1-1-1996

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April 10, 1996

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For centuries people have recognized that as family members age they become more forgetful, have difficulty attending to situations, and experience limitations in problem solving situations. Fischer (1951) was one of the first to identify a relationship between dementia and carotid stenosis, a blocking of the carotid artery typically due to accumulated cholesterol. Since that time a great number of studies have been designed to identify a clearer relationship between carotid arterial stenosis and cognitive function. It has been reported that following the clearing of the occluded carotid artery, a surgical technique called Carotid Endarterectomy (CEA), patients notice an improvement in memory function.

To date many studies have been performed in attempt to identify cognitive changes following a CEA. Unfortunately, the results of these studies have been conflicting and controversial (see Cohen, 1987 for a review). Two deficits exist in previously performed studies that contribute to the lack of conclusive findings. The previous studies relied upon modified versions of the completely randomized experimental design in which true randomization was not obtained. Such a practice brings with it many limitations, primarily in the area of unaddressed threats to validity. Many of these threats could be masking treatment effects. Cohen cites threats to validity, such as the presence or absence of practice effects, as the reason that significant results are found in some studies and not others. A second limitation of these studies is that they have relied upon standard neuropsychological batteries. These batteries have been designed to identify gross cognitive deficits in people with profound neurological dysfunction. Yet, reports of patients and physicians indicate that the cognitive changes that are taking place are relatively small, but still significant in the eye of the patient as they have an impact on the quality of life. Reports by patients and their families who have experienced CEA (Fischer, 1995) have consistently supported that cognitive improvement is taking place following the surgery.

The diminished cognitive function and subsequent improvement in CEA patients do not appear to be global in nature. More likely, dysfunction appears to be localized to specialized function within memory while other memory functions remain unaffected. This is referred to as a dissociation. Memory dissociation is certainly not a new phenomenon. Impaired and intact memory functions are typically seen within many populations like that of amnesiacs (see Schacter & Tulving, 1994 for a review). Memory dissociations have even been identified in normal elderly populations (e.g., Glisky, Poster, & Routhienaux, 1995). Such deficits would not be likely to show up on standard neuropsychological batteries. A better alternative would be to test specific areas of cognition known to be components of memory function.

The purpose of this proposed study is to determine if a CEA improves cognitive function. Tests designed to isolate the cognitive functions believed to be the most affected by carotid arterial stenosis will be used. In addition, instead of trying to work around the limitations of a modified randomized design, I plan on working with the limitations through the use of quasi experimental methods. I predict that through these changes the limitations of previous research will be minimized. Such a design would maximize the likelihood of detecting the presence of improvement in cognitive function following a CEA.

It is important to identify the aspect of memory most likely to be affected by carotid arterial stenosis. Cerebral Blood Flow (CBF) studies have shown that patients with more than 75% stenosis experience decreased CBF in the parietal, occipital, and temporal lobes (Cohen, 1987). Following a CEA an increase in CBF is observed in these three areas. The temporal, parietal, and occipital regions of the brain have also been implicated in priming (Keane et al., 1991; Polster et al., 1991; Squire et al., 1992). Therefore, it seems likely that carotid arterial stenosis limits priming memory.

Priming, the facilitation of retrieval provided by prior exposure of the item or a related item, is an integral aspect of memory function. For example, if you had to go to the store to pick up 5 items, even if you didn't write the items down you might remember them. As you walked down the aisle by glancing at cookies, you may naturally think of milk and remember to buy it. In this example, cookies primed your memory for milk.

To evaluate priming, considered to be a part of implicit memory, a standard implicit memory test will be used. Implicit memory, e.g., unconscious priming effects, can be functionally deficient independent of explicit memory, e.g., recall or recognition (Schacter, 1994). The specific implicit memory test that will be used was designed by Winocur (1996). This paradigm has been shown to identify minimal implicit memory deficits in the elderly.

Patients report memory impairment before CEA and memory improvement following CEA. Cerebral Blood Flow studies identify neurological dysfunction before CEA that improve following CEA. The cognitive function of priming has been linked to the same parts of the brain believed to be most effected by carotid arterial stenosis. A priming paradigm is available that has been successful in the past at identifying mild priming deficits when all other memory functions were unimpaired. Therefore, I predict that I will find priming deficits prior to patients needing CEA. Priming deficits will be minimized in patients who have had CEA.

Methods

Participants

Forty participants will be sought as volunteers from the practice of Associated Vascular Surgeons, Easton, Pennsylvania. Inclusion criteria are as follows: (1) 20% or more occlusion of at least one carotid artery as determined by Doppler testing (performed by a certified Associated Vascular Surgeon's technician); (2) English-speaking and literate; (3) adequate visual and auditory acuity (by patient report).

Patients will be considered ineligible if there is a prior history of a condition or situation that would directly decrease cognitive function (e.g., alcoholism, drug abuse, head injury).

The subjects are expected to be primarily above the age of 60 with an average to above average socioeconomic background. An attempt will be made to collect data from participants of both genders and multiple ethnicity.

Materials

To evaluate the degree of carotid arterial stenosis testing will be performed by Doppler imaging technicians. The Doppler imaging technique is a standard medical test designed to measure the amount of plaque in the carotid arteries.

The participants will be presented with a list of 40 words to remember. The words are identical to those used by Winocur (1996) in a previous study.

Procedure

Patients will be administered a control test designed to rule out all responses that could be answered spontaneously without prior exposure to the word list. On a separate day the patients will view a list of 40 words on a computer monitor. The list of words will be randomly presented one at a time for five seconds. Participants will be asked to report the number of vowels in each word. The participant will then be shown the same 40 words again and asked to read each word aloud. Following a 10 minute delay during which time another nonverbal task will be given, participants will be given a word stem completion task. Participants will see word stems like TRA_ _ and DRI _ _ and will be asked to say the "first word that comes to mind." The research assistant will record the answers given by the participants.

Design Issues

Randomization is one of the primary methods for determining internal validity in a study permitting a causal inference to be made when significant results are obtained. However, in the case of this study, it would be highly unethical to deny patients a treatment that has been shown to prolong life through decreasing the likelihood of a stroke. Patients with more than 75% of their carotid artery occluded are eligible for a CEA (Fischer, 1995). According to the physician who will be providing the subjects for this study, very few patients decline this risky surgery when they consider the hazards of not having the surgery.

Not only is it impossible for subjects to be ethically randomized for this study, no other control group, in the pure experimental sense of the word, is available. Together, these limitations require the use of a quasi-experimental design to infer causality by ruling out viable explanations of the studies' findings.

In the past, a common method of study has been the pretest treatment / posttest design. However this method is inadequate given the high anxiety levels of the patients preparing for major, life threatening surgery. Unlike elective surgery, patients who are eligible for CEA are normally only given a few days to a week to prepare for surgery (Fischer, 1995). Thus, it has been common practice to give the pretest to subjects the day before the procedure. It is commonly accepted in the field of cognition that anxiety has detrimental effects on cognitive function. An additional limitation with this design is that of multiple testing effects. In many studies in the past (e.g., Perry, Drinkwater, & Taylor, 1974) subjects were given the identical version of the test as a pretest and posttest. Even if a different version of the same test was used, practice effects could still be present. In the area of cognitive research, it is unacceptable to repeat memory tests due to the risk of practice effects. This is particularly true when working with test of implicit memory. Multiple tests could result in the participant recognizing the tie between the list of words they were asked respond to and the word stem completion task. In studies that have avoided these threats to validity (Matarazzo, Matarazzo, & Gallo, 1979), a link between memory dysfunction and carotid arterial stenosis was not established, leading many to question whether cognitive changes are taking place at all.

One of the most pressing concerns about completing this study is formulating a design that will eliminate alternative rival hypotheses while remaining within the limited confines of the study. The optimal design for this study is the Regression Discontinuity Design (Campbell and Stanley, 1966). The Regression Discontinuity design replaces a pure experiment "by examining the regression line for a discontinuity at the cutting point which the causal hypothesis clearly implies" (p 62). A difference in the intercepts of the two regression lines (one for the "control / no treatment group" and one for the "experimental" group) should exist when a treatment effect is present (see figure 1). If it were possible to obtain an adequate size sample of patients, for example, patients with 73 % occlusion who are ineligible for CEA and patients with 76% occlusion who just had CEA, it would be easy to see if a difference is present in memory function between the two groups. However, such grouping is not possible due to limited numbers of subjects. Grouping by larger groups of 65 - 74 % occlusion versus 75-84% occlusion could bring with it a variety of other problems like systematic variance of no experimental interest and unsystematic variance that decreases the power of the study. Regression discontinuity by-passes these problems by relying upon the regression line of the control group to estimate the performance of control group patients with 75% occlusion. Their results are compared to the regression estimate of performance for treatment group patients with 75% occlusion. Only a difference in the two regression intercepts can provide support that a significant difference is present. The slope of the line will not indicate the presence or absence of a treatment effect since a curvilinear function of cognition could be present in untreated patients. For example, if as stenosis increases, cognition decreases, there could come a point at which the decrease in cognition is no longer linear, it could simply level off. If this were the case, and the point of intervention just happened to be selected at the point of a change of slope, no intercept difference would be present even though a change in slope could be observed (see figure 2).

The Regression Discontinuity design will eliminate the concern of practice effects in this experiment since subjects will only receive cognitive testing once. In addition, the concern over anxiety's effect on cognitive function can also be eliminated since subjects will not be tested while waiting to have surgery. Instead, the control group will consist of people with stenosis of less than 75% who are ineligible for surgery. The treatment group will consist of people who have already had surgery, thus anxiety should be at a minimum.

This design is not without its limitations. Several concerns need to be actively addressed. Campbell and Stanley consider instrumentation as a common limitation in the regression discontinuity design. However, this is not expected to be a limiting factor in this study since the cognitive testing will be consistently administered to the subjects regardless of their status of stenosis. Mortality would be a problem if a follow up study was going to be performed, but no follow up is planned. Most importantly, the Regression Discontinuity design functions optimally when the cutoff point between control and treatment group is clean and crisp as in this proposed study. The assignment to the treatment group will be based solely on the reports of stenosis given by the Doppler Imaging technicians who are off site and are unaware that a study is being conducted.

A final threat to validity that needs to be addressed is that of selection- maturation interaction. Given that the regression discontinuity design makes use of a linear regression fit, if the population's underlying function is curvilinear and not linear, an intercept difference could be observed when no treatment effect is present. There is neither physiological nor cognitive evidence to support that memory would get slightly better as carotid arterial stenosis approached and past the 75% mark. Thus, selection- maturation bias is simply not a plausible threat in this study.

Expected Results

I expect to find results similar to that found in figure 1, such that following CEA patients experience an improvement in priming.

The results of this study could have a positive impact in multiple disciplines. In the field of cognitive psychology, researchers could have an easily accessible subject population to further examine the dissociation of implicit and explicit memory. Amnesiacs are typically used to study implicit and explicit memory dissociations since amnesiacs have impaired explicit memory and spared implicit memory. Carotid arterial stenosis patients have impaired implicit memory and spared explicit memory. In the field of neurocognitive psychology more support would be provided for the role of the parietal, occipital, and temporal lobes on the function of priming. Further research in this area could result in a better understanding of the neurological substrates involved in priming. In the field of medicine, physicians could provide patients with more information that could assist the patients in determine life style choices (e.g., change in diet and exercise), pharmacological choices (e.g., the use of cholesterol lowing drugs), and/ or surgical choices (e.g., CEA) that could assist in minimizing memory deficits as they age.

There are many benefits that could come from a study on cognitive changes in patients with carotid arterial stenosis. By focusing on specific cognitive functions most believed to be affected by carotid arterial stenosis and by implementing a quasi-experimental design a clearer understanding of what is happening with these patients can be obtained.[1]

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1 This does not mean that it is not possible for memory function and occlusion to have a curvilinear relationship. The possibility of an underlying curvilinear relationship between memory and carotid arterial stenosis could be evaluated through qualitative observations of the participants when they volunteer for the study. In the event that patients report that they feel their memory function is improving before getting worse a second study could be performed to verify or disconfirm this potential threat to validity.

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