from those previously described. The subjects were not inconvenienced by the small box of the receiver and

soon forgot the ear-piece of the hearing aid. The actual reception by the subject of the auditory stimulus code was monitored on one channel of the telemetry system so that when, as occasionally happened, the subject wandered out of range of the transmitter or into a radio shadow, the failure of communication was indicated on the monitor channel of the recorder. In some experiments one of the experimenters wore the stimulus receiver through which he was given instructions, for example to throw a ball to the subject whose responses were being transmitted and recorded.

The 8-channel modulator and radio-telemetry (RTE) system was that described by Kamp (1963a, b). This consists of eight identical pre-amplifiers with input impedances of about 300 kΩ, a submodulator and a radio transmitter. The submodulator provides pulse position modulation and the radio signal is frequency modulated with a centre frequency of 104 Mc/sec. The total bandwidth of the signal for the eight channels is about 400 kc/sec. This unit, including batteries, weighs only 200 g and measures 10 × 6 × 4 cm; it was worn strapped to the top of the head without inconvenience and the 3 cm stub antenna provided a range of about 30 m with the special FM receiver.

Of the eight channels five or six were generally used for EEG, one for EKG (connected to operate a cardiotachometer at the receiver output), one for recording respiration and one for the stimulus monitor (Fig. 1). Two of the EEG channels were modified to provide time constants of 7 sec to avoid distortion of the CNV; the other channels had time constants of 0.2 sec. Various electrode placements and montages were used;

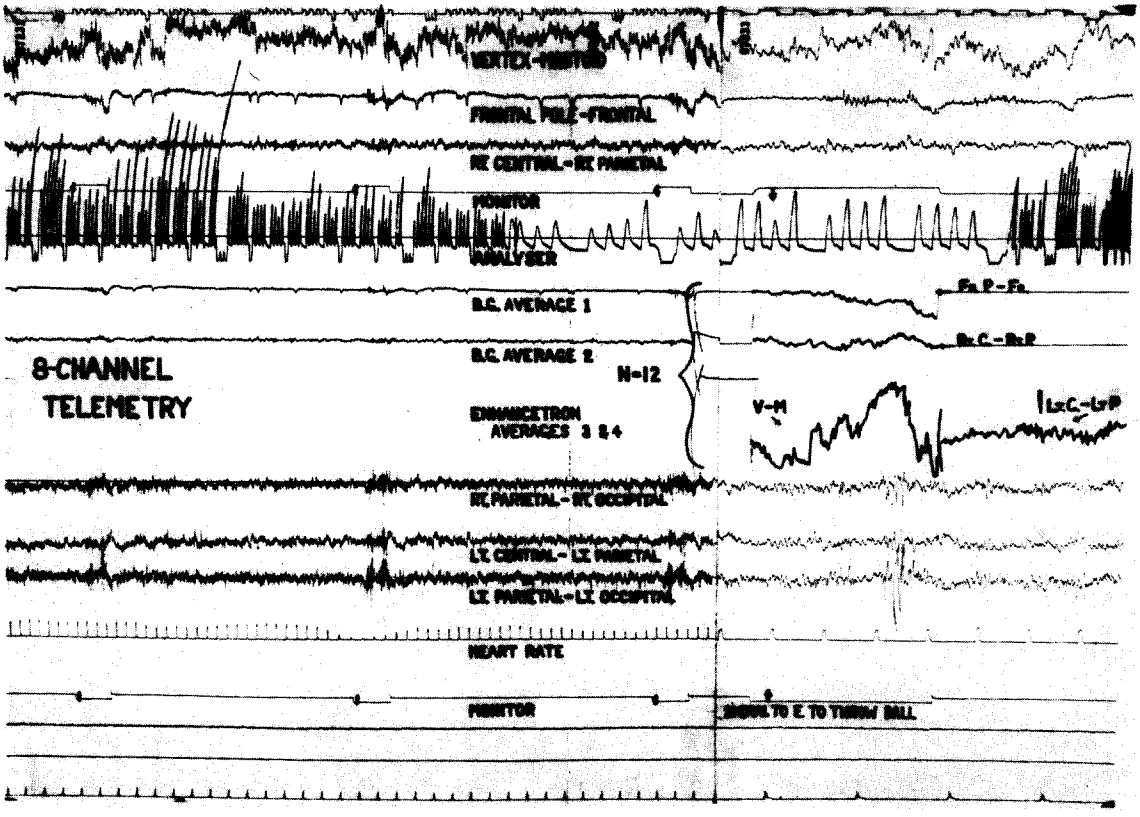

Fig. 1.
Section of 8-channel record obtained by radio-telemetry during a ball game. Normal subject. The signal to throw the ball was transmitted to the experimenter on a separate radio channel. The movement by the subject to catch is indicated by the EMG deflections in the parietal channels. The indicated heart rate was 110/min. The averages computed by the Enhancetron are written out successively on Ch. 8, those by the barrier-grid system simultaneously on Chs. 6 and 7.

for most experiments the channels with long time constants were connected between frontal and vertex electrodes in order to monitor eye movements, and vertex-mastoid, while the other channels were connected to frontal, parietal and occipital electrodes referred to the vertex or in bipolar derivation. When recording from patients with intracerebral implants, electrodes were chosen which had been found previously to be in regions responsive to conditional stimulation. These were referred to other electrodes in white matter which had been found to be unaffected by stimuli. The Average Reference system generally preferred for intracerebral recording was not convenient in conditions of telemetry because the large number of resistors needed to form the average would have taken up as much space as the transmitter. Since the intracerebral electrodes were of gold, slow potential changes were grossly attenuated but the evoked responses in non-specific cortex were clearly seen.

The responses in two EEG channels were averaged with barrier-grid tubes and in two more with an Enhancetron. The four averages were written out directly on a 16-channel Offner type TC recorder after the completion of each set of 12 presentations. Continuous frequency analysis of two channels was also provided. In most experiments the fronto-vertical and vertico-mastoid channels were connected to the Enhancetron so as to provide cancellation of vertical eye movement potentials in the cumulative write-out of the two channels during the trials. The averages of the two channels were then written out separately in succession so as to compare the anterior and vertical components. The EEG polarity convention was used: an upward deflection indicates electro-negativity at the vertex.

The procedure was first to record responses to the radio-control signal with the subject lying on a bed and directly connected to the equipment in the usual way. The radio-telemetry link was then substituted for the direct connection but with the subject still lying in the same position, and records were obtained in the same situation as before. The subject was then allowed to get up and walk around or asked to sit in another room while the signals were being transmitted to him. Subjects who were particularly interested in the technique were allowed to watch their own recording; some were encouraged to follow the growth of their average responses to the signals on the oscilloscope. When satisfactory records had been obtained by telemetry in standard conditions, various activities were introduced; the subject was engaged in conversation, or asked to read a magazine while the conditional and imperative signals were being transmitted from the programmer. Later, some subjects were driven in a car in the courtyard, others were engaged in a ball game with the experimenters. Two subjects were asked to ride bicycles; a single click on the radio-control channel was used as a warning to prepare to stop and a tone as a final command. Some subjects were asked to insert pegs in a peg-board, the clicks again being a signal to start and the tone to complete the task.

RESULTS

The general appearance of the records obtained by radio-telemetry was similar to those with direct connection in the same situation (Fig. 2). When the subjects were moving about quickly, and particularly when talking, there was naturally some increase in electromyographic activity. The only intrinsic feature that seemed to change when the subjects were free-ranging was that the alpha rhythms were more persistent, even with the eyes

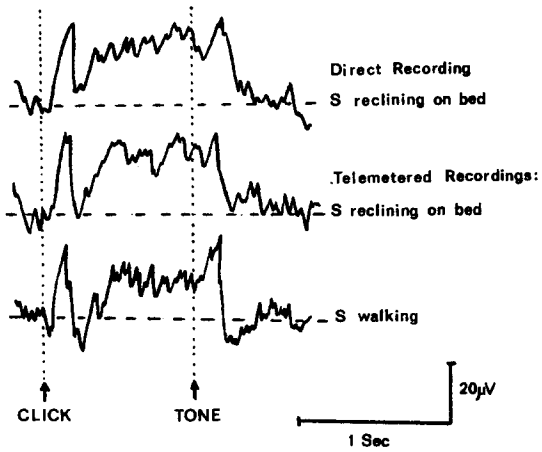

Fig. 2

Normal subject, male, 53 years. Scalp recording, vertex-right mastoid. He presses button to terminate tone. Average of 12 trials. The responses to the conditional clicks, the CNV and the responses to the imperative tones are similar in direct and RTE records while the subject was lying still but the CNV was significantly smaller when he was walking about.

open. This would suggest that the degree of restraint involved in immobilization necessary for direct recording may be enough to provide some degree of "alerting". The responses evoked by the auditory stimuli were unaffected by the insertion of the radio link and in particular, the average CNV was almost superimposable on those recorded directly (Fig. 3), provided that the subject was not too pre-occupied with other

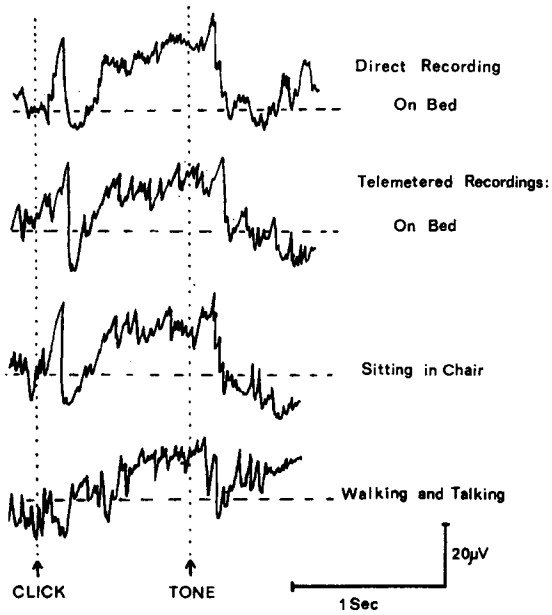

Fig. 3
Psychiatric patient, female, 28 years. Scalp recording, vertex–right mastoid. She presses button to terminate tone. Average of 12 trials. As in Fig. 2 the direct and RTE records are similar but distraction by walking and talking attenuates both the conditional click response and CNV.

activities such as conversation. When this occurred the decline in the CNV was accompanied by a lengthening of the reaction time to the radio signals, which were sometimes missed entirely. It was easy to repeat the standard tests of distraction, extinction (by withdrawal of the imperative signal) and equivocation (by interspersion of unreinforced conditional signals) and exactly the same results were obtained as with direct connections.

When the subjects were allowed to walk around there was some reduction of the CNV during the first few minutes, while the behaviour was rather self-conscious, but as soon as a subject accepted that he was really free the brain responses to the radio commands returned to the canonical form. Other activities which involved conscious attention to events unrelated to the radio signals, such as conversing and reading, attenuated the CNV even in the normal subjects, but trivial interference by other people's movements and conversation had no such effect in the normal subjects. However, one patient with a long history of obsessional neurosis showed a marked reduction in the CNV when he was sitting alone in an almost empty room, entirely out of contact with other people (Fig. 4). This patient had been treated by paracingulate coagulation and by this time was almost free from obsessional thinking except when he was left alone with no company, and it seems possible that the rather unusual attenuation of the CNV may have been due to the sense of isolation combined with remote surveillance.

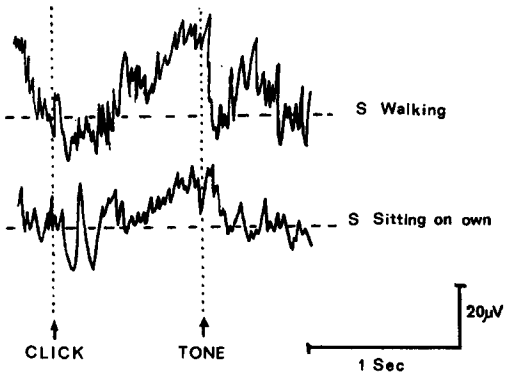

Fig. 4
Psychiatric patient, male, 34 years. Scalp recording, vertex–right mastoid. He presses button to terminate tone. Average of 12 trials. While the subject was walking about the click response on the scalp was small and the CNV of normal size, but when sitting alone the click response was larger and the CNV smaller.

The records obtained by RTE from patients with implanted electrodes showed the same features as with direct connection. For example, averages from electrodes in the orbital frontal cortex of the patient just described showed responses to the warning clicks while the CNV was present on the scalp (Fig. 5) but these dwindled when the CNV was attenuated during isolation. In another patient responses were evoked in the

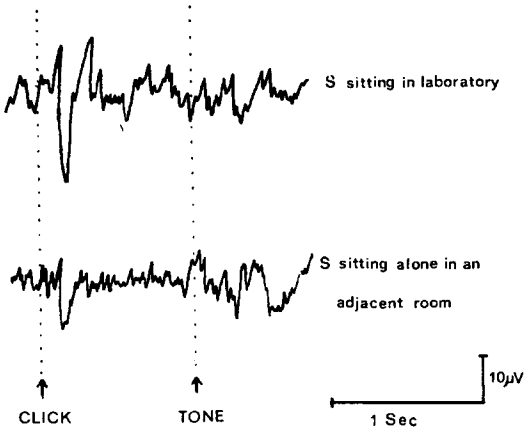

Fig. 5
Psychiatric patient, male, 34 years (same subject as Fig. 4). Bipolar intracerebral recording from orbital frontal cortex. He presses button to terminate tone. Average of 12 trials. While sitting with others the conditional click response in the orbital cortex was large but was diminished in isolation, in contrast to the changes seen in scalp records of Fig. 4.

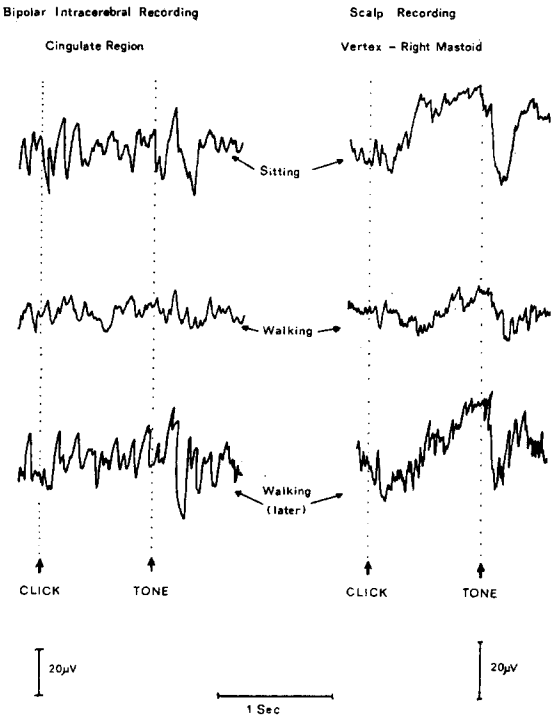

Fig. 6
Psychiatric patient, female, 48 years. She presses button to terminate tone. Average of 12 trials. Comparison of bipolar intracerebral cingulate and scalp derivations. While the subject was sitting down the responses to imperative tones were prominent in the cingulate derivation and the CNV was of normal size. When first tested while walking both features were attenuated, but returned when she became accustomed to the exercise.

cingulate region by the imperative tones (Fig. 6) and these responses diminished, together with the scalp CNV when the patient was first asked to walk around in another room. As she became accustomed to the exercise both the CNV and the cingulate imperative responses reappeared.

Similar relations between variations in the CNV in the superficial frontal cortex and evoked responses in the orbital and cingulate regions have been seen also with direct recording in laboratory conditions, but their demonstration in more natural conditions suggests that they may play a part in the normal fluctuations of attention and distraction.

During these experiments the average motor reaction time of the operant response was increased by 15–20% in distracting situations when the CNV was attenuated. The difference of the means is barely significant; the source of the difference was due to occasional very long reaction times during distraction.

In order to discover whether a CNV would develop in less formal and more familiar situations than the operant conditioning provided by associated auditory signals, the subjects were asked to perform commonplace actions such as walking and stopping, and turning the pages of a magazine to signals in the radio-receiver. Such actions were in fact accompanied by a CNV although this was often obscured by variations in attention. The clearest records were obtained when the task was a more clear-cut one in its time relations, so that the computers could be synchronized accurately with the initiation and completion of a particular stage. The insertion of pegs in a peg-board used for the estimation of manual dexterity satisfied this requirement: the subjects were asked to pick up a peg when they heard a click in the receiver and to insert it in a socket when they heard the tone. Fig. 7, *A* shows the development of the CNV during such a trial when the interval between start and stop signals was 2 sec. As in the operant conditioning situation, the click response is followed by a rapid rise of potential which lasts until the tone response

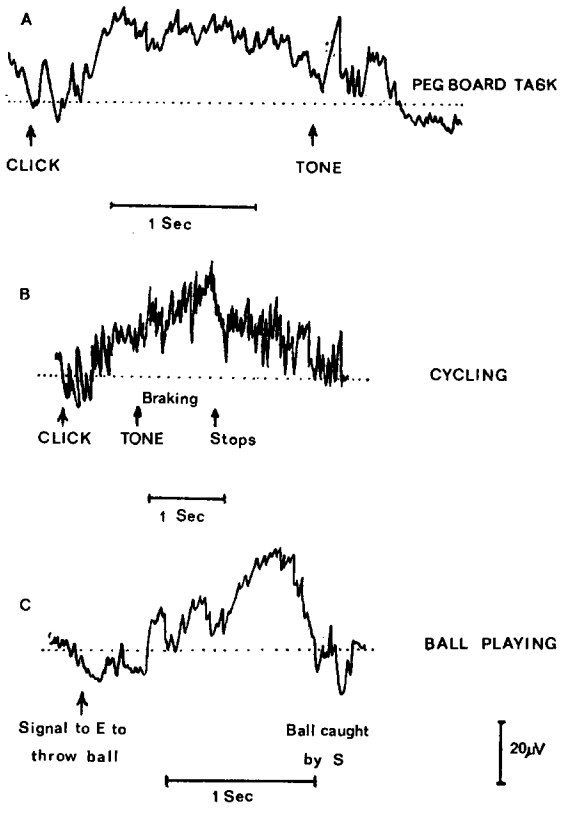

Fig. 7

A: Psychiatric patient, female, 28 years. She picks up peg on hearing click; inserts in socket on hearing tone. Average of 12 trials. The CNV is sustained over the longer period and falls to zero only when the task has been completed on reception of the imperative signal.

B: Normal subject, male, 9 years, riding bicycle. Instructed to stop on hearing tone. Average of 12 trials. The warning click is followed by an evoked response leading to a CNV during the braking manoeuvre, which peaks and falls only when the cycle has come to rest about 1 sec after the imperative tone.

C: Normal subject, male, 53 years, catching ball. Average of 12 trials. The experimenter receives a radio signal to throw ball to subject. The CNV starts only when the subject sees the ball in flight and peaks just before the catch.

and then subsides to the baseline. These observations show that a CNV is a normal accompaniment of everyday tasks and actions and does not depend on the operant relation between stimulus and response although it is particularly prominent when this relation is established.

The full freedom of action provided by telemetry was exploited by having subjects ride a bicycle around the yard. They were instructed to stop as quickly as they could on hearing a tone in the receiver. Each tone was preceded by a warning click 1 sec beforehand. Fig. 7, *B* is an example of how these commands were reflected in the CNV. During the first set of trials the warning click evoked only a brief response and the final command was followed by a large surface negative wave which persisted for some time. Gradually, however, as the subject learned the drill, the warning click began to evoke a late negative component which was augmented by the final command. This wave reached a peak at the instant when the bicycle came to rest and then declined to the baseline.

This pattern of development is also seen with direct recording in laboratory conditions; it demonstrates the gain in precision in a drill situation as the rhythm and sequence of warning and final commands come to be appreciated. A further extension was to the study of games. One experimenter wore the radio-receiver and was instructed to toss a ball to the subject when he heard a click. The time of flight of the ball was adjusted to provide about 1 sec between its release and being caught by the subject. Again in the first trials (Fig. 7, *C*) the largest negative wave appeared as the ball was caught (or occasionally dropped), but as the subject became more expert a CNV appeared while the ball was in the air. In order to reproduce the laboratory situation of equivocation by partial reinforcement, the experimenter was instructed to feint when he received a tone instead of a click; the average of these trials showed a CNV only for the first few while those in the same series in which the ball was actually thrown showed a normal CNV. The subject reported that he had learned to plan his catch only when he actually saw the ball leave the experimenter's hand.

As well as the CNV and early responses to the auditory signals, variations in pulse rate, respiration and muscular activity were also recorded. These followed the expected pattern, related to the amount of exercise and excitement before and during the experiments. During the ball games the EMG activity due to grasping the ball appeared only some 300 msec after the peak of the CNV, while in the standard operant situation (in which motor anticipation is ineffective) the CNV peaks

with the muscle response. This discrepancy may be related to what is usually called "follow-through", that is, deliberate planning and practice of an anticipatory movement leading to an automatic termination.

DISCUSSION

These observations confirm that the vertex negative wave, first described in relation to operant conditioning as the Contingent Negative Variation or CNV, is associated also in various ways with the performance of everyday actions and decisions in free-ranging subjects.

The technique presents no special difficulties except that in order to exploit the advantages of averaging computers some aspect of the signal or the subject's behaviour must be synchronized with the initiation of the computer so as to collect a number of comparable samples. In these experiments this was effected by providing an auditory stimulus from the Digitimer which initiated the computers as a warning or conditional signal either to the subject or an experimenter. Since these trials the system has been modified so that the computers can be triggered by the subject, either by his voice or pressing a button. In this way the procedure can be extended to include analysis of events during entirely voluntary actions by the subjects. Computation from tape records with appropriate delays permits identification of changes in potential *before* the subject actually performs an action. In this way the spontaneous "readiness" or intention wave described by Kornhuber can be investigated, as well as the effects which are contingent on the association between external signals, mental attitude and actions.

With these additions and improvements the computation of multi-channel telemetered data can provide a new range of investigation, including the cerebral and somatic correlates of conditioned and spontaneous decisions and actions during everyday life.

Perhaps the most important feature of the telemetry system is the provision of eight channels, so that somatic variables and sources of contamination could be monitored as well as the EEG and evoked responses. In free-ranging subjects physical exercise, accidental distraction, sudden movements of the head and eyes must be accepted as inevitable features of the experimental situation and it is essential that these should be allowed for in appraising the significance of variations in brain activity.

An obvious precaution is to ensure that the modulation systems in the radio link indicate clearly when there are "drop outs" so that these cannot be confused with bio-electric phenomena; in some systems over-modulation or fading can generate an output wave form which resembles a wave and spike discharge.

SUMMARY

1. Using an 8-channel radio-telemetry system (RTE) records were obtained of the EEG, pulse rate, respiration, evoked responses and Contingent Negative Variation (CNV) in four normal subjects and three patients with intracerebral electrodes. The subjects were free to move about within 30 m of the receiving aerial. Two RTE channels were modified to provide time constants of 7 sec.

2. Auditory stimuli, synchronized with the operation of average response computers, were transmitted to the subjects by a separate radio-control link. These were used as conditional and imperative signals to the subjects to perform various tasks: pressing a button to arrest the imperative signals, turning the pages of a book, inserting pegs in a peg-board and coming to a stop on a bicycle.

3. Responses to the signals were averaged on line with two barrier-grid tubes and a 2-channel Enhancetron and the intrinsic rhythms were analysed with a 2-channel frequency analyser. The pulse rate was indicated by a cardiotachometer.

4. The initial responses and CNV during the reception of paired auditory signals were similar to those seen with direct connection, provided that the subjects were engaged in some task related to the signals. The CNV was attenuated during exercise or conversation only while the subject was inattentive to the signals.

5. The amplitude of the intracerebral responses to the conditional and imperative stimuli in the patients with implanted electrodes was reduced when the scalp CNV was attenuated by isolation or distraction.

6. During the performance of fairly complex tasks following the auditory signals, the CNV

terminated only at the completion of the task, not at the moment of muscular effort.

7. The radio-control link was also used to instruct an experimenter when to toss a ball to a subject or to feint. In this situation also the CNV developed only when the subject was sure the ball was in the air and terminated when it was caught.

8. These observations suggest that the interactions of evoked responses and CNV seen in laboratory conditions also accompany normal activity and the performance of everyday tasks.

RÉSUMÉ

VARIATION CONTINGENTE NÉGATIVE ET RÉPONSES ÉVOQUÉES ENREGISTRÉES PAR RADIO-TÉLÉMÉTRIE CHEZ DES SUJETS PRIS AU HASARD

1. Grâce à un système radio-télémétrique à huit canaux, l'EEG, le pouls, la respiration, les réponses évoquées et la variation contingente négative (VCN) ont été enregistrés chez quatre sujets normaux, et chez trois malades porteurs d'électrodes intracérébrales. Les sujets étaient libres de se mouvoir dans un espace d'environ 30 m du système récepteur. Deux canaux RTE ont été modifiés pour disposer d'une constante de temps de 7 sec.

2. Des stimuli auditifs, synchronisés avec un calculateur de moyennes de réponses, ont été envoyés aux sujets par une chaîne radio indépendante. Ces stimuli étaient utilisés comme signaux conditionnels et impératifs, indiquant aux sujets d'accomplir diverses tâches: presser un bouton pour arrêter les signaux impératifs, tourner les pages d'un livre, insérer des fiches dans un tableau et aller à bicyclette jusqu'à un arrêt.

3. Les réponses aux signaux étaient moyennées en ligne grâce à deux tubes à mémoire et un Enhancetron à deux canaux; les rythmes intrinsèques étaient analysés par un analyseur de fréquences à deux canaux. La vitesse cardiaque était indiquée par un cardiotachomètre.

4. Les réponses initiales et les VCN obtenues pendant la réception des signaux auditifs couplés étaient semblables à ceux vus sur les enregistrements par connection directe, à condition que les sujets soient engagés dans une activité liée aux signaux. La VCN n'était atténuée pendant l'exercice ou la conversation que lorsque le sujet était inattentif aux signaux.

5. Chez les malades avec électrodes implantées, l'amplitude des réponses intracérébrales aux stimuli conditionnels et impératifs était réduite quand la VCN au niveau du scalp était atténuée par isolation ou distraction.

6. Pendant l'accomplissement de tâches relativement complexes consécutives aux signaux auditifs, la VCN ne se terminait que lorsque la tâche était achevée, et non pas au moment de l'effort musculaire.

7. La chaîne de contrôle radio était aussi utilisée pour indiquer à un expérimentateur à quel moment lancer une balle à un sujet, ou faire semblant. Dans cette situation également la VCN ne se développe que lorsque le sujet est sûr que la balle est en l'air et la VCN se termine quand elle est saisie.

8. Ces observations suggèrent que les interactions des réponses évoquées et de la VCN vue dans les conditions de laboratoire accompagnent également l'activité normale et l'accomplissement des tâches quotidiennes.

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