

SOURCE MODELLING OF THE P300 WITH VARIATION OF
PROBABILITY IN TWO MODALITIES USING THE
DIPOLE LOCALIZATION METHOD

by

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Source Modelling of the P300 with variation of probability in

two modalities using the dipole localization method

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ABSTRACT

Available evidence suggests that the P300, an endogenous activity believed to be an index of cognitive activity, is comprised of functionally distinct multiple sources that overlap spatially and temporally. Specifically, two questions are addressed in the present thesis. Is the P300 a reflection of more than one neural source, and if so, are these multiple sources indexing distinct cognitive processes? The classic oddball paradigm was used with visual and auditory stimuli occurring at two levels of probability. This design was used since the literature suggests that these variables may independently influence the subcomponents of the P300 and therefore distinguish them. As well, if the P300 reflects a unitary source of processing, then this source should be invariant across sensory modalities. A spatio-temporal dipole localization modelling procedure was applied to the data to determine whether the P300 is comprised of a single source or multiple sources and to determine whether the sources varied as the experimental variables of modality, task and probability were varied. The rationale was that functionally distinct sources should produce different localization results across conditions. This localization procedure models sources of neural activity as equivalent dipoles and models the head as a four-sphere volume conductor. The model employs a least-squares iterative procedure to compare observed electrical fields to those produced by the assumed sources in the spherical volume conductor. While this modelling procedure has necessary limitations, the results suggest that it was useful in determining that multiple, distributed sources comprise the P300. Furthermore, the results demonstrate that visual and auditory components are distinct, as are the sources which are involved with processing information about the frequency of events. It is not clear whether target and nontarget events are processed by functionally distinct sources. It is concluded that the umbrella component P300 is actually a manifestation of multiple modes of cognitive processing which overlap in space and time.

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Event-related potentials (ERPs) index brain activity during various cognitive tasks and therefore allow non-invasive electrophysiological analysis of psychological processes in humans. The division between brain neurophysiology and the study of human behaviour is thus narrowed (Desmedt, 1981). In effect, the study of electrophysiological changes associated with mental task performance provides the opportunity to observe the concurrent operation of brain activity and mind activity. We can attempt to resolve issues of the interrelationship between body and mind in a direct and empirical manner. In order to do so, the identification of neural sources of ERPs is important. Presently, the exact neural origin of cognitive processes is unknown (Donchin & Coles, 1988) and, therefore, attempts to localize sources are of theoretical significance. Another point of view on this matter holds that disregard for the neural basis of ERP components and a focus only on the psychological correlates might eventually allow the ERP field to drift into an unrealistic context reminiscent of the black box approach (Desmedt & Debecker, 1979). Evoked potentials may therefore be useful to identify and correlate physiological processes with psychological events.

In order to understand this relationship, at least two pieces of information are crucial: what is the psychological process being indexed and what is the neural mechanism? Typically, the ERP of choice for such inquiries is the P300, a positive polarity waveform occurring at approximately 300 msec poststimulus. It has been intensively scrutinized because it is evoked by stimuli that are important to the subject in some way, hence, it is generally regarded to be an index of cognitive processes (Verlager, 1988; Regan, 1989). A more trivial reason is that the P300 is so large that it is rather difficult to overlook (Verlager, 1988 cf Sutton, 1979). However, attempts to describe the neural source are complicated. Two distinct possibilities regarding neural source emerge from the broad centroparietal scalp distribution of the classical P300: it may either be generated by diffuse cortical sources, or by a small but deep subcortical source (Regan, 1989). Therefore the crucial first question to be addressed by any attempt at source localization is whether the P300 ERP is the manifestation of a unitary neural generator or of a distributed system of simultaneously active

sources. One of the main purposes of the present thesis is to apply a model-dependent technique, the spatio-temporal dipole localization method, to scalp-recorded P300 in order to establish whether a single source or a multiple source model best describes the observed data, and thus to enhance our understanding of the nature of neural sources of cognitive brain activity.

A second important question addresses the issue of what psychological process or processes P300 indexes. Generally stated, is the P300 an index of a single cognitive process or of multiple cognitive processes? An extensive literature exists to review as a starting point for evaluation of the P300 in terms of either a single or a multiple mode of information-processing.

There is little consensus on what the specific nature of the process underlying the P300 is; various overlapping psychological correlates have been proposed. Some specific candidate interpretations include Desmedt's 'closure of cognitive epochs', Squires' 'expectancy concept', Deecke's 'relaxation positivity' that occurs upon completion of a task (which serves well to account for the correlation of P300 to so many variables) as well as Donchin's 'context updating' which is further distinguished by Verleger's 'updating of subjective expectancy' and 'updating of internal representations' (Regan, 1989). Regan (1989) offers the succinct generalization that a P300 will be produced by task-relevant stimuli that occur somewhat unexpectedly (i.e. the subject expects a stimulus to occur, yet it does so infrequently or unpredictably) and requires a motor response or cognitive decision. Before this generalization is accepted as satisfactory, the caveat of Sutton and Ruchkin (1984) merits consideration:

...with the attempt to generalize, we believe that this is an undertaking fraught with peril. Karl Lashley is reported to have said that he would rather be specific and wrong than vague and right. We hope we will not achieve the worst of both, that of being vague and wrong...(p.1)

Precision is essential if any meaningful relationship between psychological processes and physical events is to be revealed. Present generalizations remain unsatisfactory; to date, both the

neural mechanisms of the P300 and the precise psychological function it indexes remain unclear. While in the past the P300 was applied in a prejudicial manner to index one or another psychological construct, more recently the horse has been properly placed before the cart with the question posed: of what function is the P300 a manifestation ?

The P300 is one of several endogenous components that comprise the late positive complex (LPC), which is a series of event-related potentials (ERPs). ERPs of the brain are typically classified as endogenous or exogenous components according to specific criteria. Exogenous components are evoked by external events and have a short latency. Their onset begins shortly after stimulus onset and lasts for about a quarter of a second (Donchin, 1978). Exogenous components are affected by the physical parameters of the stimuli, and their scalp distribution varies as a function of stimulus modality. Endogenous components, however, are those which may be evoked by external stimulus events but whose latency and waveform are determined by cognitive processes rather than the physical characteristics of the stimulus or the modality through which it is delivered. Therefore, endogenous components are characterized by a modality-nonspecific scalp distribution and are independent of physical parameters of the evoking stimulus. Such independence from physical attributes is dramatically illustrated by the fact that these components can be elicited by the absence of a stimulus, if the absence has an appropriate role (i.e. it is relevant) in the subject's task (Donchin, 1978).

The P300 is apparently endogenous since it has a long latency and can be elicited in the absence of expected stimuli. Simson, Vaughan and Ritter (1976) demonstrated that the P300 occurs in response to missing visual and auditory target stimuli. Weinberg, Grey Walter and Crow (1970) noted that the absence of expected stimuli elicited potentials within the P300 latency range which resembled those evoked when real stimuli were presented. If a component can occur in the absence of any stimuli then certainly it is independent of any physical attributes the stimuli may have. Therefore, the P300 satisfies this criterion of endogenous components.

Because endogenous components are invariant to changes in the physical parameters of the eliciting stimulus, quite disparate stimuli with equivalent tasks, even stimuli in different modalities, will elicit the same component. Therefore, if the P300 represents a unitary, endogenous source, this source should be invariant across different sensory modalities. This issue is controversial; the evidence is contradictory. Furthermore, its resolution is important since it has implications for the issue of whether a single source or multiple sources produce the P300.

Several researchers have reported that P300 are invariant across modalities. Simson, Vaughan and Ritter (1977) used visual and auditory stimuli in a go/no-go paradigm, as well as a missing target stimuli paradigm (1976), to demonstrate a late positive component possessing a mid-parietal topography which was independent of stimulus modality. Desmedt and Debecker (1979) used an oddball paradigm to elicit a P300 with a similar profile and topography across somatosensory and auditory modalities. While Squires, Donchin, Hering and McCarthy (1977) initially found differences between visual and auditory stimuli in an oddball paradigm, a second experiment by the same researchers found no such cross-modal differences when the discriminability of the stimuli was equated. Snyder, Hillyard and Galambos (1980) meticulously controlled for equality of stimuli with a signal detection paradigm. While they found reliable latency and amplitude differences, the scalp distributions of P300s revealed no substantial differences among three modalities - visual, auditory and somatosensory.

These findings are in conflict with other studies that reveal P300 to be modality-specific. There is evidence from clinical, magnetoencephalography (MEG) localization studies and studies on subjects with temporal lobectomies that visual and auditory P300s arise from different brain sources. In the clinical disorders autism and developmental dysphasia, the auditory P300 is aberrant but the visual P300 is less aberrant (Regan, 1989). In localization studies using MEG, evoked magnetic fields correlated with the scalp-recorded P300 have yielded mixed results. Okada, Kaufman and Williamson (1983) localized an apparently endogenous magnetic field

generator in a visual oddball task in the medial temporal lobe. However, Richer (1983, c.i. Halgren, Stapleton, Smith, & Altafullah, 1986) localized generators in the auditory association cortex during an auditory oddball task and in the visual association cortex in the visual oddball task. Johnson and Fedio (1984) used the oddball paradigm to compare auditory and visual P300 in patients with left or right temporal lobectomies (LTLs or RTLs respectively) and found scalp distribution differences between the two groups that suggest the possibility of separate P300 generators for each stimulus modality. Specifically, they found that P300 activity in the auditory task was essentially identical for the RTLs and the normal controls (NCs). LTLs, however, had smaller P300s. For the visual modality, the RTLs had smaller P300s than either the LTLs or NCs.

What these findings suggest is not just modality - specificity, but the possibility of more than one generator contributing to the P300. A review of intracranial depth electrode studies points to converging evidence that multiple sources comprise the P300. Johnson and Fedio's (1984) data suggest this, as well as the possibility that the processing of auditory and visual material is, to some extent, hemispheric dependent. Likewise, Wood and McCarthy (1985) recorded scalp P300 with similar morphology in auditory and visual modalities but they identified a depth recorded frontal source in addition to medial temporal lobe (MTL) structures as a candidate generator for P300. Stapleton and Halgren (1987) obtained intracranial recordings in auditory, visual and omitted stimulus oddball paradigms. They demonstrated a P300-like endogenous component which was modality non-specific. However, their findings reveal at least two spatially (in terms of depth) distinct potentials in MTL during the latency range of this component. Commenting on this study, Johnson (1988a) has suggested that since major aspects of scalp distribution remain the same in both groups, i.e. maximal P300 activity at Pz with the usual reductions in the anterior direction, the data indicate that if the generators are separate, they are located in close proximity to one another. If this is true, then it is possible that volume conduction to the scalp would render slight differences between modalities indistinguishable. This appears to be precisely the finding of Squires, Wilson and Crandall (1983) who obtained depth recordings in human limbic structures.

Evoked limbic potentials in auditory and visual oddball tasks produced auditory and visual P300s with similar polarity and morphology. Peak latencies of the visual evoked limbic potentials (ELPs) were somewhat later than those of the auditory ELPs, corresponding to the latency differences in the surface P300s. However, clear dissociation between the auditory and visual ELPs did occur at some electrode sites. ELPs from the hippocampal electrodes showed the greatest cross-modal discrepancy; the right hippocampal ELP was larger in the auditory condition whereas the left hippocampal ELP was larger in the visual condition. Squires et al. (1983) conclude that true cross-modal differences in ELPs exist at some sites. Importantly, to account for previous reports of modality aspecific topographies, they suggest that such differences would be indistinguishable at distant recording sites since, conceivably, the local field potentials could summate. That is, subtle differences in auditory and visual activation of hippocampal fields might not produce distinct waveforms at the scalp. This is even more likely to be the case if other areas are active at the same time and do not show modality differences in the ELP - for example the frontal lobe contribution reported by Wood and McCarthy (1985). It is possible, then, that studies which demonstrate P300s with similar scalp topographies across modalities are not inconsistent with those demonstrating the possible existence of multiple generators. The important point is that identical scalp distributions in two conditions need not imply identical activation at the depth.

In light of these direct reports of multiple generators, it is no longer possible to assume that all of the functional properties attributed to the third positive slow wave are exclusively properties of one component. It is possible that several components in the same latency range overlap temporally and spatially. Early studies describing the P300 did not report scalp distributions, one characteristic used to define a component. Studies which do report this detail suggest that several varieties of P300 exist. Some examples of various P300s include those associated with a more anterior scalp distribution than the 'classic' parietal P3b (Courchesne, 1978; Munson, Ruchkin, Ritter, Sutton & Squires, 1984), and the P3e component which can apparently be differentiated from a P3b by manipulating probability (Ruchkin, Sutton & Mahaffey, 1987).

If a change in scalp distribution of an ERP component reflects a change in the location and geometry of the neural source of the component (Donchin, 1978; Johnson, 1988a), and if it is also possible that different cognitive processes occur in different neuronal populations (Johnson, 1988a), then it is possible that functionally and anatomically distinct ERPs have come to be lumped under the umbrella component P300. Hence the confusion regarding the large number of psychological correlates of P300, as well as the plethora of constructs advanced to account for variations in P300 amplitude. While some progress has been made in characterizing determinants of amplitude and latency of P300, a thorough understanding of the relation between these quantitative measures of P300 and cognitive functioning remains elusive (Johnson 1988a). If the functional role and neural source of the P300 is to be clarified, then a necessary first step is to more precisely tease apart distinct components which may represent different modes of processing. What is required is a valid method to separate the P300 out according to overlapping task-specific components.

Two complimentary approaches can be used simultaneously in an attempt to achieve this. The first approach relies on the premise that, if there exists a single neural generator of the P3, then it must be responsible, by definition, for all P300 activity, regardless of the stimulus modality. That is, there should be no significant difference in scalp distribution of P300 evoked by stimuli in different modalities (Johnson & Fedio, 1984). The second approach applies the assertion of Johnson (1988) that two variables independently influence P300 measures: subjective probability and stimulus meaning.^{*} If these two factors are independent and they engage different

^{*}This hypothesis is based on the argument that, although the P300 evoked by the counted stimulus contains both a subjective probability and a stimulus meaning factor, the uncounted stimulus involves only the former factor (Johnson, 1988). The dimension of probability is the independent sum of the following three subfactors: global or a priori probability, preceding sequence of stimuli, and alternation sequence (Squires et al., 1976 c.i. Johnson, 1988). Stimulus meaning subsumes three variables: task complexity, stimulus complexity and stimulus value. Johnson (1988) argued that, while both stimuli demand equal amounts of attention for identification and categorization and both convey probability information, only one stimulus requires the additional processing involved in counting. This difference is presumably responsible for the 'target effect': the counted stimulus always elicits a larger P300 than the uncounted one.

cognitive processes, then it is possible that different neuronal populations may be activated. This would mean that it should be possible to alter the scalp distribution by varying one dimension independently of the other. If so, then it is arguable that the P300 activity associated with each variable would originate from separate neural generators, i.e. P300 represents a summated, distributed source of activity. Furthermore, because the different variables presumably engage different cognitive processes, this result would suggest that multiple modes of information processing had also summated ✓

In defense of this approach, the following is a review of evidence that different types of information-processing produce distinct scalp topographies. This evidence is support for the notion that different tasks, and, thus, different types of processing, call upon distinct neuronal populations. Johnson and Donchin (1985) used identical stimulus conditions in two tasks: an auditory go/no-go time estimation paradigm with feedback, and a counting task. Large differences between the scalp distributions of the P300s were observed in the two tasks. Whereas P300 was maximal at Cz during the time estimation task, it was maximal at Pz during the counting task. Further examination of the single trial records provides support for multiple P300s: one associated with the go/no-go task (process of stimulus identification and categorization), the other associated with processing of the time estimate. The intracranial recordings of Stapleton and Halgren (1987) used six variations of the oddball task to differentially evoke P300 subcomponents with significantly different topographic characteristics. They concluded that two distinct sources in medial temporal lobe represent distinct types of processing. Courchesne (1978) reported evidence for two distinct neural generators of P300 over time as novel visual stimuli become less novel. Recognized stimuli had a parietal distribution, novel ones a frontocentral one. Thus, as the meaning of the stimulus changed, so did the scalp topography. Lastly, there is evidence that the scalp distribution of P300 is sensitive to temporal lobe lesions but in a highly task-dependent fashion (Smith, Stapleton, Moreno, & Halgren, 1985; Daruna, Nelson, & Green, 1989). Daruna and colleagues also tested the findings of Fitzgerald and Picton (1981, c.i. Daruna et al., 1989) ✓

that increasing the interstimulus interval resulted in the augmentation of P300 amplitude, particularly over the parietal region of the scalp. Daruna et al. (1989) used this augmentation in amplitude to separate frontal and parietal components since the manipulation affected the parietal more than the frontal component. Thus, there is support for the notion that a variation in scalp topography, which represents a shift in active neuronal populations, is dependent upon different tasks and thus reflects different types of cognitive processing.

To summarize, there is accumulating evidence that the P300 is comprised of multiple components. If so, then in order to more precisely define the function and neural source of the P300 a valid method of separating functionally distinct subcomponents of the P300 is an essential first step. What is needed are independent variables which can be used to vary the P300 scalp topography and thus the neural generators so that components can be isolated by function for localization.

Probability appears to be one such variable since there is evidence that changes in probability can be used to distinguish subcomponents of the P300. Ruchkin et al. (1987) varied event probability in an attempt to contrast the functional roles indexed by the classic parietal P3b from the more centrally distributed P3e. They found P3b amplitude clearly varied as an inverse function of probability while there was no such effect upon P3e amplitude. This result of varying probability clearly establishes a distinction between P3e and P3b on the basis of both functional role and scalp location of maximal activity. This difference strongly suggests that they are different components.

Similarly, Banquet, Renault and Lesevre (1981) demonstrated the existence of at least two different P300s which were distinguished by latency, topography and functional significance. They analyzed these according to probability and task (go/no go) in order to better understand the significance of each of them in terms of information processing. For an equal change in probability,

the gradient of the absolute change in amplitude was more than twice as large for Pz as for Cz. They interpreted this as representing two functionally distinct components. Polich (1990) demonstrated an interaction between probability and electrode site where probability effects were larger at Cz and Pz relative to Fz. This amplitude effect for different probabilities was confirmed with a post-hoc analysis which also demonstrated little effect for probability at the Fz electrode but strong effects at Cz and Pz. From these experiments, it is concluded that variations in probability should be useful for separating overlapping components.

Stimulus meaning as defined by Johnson (1988a) may be another useful variable. Johnson (1988) has provided evidence (unpublished data from Duncan - Johnson & Donchin, 1977) that different scalp distributions might be obtained for the two event categories of this task, presumably because the cognitive processes underlying each are distinct. Specifically, the P300 for the counted (target) stimuli represents processing of subjective probability *and* a stimulus meaning while uncounted (nontarget) stimuli possess only a probability component. An ANOVA of that data revealed that the P300 scalp distribution for counted and uncounted stimuli were significantly different from one another. Whereas P300 amplitude was consistently larger at Pz than at Cz for the counted stimuli, this was not the case for uncounted stimuli - at 3/9 levels of probabilities Cz amplitude was greater than or equal to that at Pz. Also, uncounted stimuli elicited larger P300s at Fz than counted stimuli for all nine levels of probability. Implicit in the concept of a robust 'target effect' (a much greater amplitude to counted stimuli) is the suggestion that two types of processing are occurring.

Therefore, subjective meaning and probability are two variables which can apparently influence the P300. If there is a difference in task (counted or uncounted), there is a differential change in amplitude. As well, a change in probability results in a change in scalp distribution. However, most studies of the P300 using the oddball paradigm employ only one level of probability where the target is rare and the nontarget necessarily occurs frequently. Therefore, in many instances the

probability and stimulus meaning have been confounded and it is not clear whether the 'target effect' is largely due to the rarity of the event or the type of task. Johnson and Donchin (1980) demonstrated that the P300s elicited by the uncounched stimuli were extremely similar to those elicited by an uncounched stimulus which was twice as probable. Therefore, an oddball paradigm which included at least two levels of probability would be a powerful design to separate functionally distinct subcomponents of P300. If probability and task are each held constant as the other varied, with resultant changes in scalp topography, then it would become clearer that the two variables influence the P300 independently.

To summarize, there is mounting evidence that the P300 is comprised of multiple neural sources and that these multiple sources may represent functionally distinct cognitive processes. Stimulus probability, stimulus meaning, as well as scalp distribution appear to be major factors which allow the differentiation of multiple endogenous components, each related to distinct aspects of cognitive behaviour. Therefore, systematic variation of probability and stimulus meaning should be useful to separate distinct processes for the purpose of localization. In addition, it has been argued that any component representative of a single mode of processing must, by definition be invariant across sensory modalities. An experimental paradigm which employs probability and stimulus meaning as independent variables, presented through two modalities, would be powerful to test the hypothesis that the P300 is comprised of functionally distinct, multiple distributed sources. To this purpose, the present experiment will use an oddball paradigm which requires that the subject keep silent count of one of two stimuli. Both visual and auditory stimuli will be used. Furthermore, the paradigm will utilize two levels of probability so that counted and uncounched stimuli will each be presented at the a priori probabilities of 20% and 80%. Therefore, the oddball paradigm will be used with two levels of probability across two modalities to test the hypothesis that P300 is comprised of functionally distinct, distributed sources. Specifically, it is hypothesized that a multiple source model will better account for the scalp distribution of the P300 in all conditions than a single source and that, while scalp topography is similar, the sources

between modalities will be distinct. Furthermore, it is predicted that P300s evoked by target and nontarget stimuli will also vary in location from each other, as will location of sources with varying probability for the same kind of task. Therefore, there are two specific issues addressed in the present study: is the P300 a manifestation of multiple distributed sources, and are these sources functionally distinct cognitive processes?

In order for the relationship between P300 evoked by different variables and underlying neural sources to be understood, some method of relating the two is required. Before the chosen method of analysis is discussed, it is worthwhile to consider a review of methods and justifications in order to appreciate the benefits of the method chosen for the present study.

Typically, either as an arbitrary measure or as a result of few recording channels being used, most investigations have used the latency and amplitude of P300 as the only significant measures of the P300. Such single time point measures assume that all of the relevant information contained in a waveform resides at a single point in time, at for example, the peak of a given component. Yet, this is contrary to mounting evidence regarding the origin of most late components. As stated earlier it appears that the P300 is comprised of at least four and possible more subcomponents that overlap in time (Courchesne, 1978; Ruchkin et al., 1987; Squires et al, 1977; Sutton & Ruchkin, 1984). Examination of the amplitude at a single point in time ignores the different latency and topography of each of these potential generators (Karniski & Blair, 1989). That is, if several peaks in one waveform overlap, then identification of distinct components is problematic, especially when some peaks are independent of each other and some are not. As well, in principle, more than one brain site or event can contribute to more than one peak (Regan, 1989) so it is difficult to infer anything about the number of sources involved.

Squires, Donchin et al. (1977) have produced an example of how misleading an analysis relying on amplitude and latency alone can be. In that study, P300s were elicited by visual and auditory

stimuli in an oddball paradigm. An ANOVA revealed no statistically significant effects of modality on amplitude. While this would seem to imply some similarity of processing between the two modalities, further analysis revealed a significant effect for electrode site and modality. Thus, the importance of examining scalp distribution in a cross-modal comparison rather than just comparing amplitudes became clear. Therefore, for the present purposes, simple amplitude comparisons will not be useful in determining single or distributed sources.

It has been argued that, although topographic analysis of surface recorded ERPs in both intact and brain lesioned humans is useful, only detailed intracranial mapping can provide complete and unambiguous information for generator localization. However, any invasive recording procedure suffers from several inherent limitations. Firstly, it is questionable as to whether or not observed events under these circumstances correspond to normal events, particularly if a clinical population is used. Secondly, subcortical loci explored with depth electrodes are limited to the targets and trajectories used for surgical treatment of patients and as a result may be remote from potential generators under study; proximity was to be one of the advantages over scalp recordings (Velasco, Velasco, Almanza, & Olvera, 1986). Furthermore, ambiguity remains since the temporal variations of scalp endogenous potentials do not resemble most of those recorded by intracranial electrodes (Okada et al., 1983). It is not known if the scalp and depth-recorded endogenous potentials are simply correlated or if some component of the scalp potentials is in fact a passively volume conducted reflection of the former (Halgren, Squires, Wilson, Rohrbaugh, Babb & Crandall, 1980). Also, while it is a well accepted fact that brain stem potentials are volume conducted to the scalp, the reverse current paths have often been neglected; cortical polarizations necessarily and always cause potential changes in deeper structures. (Braun, Lutzenberger, Miltner, & Elbert, 1990). The point is that an extended cortical source produces considerable changes everywhere in the brain. Thus, intracranial measurements can hardly resolve the issue in a more definite manner than some of the other approaches.

For the purposes of the present study an alternative modelling method, described by Scherg and Von Cramon (1986), is applied. This method, the spatio-temporal dipole localization method (STDLM), constructs a mathematical model that attempts to describe neural sources which could vary in strength and orientation over time to produce the potential distribution seen at the scalp. To localize sources of functional activity, this approach constructs models of the source and the volume conductor. A brief description of the source modelling is considered first. (For a thorough description and justification of the assumptions underlying this modelling, the reader is referred to the Appendix).

It is generally accepted that the electroencephalogram (EEG) is caused by postsynaptic activity in apical dendrites of neurons and that the resultant current can be modelled as a dipole (Stok, 1986; Nunez, 1990). A dipole is a theoretical entity that represents two charges of equal and opposite polarity separated by space. These postsynaptic potentials are caused by substances released by the synapse which in turn cause small local changes in membrane resistivity. When the apical end of an elongated neuronal process such as those of neocortex pyramidal cells becomes positive or negative with respect to the opposite end, a current is drawn and the structure resembles a dipole. (Schlag, 1973).

Any source large enough to manifest itself in the EEG will involve a small area of neurons which are synchronously active. If the area is small enough, it may be conceptualized as an "equivalent dipole" (Henderson, Butler, & Glass, 1975). The assumption that neural sources underlying scalp recorded potentials can be regarded as simple current dipoles simplifies the mathematical model used in the STDLM. Generally this model operates in the following manner. An assumed dipole is located within concentric spheres of differing conductivities which represent a volume conductor, the head. Electric field theory is invoked to calculate theoretical potential distributions at the surface. The source is varied incrementally until the summed squared difference between the theoretical field and the observed data potential field is minimized. By examining the anatomical

plausibility of the localization, and goodness of fit (variance accounted for - VAF) by the modelled source, conclusions can be drawn about the nature of the neural generators producing the evoked potentials.

Dipole localization has become a common approach. Okada et al. (1983) used the single equivalent dipole model to localize P300 recorded by magnetoencephalogram. Sidman, Ford, Ramsey, and Schlichting (1990) used the method to characterize age-related features of P300. From that study it was concluded that this method appears useful for distinguishing clinical conditions since it enhances the discriminatory power of traditional electrophysiological measures. Sidman and colleagues concluded that clinically useful interpretation of scalp potentials have been gained through the use of this model.

However, these studies relied on the assumption that the source of the potentials under study can be effectively modelled as a *single* equivalent dipole. This assumption is questionable, particularly with regards to models of cognitive activity. Geisler and Gerstein (1961) compared a mathematical model to experimental data from monkey and demonstrated that the averaged evoked response does not behave as if it had been produced by a simple dipole-like field, even though the animals had been anesthetized; hence many cortical processes diminished. They concluded that the electrical activity of auditory cortex is too complex to be accurately described by a single dipole. Weinberg, Brickett, Coolsma and Baff (1986) concluded that while the concept of the current dipole has proven useful as a means of making source localization possible, it is not an adequate representation of the complexity of anatomical structures. Indeed, a complex obstacle for source localization is the predominance of multisource activity in most clinical and psychological applications. Multisource activity is to be expected, based only on anatomical or physiological, considerations (Nunez 1985).*

* most of the 10^{10} cortical pyramidal cells send an axon into white matter which re-enters the cortex at tangential locations with an average separation of several centimeters (Braitenberg, 1978 c.i. Nunez, 1990).

When the potential distribution is the result of simultaneous activity of a number of cerebral brain areas, the assumption that the source is restricted enough to be adequately represented by a dipole is violated. A single dipole may account for a large portion of the data variance and yet be localized far from any of the active brain areas (Achim et al., unpublished). However, fitting multiple dipoles to a single scalp topography is problematic since the number of unknown parameters quickly approaches the number of data values - 6 parameters per dipole to identify location, orientation, and strength for 21 data points (assuming full montage) per point in time. Given that single dipole source modelling is inadequate for identifying the source(s) of the P300 and considering that it is not possible to clearly define what is meant by these "sources" without indicating both the temporal and spatial scales involved (Nunez, 1990), the more recent developments in modelling appear more appropriate.

The spatio-temporal modelling approach described by Scherg and Von Cramon (1986) is suitable for modelling multiple sources. This method takes time into account as a variable and thus it is possible to study the activity and interaction of multiple simultaneously active brain sources over the entire time domain of a physiological process. Because this model can be used to characterize sources whose activity overlaps spatially and temporally, it is an appropriate method to apply to address the issue of whether or not the P300 is an index of multiple, functionally distinct sources.

Various data suggest the likelihood that localized afferent input to the cortex will spread to the distant regions of the cortex in much less than 100 msec, perhaps in times of the order of 10 msec. Moreover, there is no apparent reason to believe that most cortical sources are stationary.

Method

Subjects and Recording Conditions

Nine (9) adult right-handed subjects, 2 females and 7 males between the ages of 23 and 35 were used (mean age was 26.11). All of the data from one of these subjects (male) was excluded due to excessive artifacts. Twenty-three silver-silver chloride electrodes were applied according to the international 10-20 system. Linked reference electrodes were applied to earlobes and a forehead ground was used. Impedences were never higher than 7 kohms and were re-tested once the subject was in place as well as between conditions when headphones were worn or removed. Subjects were seated comfortably in a soundproof booth which was held at a constant illumination of five footcandles. Stimuli in visual and auditory modalities were presented at a rate of .4 per second and the recording epoch was 1024 ms with a sampling rate of 250 points per second. Auditory stimuli were generated by the Bio-Logic System and visual stimuli were triggered by an external microcomputer. All data were recorded by the Bio-Logic using Brain Atlas software, version 2.30. The high and low pass filter settings were .1 and 70 Hz respectively. Gain was set at 20,000 and the 60 Hz notch filter was on. The built-in artifact rejection was also used. Approximately twenty samples were averaged for each condition and if fewer than seventeen were obtained then the trial was re-run.

The auditory stimuli were two tone bursts presented binaurally through Sony Dynamic Stereo DR-S3 headphones. The nontarget and target frequencies were 1000 Hz and 2000 Hz respectively. Subjects were instructed to close their eyes during the auditory task. Both tones had a rise and fall time of 10 ms, a duration of 50 ms and an intensity of 60 dB. The visual stimuli consisted of two spatial frequencies: white bar gratings against a dark background occurring at one or three cycles per degree.* The high spatial frequency (3 c/d) represented the target stimulus for all visual

*Subjects were seated with measured distance from eyes to screen of 1 meter. Spatial frequency is defined as: $\text{tangent of the visual angle} = \text{size} / \text{distance}$. Therefore, to achieve a spatial frequency of 1 cycle per degree at a distance of one meter, the width of one cycle (a complete alternation of white and black), is 1.7 cm. The width of a cycle for three cycles per degree is .57 cm.

conditions. The lower frequency stimulus had a luminance of .125 log ft-L; the high frequency had a luminance of .38 log ft-L. Visual stimuli were presented through a Data Train DC355 EGA monitor.

Procedure

In the oddball paradigm, two stimuli are randomly presented - one frequently and one infrequently. As in typically run oddball tasks, subjects were instructed to silently count the oddball or rare stimuli so that they could report at the end of a run the number of times that this infrequent stimulus was presented. Because the present study is examining the effects of probability at each level of the task dimension, another condition was added. In this condition, subjects were instructed to count the target stimulus when it was frequent. Frequency was defined as having an a priori probability of occurrence of 20% or 80%. Subjects were allowed a short trial to experience the stimuli, and to ensure that both the task and the target were known. They were then instructed to relax and count the target stimuli silently to themselves. It was made clear that they would be asked after each trial how many targets were observed.

All conditions were run for both visual and auditory modalities. The order of the conditions was counterbalanced and nested within the larger counterbalanced order of modality condition. Subjects receiving the visual stimuli first were dark-adapted to both conditions for twenty minutes before the trial was run. It was assumed that those receiving the auditory condition first would visually adapt during the first part of the experiment.

Quantitative Evaluation of Dipole Sources

Peak latency measures were taken from stimulus onset and peak amplitude was defined as the maximum positive peak at the Pz electrode site. Maximum peak was determined by visual inspection after a baseline adjustment was performed. This adjustment was made by averaging all

data points in the epoch to create a baseline. Data was then digitized with the Bank Math process of the Brain Atlas software version 2.30.

In order to perform the dipole analysis, a position file recreating the electrode montage (including references) was first constructed. For EEG data, the electrode positions are assumed to lie on a sphere 8 cm in radius. An x axis runs from nasion (positive end) to inion (negative). A positive y axis runs from left pre-auricular to the right (negative y axis). A z axis runs at right angles to x and y with intersection as origin. Superior z axis is positive. Electrode position and subsequent dipole localization are converted to cartesian x, y, z co-ordinates.

Next, for both the target and nontarget data at each level of probability a 'window' of 300 msec was selected: 150 msec on each side of the peak P300 amplitude obtained from each individual subject for each condition. These windows of data were then subjected to a spatio-temporal dipole fitting analysis. The goal of this type of computer model is to determine what combination of one, two or three spatial dipole patterns weighted by three respective temporal fitting waveforms would yield a combined spatio-temporal electrical field distribution that most closely fit the recorded data.

The specific model used, Sdip Version 1.1, computed the forward solution (the scalp electrical potential for an assumed dipole location) using a modification of the solution provided by Stok (1986). This model assumes a volume conductor consisting of four concentric shells which are isotropic and homogenous. The shells represent the following tissues with respective electrical conductivities and radii:

<i>tissue</i>	<i>radius (cm)</i>	<i>conductivity ((ohm-m)⁻¹)</i>
brain	7.0	0.3300
csf	7.2	1.0000
skull	7.7	0.0042
scalp	8.0	0.3300

For a given number of current dipoles of with assumed parameters, an iterative fitting procedure varies the starting parameters incrementally until an optimum, defined as the minimization of the sum of squared differences between theoretical (modelled) and observed data, is obtained. In this spatio-temporal model, the solution requires that during each fit the sources be fixed in space with orientation and strength varying over time. Each dipole therefore is modelled with six parameters: three for location in space and three for dipole orientation or direction of the vector sum of dipole moment in three orthogonal directions. Dipole strength represents the net dipole moment of the source which flows in the direction indicated by the orientation vector. The residual variance or percentage of observed data not accounted for by the model when optimization is reached, is the sum of squared differences between theoretical and observed fields normalized by the total observed field.

In this analysis, one, two and three dipole models were run to determine whether a single source or multiple sources best accounted for the data. Starting parameters were determined in a previous analysis which used single source, single time point fitting to the peak amplitude of P300 for each subject. It was determined that for the visual data, occipital lobe and central starting points produced the smallest residual. For auditory data, central and inferior temporal lobe parameters did the same. Thus for single dipole spatio-temporal fitting, right central starting parameters were used for both modalities. The two-dipole model added a left inferior temporal lobe or left occipital lobe source to auditory and visual data respectively. The three-dipole model added right inferior temporal lobe or right occipital lobe to the above sources.

After all three models were run for all conditions a post hoc analysis was attempted using a predictor model derived from the first analysis. Since the three-dipole model fit the auditory and visual rare target best, these conditions were used to create the visual and auditory predictor models. The predictor models were created as follows. A subsegment of the time window for the rare target condition where the model was fitting best was selected. This process involved

subjective assessment (visual inspection) to determine the time points over which there was the longest continuous run of point by point fits with extremely low residuals for each subject. The end points of the windows were averaged across subjects for each modality to obtain a subsegment. For the visual condition, the subsegment spanning 432-446 msec was used. For the auditory condition, the time span was 364-378 msec. Next the x, y, z coordinates for the localized dipoles 1, 2, and 3 obtained in the first analysis were averaged across subjects in each of the visual and auditory rare target conditions. The averaged dipole sources were used as starting parameters or predictor models for all of the other auditory or visual conditions. These assumed sources were fit to the 14 msec windows (the subsegments). For each subject, these sources were iterated once and the resulting residual variances for each of the time points of the subsegment were recorded. The average of the subjects' results were compared to the average residual variances of the subsegment for each of the other conditions. The predictor model was also applied in the same way to visual and auditory rare target condition for comparison.

Results

P300 Scalp Distribution and Peak Latency

Figure one is a sample recording of the P300 evoked by rare visual stimuli. Table one presents individual peak amplitude latencies for each condition. In all but one subject, the rare target events elicited P300 waves which were maximal at Cz and Pz and produced the classic centroparietal positivity in the topographical maps. In the rare auditory target condition, one of the subjects produced a P300 with a more frontal distribution. This subject's visual P300 to rare targets resembled the others'. Consistent with previous research, higher amplitude waves occurred to rare target stimuli than to frequent target stimuli and the visual latencies were longer than auditory latencies. The latency to frequent targets was shorter than to rare targets.

Figure 1. Sample Recording of the P300 Evoked by Rare Visual Stimuli in One Subject.

This sample demonstrates a P300 with the classic centro - parietal scalp distribution. The cursor measures peak latency which is defined as the most positive point at the Pz electrode site.

Figure 1. Sample Recording of the P300 Evoked by Rare Visual Stimuli In One Subject

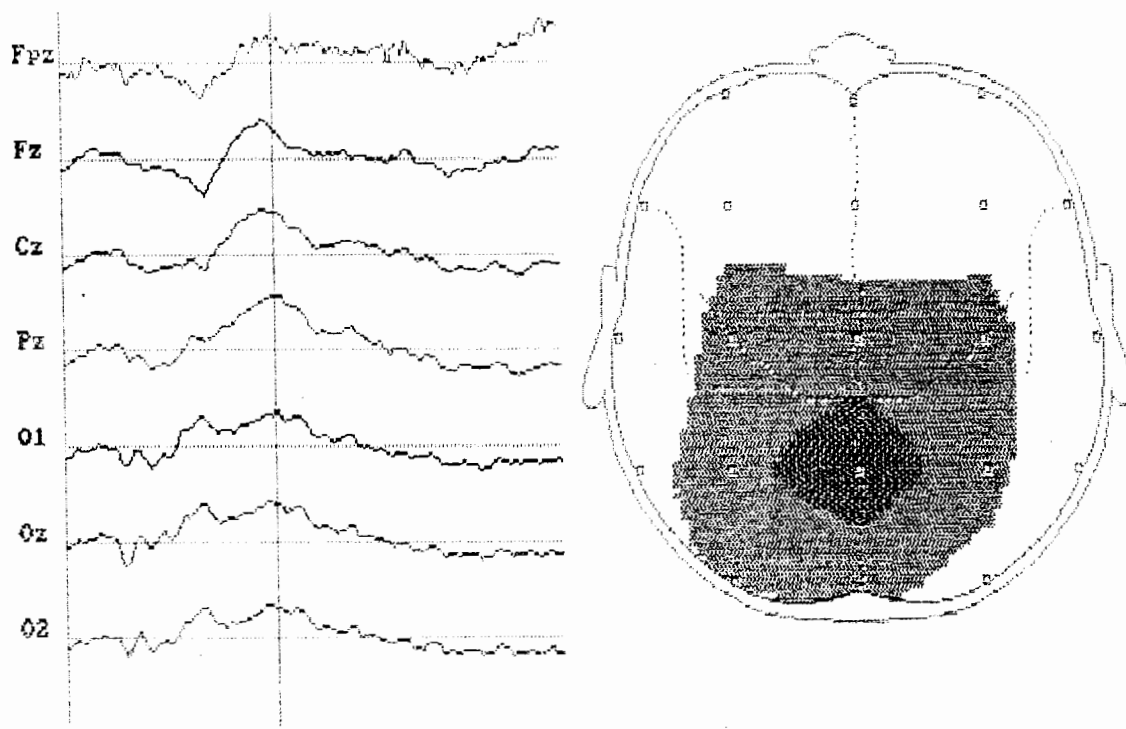


Table 1. Peak Amplitude Latencies for P300 at Pz

Peak latencies in msec are measured from stimulus onset.
Latencies for each subject are shown for all conditions in both modalities.

Table 1. P300 Peak Amplitude Latency for Each Subject in All Conditions

	AUDITORY				VISUAL			
	Target/Counted		Non-target		Target/counted		Non-target	
	Rare	Frequent	Rare	Frequent	Rare	Frequent	Rare	Frequent
	360	224	328	204	476	272	260	280
	352	160	248	344	428	236	400	260
	372	160	372	424	436	276	276	276
	392	292	476	364	464	332	448	432
	352	196	304	140	436	364	428	380
	376	308	348	308	408	372	268	440
	320	296	292	332	372	364	292	356
	332	312	344	216	464	388	384	260
Mean	357	243.5	339	291.5	435.5	325.5	344.5	335.5

In all frequent conditions, positive peaks of some subjects occurred at latencies which are earlier than the typical criterion latency for P300. Because the characteristic N2, P2, P3 pattern was not always obvious, there is the possibility that the peaks taken to represent the P300, in fact, reflect the earlier P2 component of the late positive complex. Because frequent stimuli produced considerably shorter latencies, and because the most positive peak at the Pz electrode is typically used as an index P300, the most positive peak criterion was used despite the shorter than typical latency.

Large amplitude P300s in response to rare *nontarget* events were recorded. These components resembled those evoked by rare target events. This finding is consistent with that of Duncan - Johnson and Donchin (1977) who demonstrated that when target and nontarget events are equally unexpected, the two events produce strikingly similar P300s.

Dipole Source Localization

The results are comprised of two parts: the number of sources which best model the data, and the specific localizations derived. Results from the initial spatio-temporal modelling are presented separately from those obtained using the predictor models. The results from the initial analysis which address the issue of number of sources are presented first.

Table two presents the 'goodness of fit' or the amount of variance in the original data which the modelled sources were able to account for during the time period selected. The table includes variance accounted for (VAF) for all conditions by one, two or three-dipole source models. This information is summarized in the bar graphs shown in figures two, three and four. Examination of the mean VAF indicates that the three-dipole model accounts for the most variance in all cases although the fit for the two-dipole model is very close. An examination of the variance in VAF scores across subjects indicates that values for the one-dipole model are extremely variable, less so for the two-dipole model, while the three-dipole model reflects the lowest variability in VAF

values. However, because there are fewer parameters in the models with fewer dipoles, it is reasonable to expect those models to express less variance in the localizations (Baumgartner, 1989). Therefore, lower variability of VAF values in the three-dipole model may reflect its greater adequacy at accounting for the data.

A comparison by modality in table two demonstrates that the three-dipole model accounts for the visual and auditory data equally well. While this may imply some similarity in processing of information between modalities because there appear to be multiple sources in both, specific localizations need to be considered in order to deduce this. A comparison of models in table two indicates that for the rare target condition only, differences in VAF between modalities increases dramatically as the number of assumed dipole sources decreases. This may be due to the fact that the decline in VAF with decreasing number of assumed sources is steeper for the auditory modality. In fact, the residual difference between the three-dipole and one-dipole fit for the rare auditory target data is 24.55 % while that for the visual data is 12.14%; the difference is twice as great for the auditory modality.

A comparison of target and nontarget results in table two demonstrates that in the three-dipole model, there is a difference in VAF between target and nontarget data when compared at the same level of probability, however this difference is slight when the target is frequent. The difference in residual for rare target and rare nontarget is 6.43 %(visual) and 4.54% (auditory), whereas the difference for frequent stimuli is only .33% and 2.73% for visual and auditory respectively. Therefore, this model accounts for target data better than nontarget data but only when these events are rare.

If 'fits' for target and nontarget data are compared for each model in table two, it is clear that the difference in VAF between rare target and rare nontarget increases dramatically in the visual modality as the assumed number of dipole sources decreases. Furthermore for both modalities, in

the one and two-dipole models, the difference between frequent target and frequent nontarget is greater than that found in the three-dipole model.

Table 2. Variance Accounted For by One, Two or Three Assumed Dipole Source Models for Each Subject Across All Conditions

Variance accounted for (VAF) indicates the percentage of variance in the observed data which the theoretical or modelled sources could account for.

Individual results are shown for target (T), nontarget (nT), conditions at rare (R), and frequent (F) probabilities.

The percentage of VAF is listed for models using 3 sources, 2 sources or 1 source.

Overall means and standard deviations within each condition are also included.

Table 2. Variance Accounted For by One, Two, or Three Assumed Dipole Source Models for Each Subject Across All Conditions

	3 dipoles						2 dipoles						1 dipole						
	Visual			Auditory			Visual			Auditory			Visual			Auditory			
	T	nT		T	nT		T	nT		T	nT		T	nT		T	nT		
F	91.39	88.99	95.52	87.45	81.53	83.39	86.27	81.53	89.92	85.23	81.99	83.39	76.11	40.91	59.09	75.55			
	84.60	92.76	92.83	89.78	88.36	81.99	75.78	88.36	85.23	81.99	83.39	81.99	57.10	71.89	72.52	63.57			
	95.21	93.60	91.02	92.66	84.11	80.08	78.47	84.11	80.08	90.66	90.66	46.03	52.63	70.44	46.03	71.89			
	94.49	94.06	97.02	89.77	88.15	80.66	92.03	88.15	95.14	80.66	80.66	74.77	67.92	80.20	80.20	64.07			
	96.25	94.86	92.19	87.34	90.95	89.02	89.69	90.95	89.02	73.18	73.18	83.65	77.87	75.08	75.08	55.00			
	91.73	93.56	97.75	94.10	87.79	96.43	90.03	87.79	96.43	90.26	90.26	86.57	79.61	91.23	91.23	78.02			
	96.96	97.66	93.55	93.39	89.84	89.16	95.39	89.84	89.16	89.18	89.18	92.91	78.79	76.76	76.76	78.30			
	93.00	85.47	89.75	93.27	81.75	91.31	89.98	81.75	84.62	91.31	91.31	84.70	74.92	75.21	75.21	62.49			
	92.95	92.62	93.70	90.97	86.56	85.08	87.21	86.56	88.70	85.08	85.08	75.23	68.07	75.07	75.07	68.61			
FM	3.93	3.75	2.84	2.73	3.62	6.40	6.76	3.62	5.43	6.40	6.40	15.96	14.05	9.05	9.05	8.54			
SD																			
R	97.30	80.81	90.76	91.13	72.03	85.72	94.70	72.03	80.31	85.72	85.72	88.03	50.13	58.01	58.01	73.52			
	93.83	97.08	93.88	84.78	95.49	78.05	87.54	95.49	89.08	78.05	78.05	75.95	85.46	74.94	74.94	58.48			
	94.94	89.00	92.47	89.23	82.17	85.15	91.70	82.17	85.15	78.81	78.81	78.84	71.68	65.41	65.41	59.94			
	95.99	87.79	92.65	86.27	83.02	84.26	93.81	83.02	84.54	84.26	84.26	76.29	53.67	62.10	62.10	45.31			
	90.89	91.75	92.73	87.64	84.28	82.28	88.03	84.28	90.30	82.28	82.28	81.25	77.35	48.16	48.16	52.54			
	88.56	84.34	98.01	95.99	68.05	95.58	85.02	68.05	96.68	95.58	95.58	76.35	52.09	93.16	93.16	84.12			
	97.19	90.62	95.03	93.82	87.48	89.42	96.01	87.48	93.99	89.42	89.42	90.93	51.94	85.90	85.90	81.23			
	94.33	80.22	94.42	82.75	78.07	74.00	92.70	78.07	90.36	74.00	74.00	88.26	66.20	65.82	65.82	58.47			
R	94.13	87.70	93.74	89.20	81.32	83.52	91.19	81.32	88.79	83.52	83.52	81.99	63.57	69.19	69.19	64.20			
M																			
R	3.05	5.72	2.17	4.40	8.65	6.87	3.90	8.65	5.31	6.87	6.87	6.18	13.56	14.79	14.79	13.89			
SD																			

RM = rare mean, RSD = rare standard deviation
 FM = frequent mean, FSD = frequent standard deviation
 N = 8

**Figures 2, 3, 4 Bar Graphs Representing Mean Variance
Accounted For by One, Two or Three Assumed
Dipole Source Models Across All Conditions**

Figure 2. Mean Variance Accounted For by a Three-source Dipole Model Across All Conditions

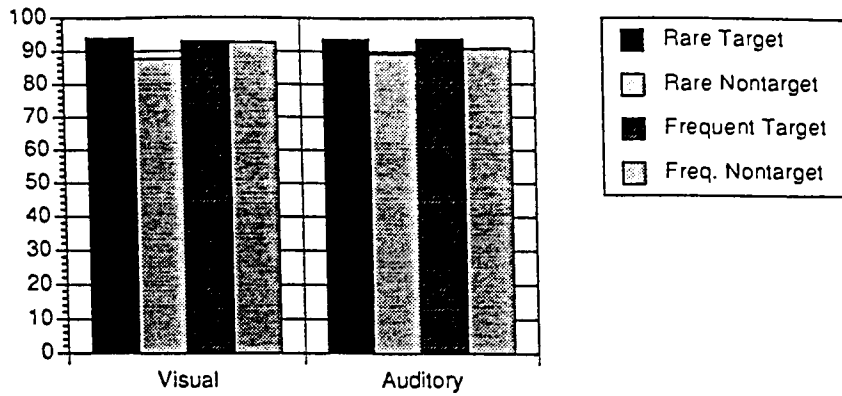


Figure 3. Mean Variance Accounted For by a Two-Source Dipole Model Across All Conditions

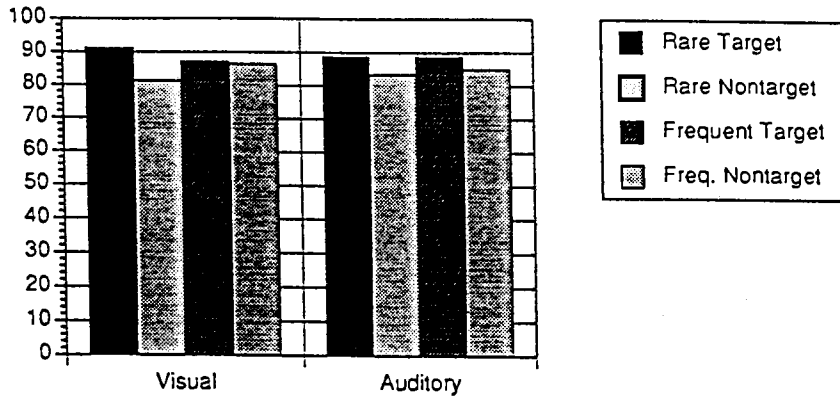
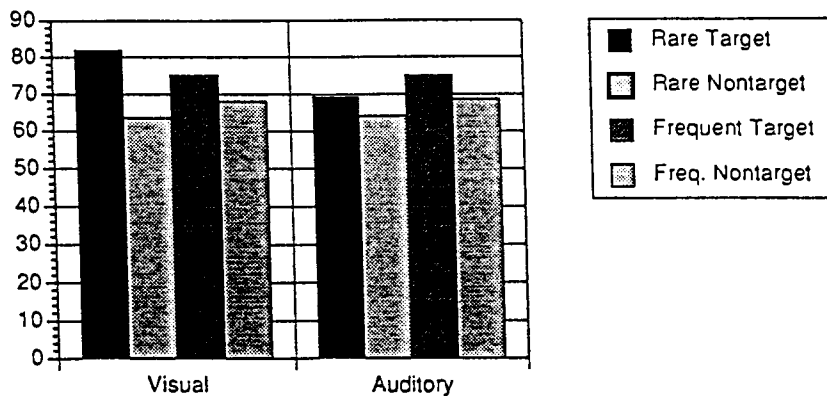


Figure 4. Mean Variance Accounted For by a One-Source Dipole Model Across All Conditions



To summarize, several patterns emerge in the VAF results presented in table two as the number of assumed sources decrease: the differences between modalities for rare target events increases since the decline in VAF is more precipitous for the auditory modality, the difference between rare targets and rare nontargets increases and increases much more dramatically for the visual modality, the difference between frequent targets and frequent nontargets increases, the difference between rare and frequent targets increases as does that for rare and frequent nontargets.

Furthermore, an interesting pattern in table two emerges when the data are examined for each task at both levels of probability. In the visual modality, rare target data was fit better than frequent target data. This difference is slight for the three-dipole model but increases as the number of dipoles decreases. Contrarily for nontargets, the *frequent* nontarget data was better fit than the rare nontargets. This pattern of reversal was similar for the auditory data, however, the differences are smaller. Thus, depending on the modality, the models accounted for target data from rare events better than from frequent ones while the opposite was true for nontarget events.

Table three demonstrates a similar pattern to table two when predictor models, evolved from the three-dipole source localization of the rare auditory and visual target events, are applied to data from all other conditions over a subsegment of time. The difference between target and nontarget fits is enhanced at both rare and frequent levels. As in the initial analysis results of probability effects for each task, rare targets were fit better than frequent ones. The reversal for nontargets, that frequent data was fit better than rare data, held for the visual modality but not for auditory modality. Across modalities, there is little difference in how well the models fit the data. However, in nontarget conditions, auditory rare data was fit better than frequent data; the opposite was the case for the visual data. Except for this, the pattern of fitting using the predictor models was the same as for the original results in table two.

Table 3. Mean Variance Accounted For by Predictor Models Using Three Assumed Dipole Sources

The overall mean VAF for each condition indicates the mean percentage of variance in the observed data which predictor models could account for.

The predictor models were derived from visual and auditory rare target event localizations in the original analysis using a three dipole model. Within each of these two conditions, sources for the predictor models were obtained by calculating the mean x, y, z coordinates resulting from the original analysis across all subjects for each of dipoles one, two and three. These three predictor dipoles were then used as assumed sources to model data in other conditions over a subset of time.

Table 3. Mean VAF by Predictor Models Using Three Assumed Dipole Sources

	TARGET		NONTARGET	
	Rare	Frequent	Rare	Frequent
Auditory	96.60	58.26	67.92	61.61
Visual	96.78	61.20	62.15	78.15

Figures 5. - 12.

Source Projections for the Three-Dipole Model For All Subjects Across All Conditions

All three dipole sources for each of the eight subjects are represented in each figure. For each subject, 1 green, 1 blue, and 1 grey dipole represent the three sources for that subject. Each figure demonstrates results for one condition.

The three views for each figure correspond to right side, posterior and superior views.

The pointwise residual variance plot under each figure indicates the point by point VAF for each time point over the 300 msec 'window' included in the analysis. The horizontal axis represents time; the vertical axis indicates residual variance between theoretical and observed fields. For example, points in time with low values on the vertical axis indicate time points where the model fits the data well.

Pointwise residual variances for all eight subjects are superimposed on the plot.

Source Projections in Head Coordinate System For All Subjects Using Three Assumed Dipole Sources

Figure 5. Rare Target: Auditory

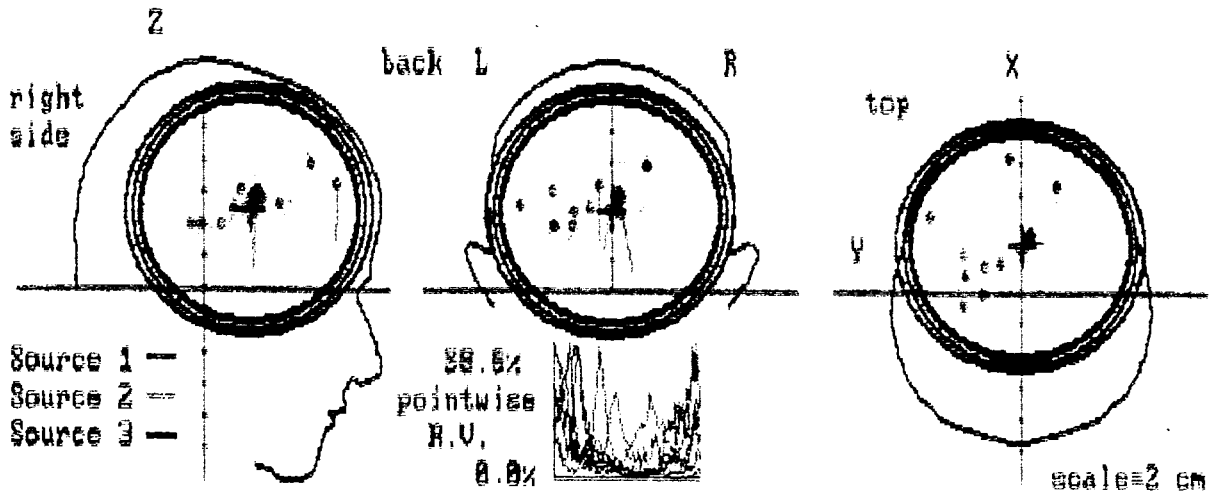
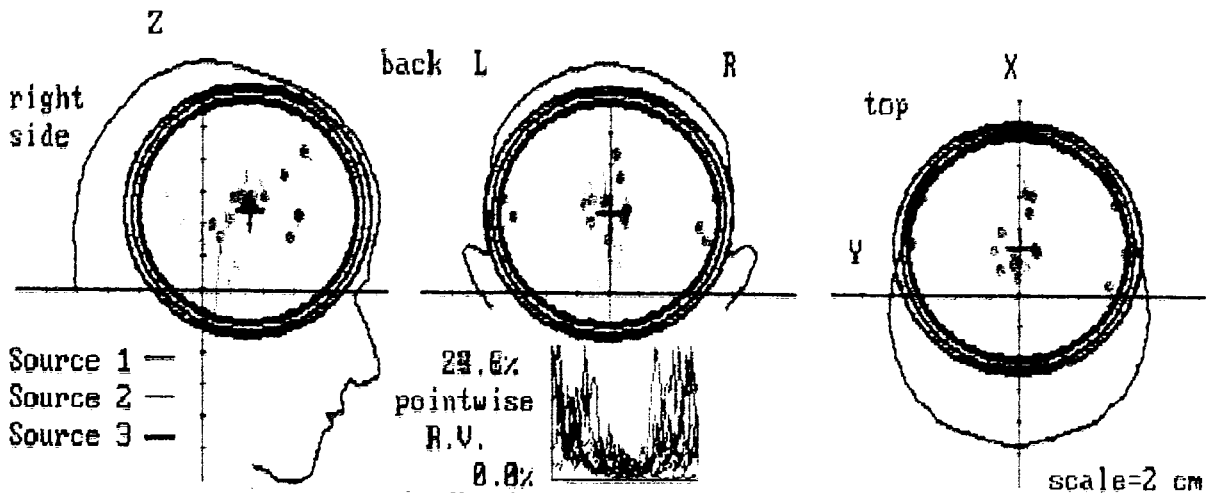


Figure 6. Rare Target: Visual



Source Projections in Head Coordinate System For All Subjects Using Three Assumed Dipole Sources

Figure 7. Frequent Target: Auditory

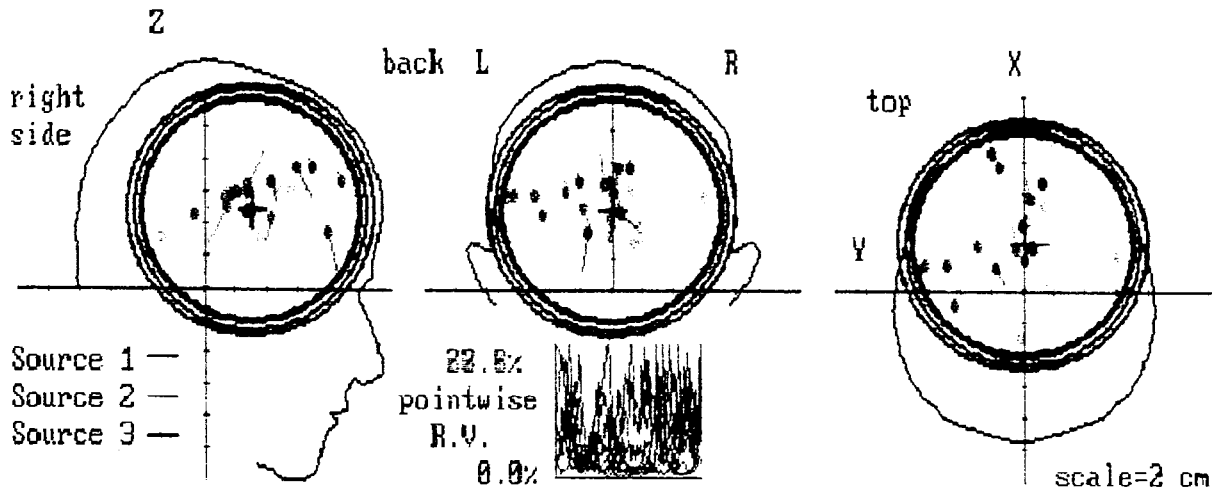
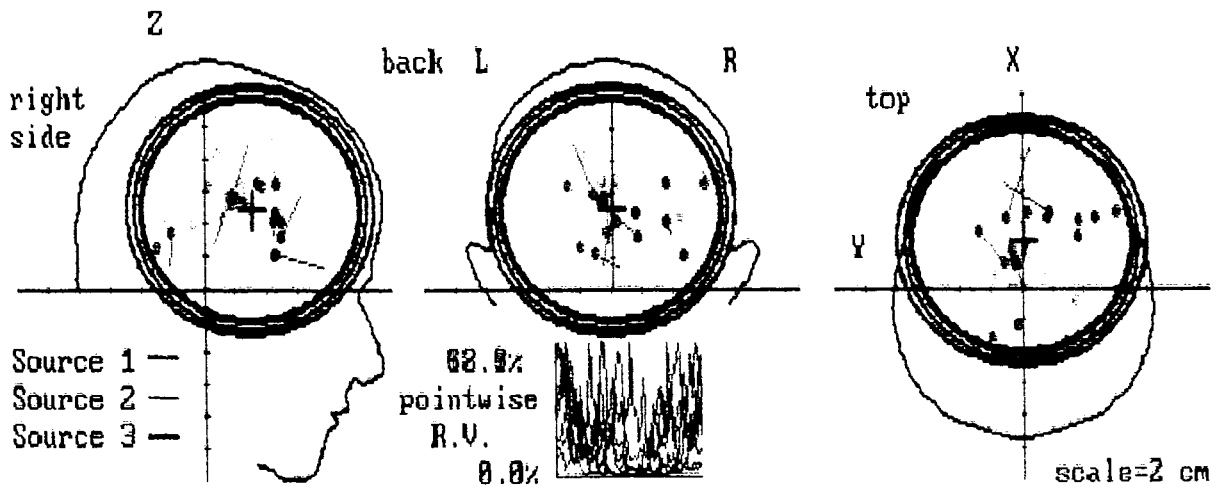


Figure 8. Frequent Target: Visual



Source Projections in Head Coordinate System For All Subjects Using Three Assumed Dipole Sources

Figure 9. Rare Nontarget: Auditory

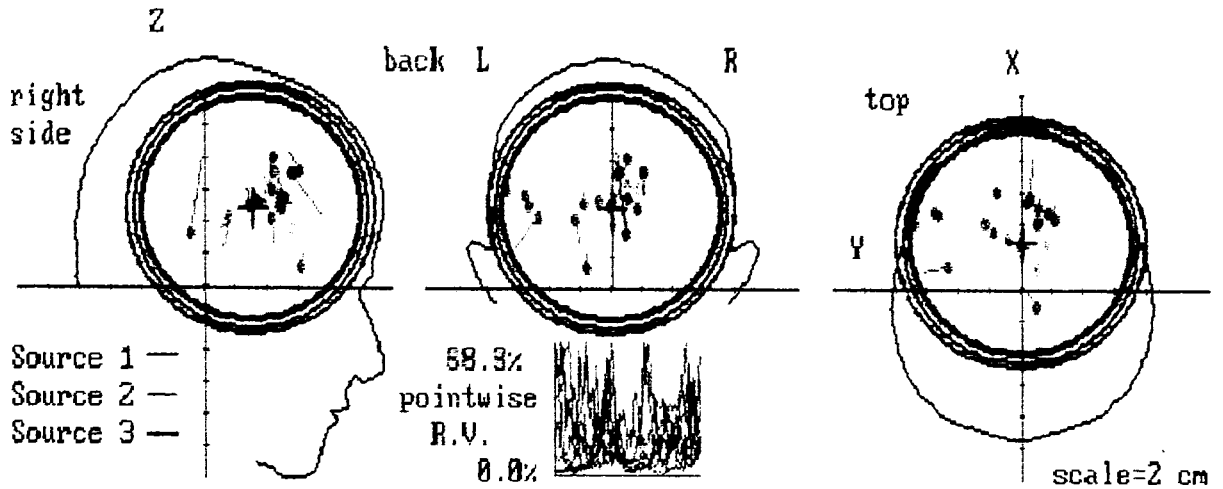
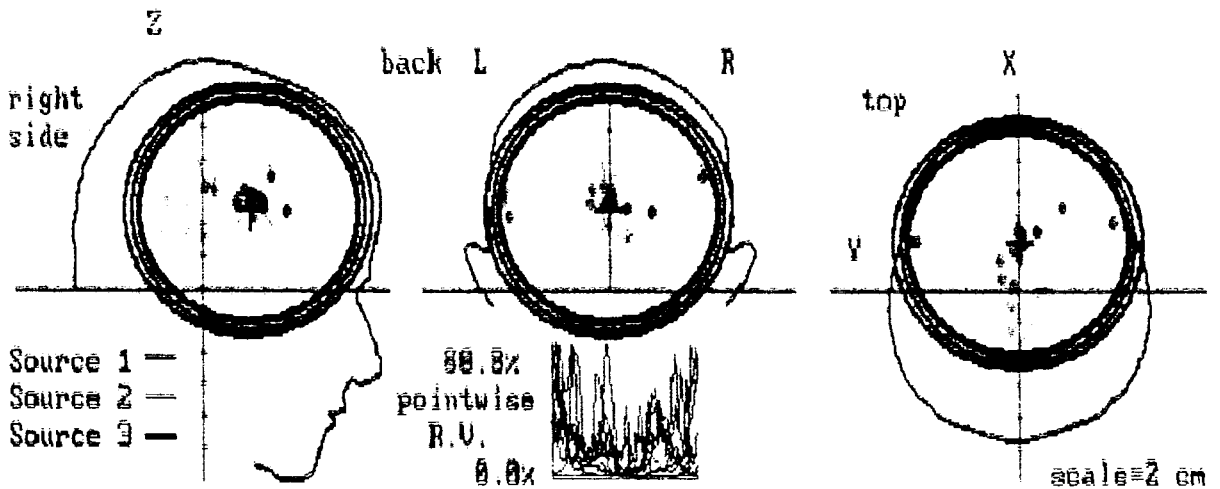


Figure 10. Rare Nontarget: Visual



Source Projections in Head Coordinate System For All Subjects Using Three Assumed Dipole Sources

Figure 11. Frequent Nontarget: Auditory

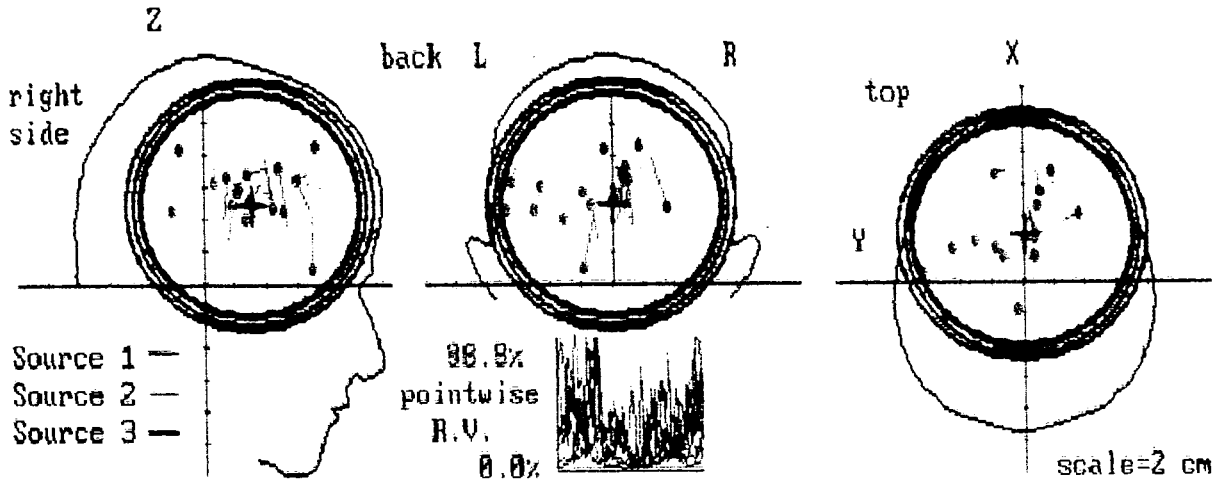
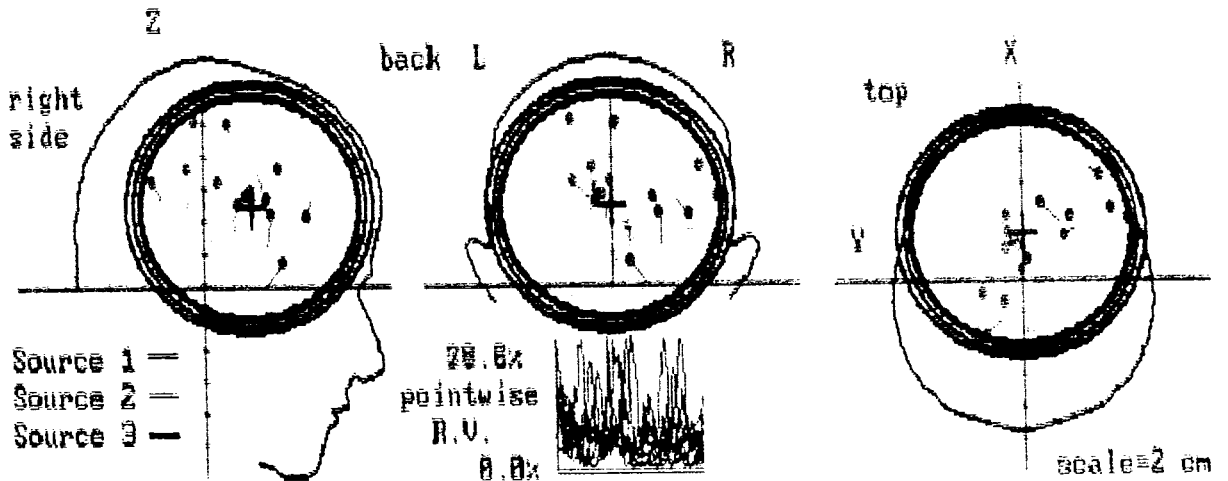


Figure 12. Frequent Nontarget: Visual



Next, specific localizations are reviewed for the three-dipole source model. The three-dipole localizations for all eight subjects in all conditions are represented in figures five to twelve. Rare events, represented in figures five, six, nine and ten, demonstrated the clearest organization of dipoles. When time point-by-point residual variances for these figures across the time interval were examined, both visual and auditory rare target conditions clearly produced a "window" or subset of time where the model fit the observed data very well. This was not the case in other conditions.

Figures nine and ten demonstrate that localizations of rare *nontargets* appear more similar to rare targets (Figures five, six) than do frequent targets (Figures seven, eight). Interestingly, frequent targets appear to have the most variable localizations.

In every condition, distributions of sources for auditory stimuli appear distinct from visual distributions. Auditory sources appear bilateral and more superficial than the more midline, sometimes deeper visual sources. As well, figures nine through twelve demonstrate that auditory sources appear to have more frontal distributions in the nontarget conditions than do visual sources.

While it is not possible to precisely identify putative anatomical structures, the localizations for the three-dipole model are physiologically plausible. The auditory dipoles may represent temporal sources while the visual sources could represent thalamic activation and perhaps deeper limbic sources. In both modalities there were frontal sources identified. One may speculate whether these correspond to the frontal contribution to P300 reported by Wood and McCarthy (1985).

Outlier sources residing in one of the concentric rings occur in almost all conditions but not for all subjects. These may be accounting for residual biological noise. When noise is present in EEG data, the spatio-temporal method is likely to exploit topographic regularities in this noise. Thus, the

spatio-temporal solution can contain spurious or displaced sources that account for topographically organized noise (Achim et al., unpublished). Source localizations for the one-dipole model consistently placed the dipole in the origin of the coordinate system. Likewise in the two-dipole solutions, one dipole was often placed in this location. Rather than representing physiologically plausible solutions, these dipoles are likely compromising source location to account for more variance.

To summarize the results of localization, lower residual variances and physiologically more plausible localizations suggest that the three-dipole spatio-temporal model is the most adequate of all the models used to characterize the cognitive events that occur during counted and uncounted rare and frequent events. However, because VAF values are quite high for all conditions, it is not possible to infer from VAF values alone whether or not neuronal sources of these different activities are distinct. To address this issue, specific localizations must be considered. While residual variances are very low for both visual and auditory data, the actual source locations appear distinct. As well, sources appear distinct between frequent and rare events. It is not clear whether sources for targets are different to those for nontargets since, for rare events, these appear similar.

Discussion

Implicit in the idea that wave forms have "components" is the assumption that ERPs represent activity of distinctly functioning neuronal aggregates (Donchin, 1978,; Johnson, 1988). That is, a component is a subsegment whose activity represents a functionally distinct neuronal population. Donchin (1978) more specifically defines a component as a neuronal aggregate whose activity has been distinctly affected by one or more experimental variables. The purpose of the present study was two-fold: to discern whether the P300 is characterized best as a unitary or multiple source component, and, to attempt to demonstrate that these sources vary as the experimental variables

of task and event probability vary which would imply distinct sources representing multiple modes of cognitive processing. The spatio-temporal dipole localization method was used for these purposes and, as with any mathematical model, the conclusions reached are only as valid as the model's underlying assumptions. Therefore a brief consideration of caveats will precede a discussion of the results.

The method used assumes that there exists a unique or at least a meaningful spatial and temporal combination of a maximum of three equivalent dipoles that generate a given spatio-temporal electrical field, and in order to model these, it is further assumed that the head can be represented as a spherical, homogenous volume conductor. The latter assumption is clearly erroneous for the following reasons: the shape of the head has many irregularities which vary from one subject to another, the human cranium is not spherical, the interior of the brain is comprised of distinct regions of varying conductivities, and the cranial conducting medium itself is not homogenous (Barth,1989). However, extensive modelling studies indicate that a multisphere model of the head, each sphere a homogenous, isotropic conductive medium, is an adequate compromise between mathematical simplicity and anatomical realism (Barth et al, 1989,;Stok,1987; Kavanagh, Darcey, Lehmann & Fender, 1978). Additionally, Stok (1987) reports that sphere radii and conductivities especially influence the strength of the EEG dipole and not its location or direction.

Likewise, the model of an equivalent dipole is used as an approximation of physiological sources that is mathematically tractable and yet is sufficiently realistic to be useful (Stok, 1986; Barth ,1989; Nunez, 1990). The spatio-temporal dipole localization model is an appropriate method to apply to the issues of the present study since this model characterizes components produced by multiple sources whose fields overlap substantially in both time and space; there is considerable evidence that the P300 is such a component (Courchesne et al., 1978; Munson et al., 1984; Ruchkin et al., 1987). As well, the researcher of the present study noted that, very often during recording, two prominent positive waveforms eventually were averaged as one large waveform.

In order to model multiple dipoles, simplifications have been made: current dipoles are assumed to remain fixed in space and vary their current in direction and strength over time (Barth et al., 1989; Stok, 1986; Nunez, 1990). One may question the degree to which this assumption of stationarity reflects reality. Nunez (1990) asserts that fundamental physiological data for a variety of EEGs recorded with depth electrodes, and a number of EP studies, indicate that distributed, *nonstationary* sources in the brain are the rule rather than the assumption. Additionally, since it is stationary events which are more likely to be stably recorded through averaging over time (Nunez, 1990), a model based on stationarity which fits well may have 'begged' the result of high VAF. These are serious concerns for the model which is simplified out of computational necessity; if location can vary for each instant in time as direction and strength do, then the number of unknown parameters greatly increases. This, besides producing an enormously complex computational task, would reduce the ratio of number of known parameters to unknowns which would result in unreliable localizations (Achim et al., unpublished).

Furthermore, a physical model involving multiple equivalent dipoles is only valid if the actual sources have, in fact, a dipolar configuration. Thus, where fits between observed and theoretical data were good, or where fewer dipoles could account fairly well for the data, it is not necessarily the case that other sources were not present. Other nondipolar sources may have been present. The assumption that neural sources can be modelled as equivalent dipoles is well supported by physiological evidence (see Appendix A). Despite this evidence however, the assumption is by no means unarguable. Based on modelling experiments comparing deep and cortical sources, Braun (1990) demonstrated that larger ERPs like P300 must have their electrical sources distributed mainly (>80%) in extended cortical areas. If the possibility of extended cortical areas being active synchronously is taken into consideration, the assumption of dipole-like current sources is no longer valid (Braun et al., 1990). Therefore, it should be recognized that the judgement of validity of models assuming dipolar sources is somewhat circular. The model

assumes dipolar sources yet this assumption, according to some, is violated when the sources are extensively distributed. In turn, the method is applied to determine if the sources are distributed.

As with all procedures using an inverse solution, the problem of nonuniqueness means that source parameters for alternate source combinations may differ substantially with little effect on the results. The fitting algorithm is prone to settle on parameters that are good but not optimum. In fact, the initial starting parameters may greatly influence whether or not optimal localizations have been found (Baumgartner et al., 1989). Because the localization results of the present study identified sources that were quite consistent across subjects for rare conditions and for modality, it is argued that the fitting procedure was successful at locating the optimum. In the future, increased certainty regarding nonuniqueness and the effects of initial starting parameters may be obtained through use of the Principle Component Analysis procedure outlined by Baumgartner et al. (1989). While this type of analysis requires limitations which are not physiologically necessary and therefore its validity is questionable, it may prove useful to objectively obtain starting values.

Furthermore, the procedure outlined by Baumgartner et al. (1989) appears useful to test the efficacy of two-dipole source models against three and to determine the degree of difference between different source localizations. The present study could have benefited from such a procedure; presently there are no formal criteria for determining the point at which a source localization is certainly distinct from another. As well, the present results demonstrate that the VAF using the two-dipole model was very close to that obtained from the three-dipole model. It is possible that the higher VAF in the latter is due to the third dipole accounting for more biological noise rather than localizing another significant source. Again, because there was some regularity in the placement of all three dipoles across subjects for some conditions, it is argued that the three-dipole model most effectively modelled the present data.

While the use of a predictor model appears to be a logical approach towards characterizing sources in the different conditions as distinct, the procedure has theoretical problems. Firstly, it is reasonable to expect that a predictor will fit other data less well than its own; by necessity the VAF would decline in the other conditions. Furthermore, it cannot be assumed that differences between conditions are due only to distinct sources; some may have more noise than others and this could have produced the decline in VAF. Lastly, it is not possible to assess the significance of the differences in VAF using the predictor model since the null case or probability of obtaining a good fit is unknown. Despite these serious shortcomings, the decline in VAF indicated by table three retained the pattern across conditions that was obtained in the original analysis presented in table two. One may speculate that the preserved pattern of differences reflect some degree of reliability at identifying true differences between distinct sources.

The present results suggest that the P300 is comprised of multiple sources and that these sources are distinct between visual and auditory modalities, and between rare and frequent events. What is less clear, is whether or not distinct neural sources are involved in the processing of counted, target stimuli and uncounted stimuli. Therefore, if the assumption holds that functionally distinct neuron populations are differentially activated by experimental manipulation, then from these results one may speculate that the P300 evoked during the classic oddball paradigm reflects not only multiple sources, but more than one type of information processing. Most clearly, it appears that the sources are dependent upon the sensory modality through which the information is delivered. Furthermore, when the type of task is held constant (counting or not counting) and the probability is varied, different sources appear to be involved. This is not to say that processing of each and every level of probability resides in different neurons (near the Grandmother cell?) but that it is possible that the cognitive activity involved with processing rare events is different from that for frequent events. While some have argued that the P300 represents a unitary mode of processing, (Simson et al., 1976; Snyder et al., 1980), the present submission that P300 is comprised of multiple sources is well supported by a plethora of other

studies (Courchesne, 1978; Wood et al., 1979; Squires et al., 1983; Okada et al., 1983; Johnson & Fedio 1984; Johnson & Donchin, 1985; Stapleton & Halgren, 1987; Smith et al., 1990).

Support for multiple distributed sources comes from the finding that localizations achieved using one or two-dipole models resulted in higher residuals than the three-dipole model, in particular, for the rare target condition. Furthermore, when the localizations are examined, the one and two-dipole models appear to be less anatomically plausible. It is worth noting that the single-dipole localization performed in the present study corresponds to the source which another group, Sidman et al., (1990) obtained using single time point, single-dipole modelling. That source localization, in the origin of the coordinate system, should perhaps be interpreted cautiously in view of the present findings that multiple sources in other areas seem to account for the data better.

Given the limitations of the model at precisely identifying activation of specific anatomical structures, it is useful to consider the derived sources in the context of what others have discovered using other techniques. Intracranial recordings have implicated the mesial temporal lobe (Halgren et al., 1980; Wood et al., 1979; Wood & McCarthy, 1985; Stapleton & Halgren, 1987). Others, including one group using neuromagnetic recordings, have interpreted these findings as indicative of a hippocampal source (Okada et al., 1983; Smith et al., 1990). Besides medial temporal lobe, Wood and McCarthy (1985) identified contributions from frontal lobe sources.

Evidence from lesion studies suggests that, because temporal lobe lesions have a task-dependent effect upon P300 (Daruna et al., 1989) but do not obliterate it, this region is involved but not is not alone. Johnson (1988b) found patients with standard en bloc lobectomy produced neither overall nor lateralized post-operative reduction of the scalp recorded P300 at central or parietal sites. While this would seem to argue against medial temporal lobe or hippocampal

sources, because in this type of resection the anterior half of hippocampus sometimes even more is removed, at least two to three cm of posterior hippocampus is spared (Knight, 1990) . If it is possible that only this portion of the hippocampus contributes substantially to scalp-recorded P300, then this structure remains a plausible candidate. Lastly, intracranial recordings have also implicated deep midline thalamic, and subthalamic sources (Velasco et al., 1986; Yingling & Hosobuchi, 1984).

While further verification would be required to draw firm conclusions, in light of previous studies, the localizations provided by the present spatio-temporal analysis appear to be anatomically plausible. The auditory sources appear bilateral and localized approximately in temporal lobe regions while the visual sources appear to represent midline, sometimes deep sources. One may speculate that these represent thalamic sources or thalamocortical connections. In both modalities several dipoles were localized frontally; perhaps reflecting the frontal contribution reported by Wood and McCarthy (1985). While it has been argued that definitive conclusions can only ultimately come from invasive procedures, this researcher disagrees. The value of modelling such as this in its present form is that it serves as a useful tool to set up a hypothesis about a complicated data set rather than to precisely answer neurophysiological questions. It has been suggested elsewhere that as the model evolves, source identification can become more precise. For example, Achim et al. (unpublished) recommend the systematic use of restrictions on where the optimization may place sources in the head. By forbidding sources from an area believed to contain one, either alternate admissible solutions will be identified or the failure to find admissible solutions will constitute strong evidence that the restricted area contributes to the data.

Whether or not the contribution of specific structures can be confirmed, the sources for auditory and visual data were clearly different for several reasons. Firstly, the localized distributions between modalities were clearly different. Secondly, as demonstrated in table two, the overall decline in VAF as the number of assumed sources decreased was greater (double) for the

auditory data than that of the visual. This would seem to imply that the auditory modality has more sources and therefore was penalized more quickly. More difficult to explain was the difference between modalities for rare events. It was demonstrated in table two that the difference in VAF for rare targets and nontargets was most affected by the number of assumed sources in the visual modality. One may speculate that the visual modality processes rare events differently. Snyder et al.(1983) reported that even when all aspects of visual, somatosensory and auditory stimuli were equated in a signal detection paradigm, the latency of P300 in the visual modality was longer and the amplitudes were greater than for other modalities. That group concluded that the visual modality accesses a common neural system in a different fashion from other modalities. If processing of visual stimuli for rare target events requires more resources than for nontarget events, then perhaps during the former there was less cognitive activity of other types occurring at the same time. Further, if it is possible that the models fit better when there are fewer different types of processing occurring (presuming more types of cognitive events would create a more complex or random pattern of sources to be fit) then this might explain why the VAF for rare targets remained quite high as the VAF for nontargets rapidly declined. Or, if it is true that the auditory P300 is comprised of more sources than the visual P300, then for auditory data the pattern of increasing difference between fits for rare targets and nontargets with less sources may be muted by the fact that the data is already not modelled adequately. Thus, the results demonstrate that while both modalities evoke multiple sources, the sources of the P300 for visual and auditory are distinct and, because these distinct sources are differentially affected by the different models, it is submitted that the distinct sources index functionally distinct components.

While the present study was not designed in a way that the results would clearly distinguish between different interpretations of the functional significance of the P300, it is interesting to speculate on what the results might mean in the context of candidate hypotheses. What is interesting about the results is that frequent targets appear to produce the most variable localizations, somewhat more so than frequent nontargets and certainly more so than rare

nontargets. One might have predicted that uncounted stimuli would be associated with more variable, less stable brain events over time since subjects are not engaged in a consistent task (counting). Perhaps subjects are engaged more vigilantly with frequent non-targets than frequent targets because during the presentation of the former, subjects are *awaiting* a rare, unpredictable and relevant event; attention may be quite focused despite the frequency of the event. This interpretation of the results is consistent with Verleger's reinterpretation of Donchin's Context Updating hypothesis of P300. Unlike previous assertions that rare events produce large P300s because they are unexpected events, Verleger has proposed that P300 indexes context closure (Verleger, 1988). P300-eliciting stimuli are those events that close the "context" and unlike previous interpretations, P300s are invoked when expectancies are *fulfilled*, not when they require revision. In this interpretation, rare events are actually the expected events and now 'expectancy' refers to 'awaiting' or the resolution of suspense. Frequent nontargets may carry more meaning or involve more processing than frequent targets because the consequences of correctly expecting the rare target or awaiting the rare target are more important than correctly awaiting a rare, nontarget event. Again, if more important or demanding cognitive activities produce a more organized source pattern over time, then this interpretation might explain why the three-dipole model accounted for nearly the same amount of variance in frequent non-target conditions as in frequent target conditions.

It was also demonstrated in figures one, two, five and six that the rare nontarget sources appear to resemble the rare target ones more closely than the frequent target sources in figures three and four do. This suggests some priority of processing of rare events over whatever process is involved in counting during the P300 paradigm. Perhaps when the target is frequent, counting becomes easy or a relatively automatic process and the subject is able to engage in other cognitive activities simultaneously. This might explain the relatively variable localizations for this condition. Or, it is possible that the activity related to processing of rare events is more synchronous and dipolar and therefore more reliable localizations resulted. It is well established

that rare events produce large amplitude P300. A larger amplitude event is likely to be more stable over time, hence localizations are more likely to be consistent over time (Karniski & Blair, 1988).

Usually, since most studies only employ one level of probability, only the target event is the rare event; the nontarget is necessarily the frequent event. Because event probability and task (counted) are confounded in such cases, what is referred to as the 'target effect' (largest amplitude to rare target events) may largely reflect the processing of the rarity of the event. The power of the design of the present study is that two levels of probability allowed for the comparison of both rare target and nontarget events. In the present study, it was noticed during recording that rare nontargets produced high amplitude waves. Target and nontarget P300s appear more similar when probability is held constant. This is precisely the finding of Duncan - Johnson and Donchin (1977). They demonstrated that target and nontarget stimuli, equally unexpected, yield the same P300 amplitude. Insightfully, they noted that, if subjective probability is comprised of a priori probability and local sequence effects, then the first nontargets which occur after the rare target are perceived as rare events. That is, the first of a series of frequent events is perceived as a rare event. These researchers were perceptive in realizing that, while there appears to be an orderly relationship between a priori probability and P300 amplitude for task-relevant stimuli, the effects of stimulus sequencing are obscured by the process of averaging all EEG records associated with a specific stimulus. Because the nontarget event is usually designated as the *frequent event*, *obscuring would have a more pronounced effect on the amplitude of the nontarget*. Therefore, as was demonstrated by Duncan - Johnson and Donchin (1977) and as was demonstrated in the present study, target and nontarget data appear similar when the events are rare.

This finding may be interpreted in terms of Donchin's context updating hypothesis of P300. If the interpretation of this hypothesis is that P300 is associated with updating of the schema, then the degree to which an event requires a revision of the model will determine whether a high amplitude

P300 occurs or not. It makes intuitive sense that rare events might require more updating so that if P300 is the manifestation of the processing activities that are involved in the maintenance of representation of external events, then where representations are weak (rare events), more updating must occur. The assumption that a class of processes are concerned with the maintenance of a proper representation of the environment is one commonly held among cognitive theorists (Donchin & Coles, 1988). If such a process lacked an updating component, it would be useless because it would fail to meet the most basic requirement- that of reflecting the ongoing context. The sensitivity of P300 to the probability of events adds plausibility to the suggestion that it is associated with maintaining the schema and the results of the present experiment support this interpretation.

If the ultimate goal is to understand the process which manifests itself as the P300, then description of the relationship between variables that control the output of this process (amplitude, latency) may not be so useful; what we seek to characterize exists between inputs and outputs of the P300. It is possible is that the functional significance of a component is best understood by knowing which anatomical structures produced it. Of course this approach is dangerously circular since we require a priori knowledge about what function various structures perform.

In conclusion, the procedure employed here has been useful since it was possible to identify sources of neural activity or functional components which were associated with various experimental variables. Before a waveform such as the P300 can be functionally characterized, it is crucial that functionally distinct but spatially and temporally overlapping components be identified. The results demonstrated distinct components for auditory and visual P300s. As well, the sources which contribute to the P300 evoked by rare events appear distinct from those to frequent events. Because rare nontarget P300s resemble rare target P300s, it is not possible to say whether the different tasks (counting or not counting) involve functionally distinct

components. Furthermore, it is possible, given the results, that what is referred to as the 'target effect' may, in large part, be due to the rarity of the event and not the fact that it is counted.

It was also demonstrated that the multiple (three) dipole model was the most adequate at accounting for the data in all cases. There were differences in the residual variances across conditions and it became clear that these differences increased as the number of assumed dipoles decreased. The implications are that an inadequate number of modelled sources may produce apparent differences where, given more assumed sources, there might be none. Given this possibility, the present results which suggest distinct sources should be viewed cautiously until a spatio-temporal model utilizing more sources is applied to the data.

Finally, it is unarguable that scalp-recorded ERPs are produced by patterns of activity associated with different populations of neurons. Whatever those activated sources are, the patterns of interaction over time and space reflect intimately the transmission of information and the resultant information-processing activities within intracranial structures. The ultimate utility of spatio-temporal dipole localization models is to establish patterns of timing, sequence, identity or non-identity of brain generators which are invoked by different and systematically varied events. This knowledge may in turn eventually lead to a meaningful reinterpretation of the electric data and to correlations with cognitive data that can provide mutual corrections of hypotheses in both fields.

APPENDIX

THEORETICAL CONSIDERATIONS OF THE SPATIO-TEMPORAL DIPOLE MODEL

The Nature of the Source

In order to estimate source location from scalp-recorded electrical potentials, it is necessary to make some assumptions about the nature of the source. Brazier (1949, c.i. Henderson et al., 1975) proposed that an electric dipole within a spherical conductor would serve as a useful model to account for sources generating the electrical fields observed at the surface of the head. She indicated that electrical field theory can be employed to deduce the locus and orientation of the dipole (source) from the pattern of potentials it creates at the surface of the sphere. Therefore, the initial assumption of the dipole localization method is that a generator of electrical activity within the brain can be conceptualized as a dipole. Justification for this assumption is considered next.

It is generally accepted that EEG is mainly caused by transmembrane current due to synaptic activity that arises in dendritic tree structures of neurons (Stok, 1986). At sites of synaptic activity, this transmembrane current is the result of an actual exchange of electric charges. The active region of the membrane is negative with respect to the inactive region and a resultant current then runs longitudinally in the extracellular and intracellular fluids. When a potential change occurs at one end of an elongated neuronal structure and thus draws current from the other end, the structure appears polarized; i.e. it becomes a dipole (Schlag, 1973). An electric dipole is a theoretical entity consisting of a positive point charge (+q) and an equal-and -opposite negative point charge (-q) with the two charges being separated by a very small distance, d (the dipole moment or strength, is defined as qd). The entire neocortex consists of approximately 10^4 to 10^5 macrocolumns of neurons which may be conceptualized as a dipole layer covering the entire brain surface (Nunez, 1990).

In reality, what is recorded by EEG does not correspond precisely to simple one-dimensional dipoles. for several reasons. Resolution of the dipole even at the macrocolumn scale which contains approximately 100-300 neurons (Regan, 1989) is beyond current technology. As well, since the scalp electrode is separated from neural sources by both distance and the poorly conducting skull, the spatial resolution of the scalp recordings is much less than 1 cm (Nunez, 1990). This means that surface potentials recorded by a scalp electrode are due to neural sources averaged over a surface of cortical tissue that is typically at least several centimeters. Therefore, single electric dipoles are not what is recorded by EEG. Instead, the distant electrode 'sees' a dipole when neurons within a small area of cortex are simultaneously active. If the area is small enough, it may be conceptualized as an 'equivalent dipole' (Henderson et al., 1975).

Direct evidence for the assumption that an equivalent dipole can account for the observed surface electric potentials has been obtained experimentally. When a measuring electrode follows a track perpendicular to the surface of an active patch of cortex, there is an observed negativity on one side, positivity on the other and an abrupt polarity reversal in between (Stok, 1986). Furthermore, the dipole model is physiologically plausible. Pyramidal cells of the neocortex are located in orderly palisade arrangements with cell axes perpendicular to the surface.*

Assuming that EEG records intracellular currents in the direction of the cell axis, then a flat patch of cortex comprised of rows of palisades that are activated in a coherent fashion will, seen at a distance, act as a current dipole (Stok, 1986).

*It is very unlikely that cells with a predominantly radial and symmetric arborization of dendrites (spiny satellite cells, Golgi Type-ii cells) contribute to vertical current flow since their processes extend sphere-like and the synaptic events produce closed fields (i.e. which produce no externally detectable signals due to self-cancellation effects). The transmembranous currents produced by APs are also very unlikely to sum up to spatially separated extracellular sinks and sources (Petsche, Pockberger, & Rapplesberger, 84)

Volume Conduction and the Forward Problem

Accepting that generators within the brain can plausibly be modelled as equivalent dipoles, what is required next is a model to account for the surface electric potentials which dipoles of a given location would create. This procedure is the forward solution.

The head is modelled as a volume conductor comprised of four concentric spherical surfaces of different resistivity that represent brain, cerebrospinal fluid, skull and scalp. A computer program employs the equations of field theory to calculate the electrical field at the surface of the conducting volume given the locus, magnitude and orientation of a dipole within it. The calculation of scalp potential from known sources provides a unique solution and is the basis for solution to the inverse problem.

The Inverse Problem: Dipole Localization

The process of source localization begins with the forward solution: a series of assumptions about the location of the dipole at each fixed point in time is made and resultant surface potential distributions are calculated. These theoretical surface potentials are compared to measured surface potentials (from the EEG). A nonlinear optimizing computer algorithm employs an iterative fitting procedure to vary the co-ordinates of the theoretical dipole incrementally until a minimum summed squared difference between observed and theoretical potentials is obtained. Thus, the procedure finds a dipole whose field is a "best fit" to an observed field.

Each dipole used to model the source of the EEG is given by six parameters: three to establish its position and three to define its orientation within a three-dimensional sphere where the x axis represents nasion to inion, y axis= left to right preauricular and the z axis is the vertical with origin at x, y intersection. A seventh parameter, dipole moment is calculated as the vector sum of orientation of x, y, z values.

Spatio-Temporal Modelling

While the concept of a single equivalent dipole has been useful for source localization, it is not an adequate representation of the complexity of anatomical structures (Weinberg et al., 1986). When, for example, the potential distribution at a specific latency results from the simultaneous activity of distributed sources, the assumption that a single equivalent dipole can adequately represent the source is violated (Achim et al., unpublished). The difficulty in employing a multiple source model to correct this violation is that the number of free parameters (6 per dipole) or unknowns approaches the number of data values (21 recording channels per time point). Under these circumstances, even low amplitude residual noise will be accounted for with resultant unreliable localizations. Thus, the problem of localizing multiple distributed sources is more adequately modelled by simultaneously using data from a series of consecutive time points. That is, rather than applying dipole localizations to individual time slices of EPs, all data points over a specified range of time are used.

The spatio-temporal sources model (STSM) assumes that EPs involve neural sources which remain active over a given time interval, so that while equivalent dipole sources may change their strengths, location and orientation remain constant over the prescribed time interval. The use of these constraints allows a more practical inverse solution for multiple dipole sources, since, if dipoles are allowed to change location and or orientation, the number of unknown parameters is greatly increased as is the complexity of the problem.

Although spatio-temporally organized noise prevents the exact localization of temporally overlapping multiple sources, reliability testing of the STSM approach suggests that this method is reliable for decomposing spatio-temporal EEG data into contributions from distinct brain areas. However, in contrast to the Forward Solution, any inverse solution including those employing the STSM approach, has no unique solution. That is, a number of distinct solutions (source localizations) are simultaneously compatible with the data. As a result, it is not possible to

unequivocally specify the source distribution throughout the brain without additional information. However, the methodology is in evolution and some innovative approaches have been suggested. For example, by placing limitations on where sources may be localized, alternative source combinations may be identified. Or, the inability to produce a solution could build a negative case in favour of another putative generator.

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