Cognitive Neuroscience and Neuropsychology
Lecture 1 Notes

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1 Methods

1.1 Introduction

A multitude of research methods are necessary to begin to obtain a holistic impression of some given brain function. These methods may be designed to gather information at neuroanatomical, neurochemical, levels neurophysiological, in addition to behavioral information. Information gathered in any investigation in the realm of cognitive neuroscience or neuropsychology can be biased towards collecting a specific type of information by the choice of population and method, and so a single phenomenon must often be approached in multiple ways using multiple methods. The technique of examining whether all data obtained from a set of interrelated experiments lead to the same conclusion is known as the method of converging operations.

The ensuing discussion will focus on specific subject populations and specific research methods.

1.2 Populations of Research Participants

The following three major types of populations each have differing advantages and disadvantages.

1.2.1 Patients with Circumscribed Brain Damage

The method of comparing individuals with brain damage with those without is ancient; in Roman times, it was first discovered that the brain is the centre of thought after it was observed that gladiators lost cognitive ability only after trauma to the head. If damage to a particular brain region results in an inability to perform a specific mental function, as in the lesion method, a link therein may be inferred. This method has lead to the discovery that particular mental functions can be specific regions of brain tissue, a concept called localization of function.

Localization of function was predated by the now obsolete theory of mass action of the early twentieth century, which posited that each portion of the brain contributed to all mental abilities; the theory of mass action was initially supported by the fact that increasing amounts of brain damage leads to increasing loss of mental ability and was discredited only after more advanced tools and methods lead to the ability to demonstrate localization of function.
It is important to remember that localization of function must be supplemented by a great degree of communication between different parts of the brain in order to be able to produce the sum total of mental ability that is observed. For example, damage to one area of the brain may disrupt not only one type of mental function but also disrupt communication between other parts of the brain and cause a gamut of deficits, not all of which are in functions localized entirely to the site of damage.

**Uses of the Lesion Method** The main strength of the lesion method is that it allows a specific region of brain tissue to be directly linked to a specific aspect of mental processing. Artificially induced lesions are extensively used in animal experiments and have led to a wealth of understanding. However, for many reasons, such experiments cannot be performed on humans; major advances in understanding of the human brain have been mediated by patients who sustained brain damage in some accident (and who are cooperative in being studied).

When using the lesions method, one may emphasize either knowledge about neural substrates or knowledge about cognitive function. If the former, a good experimental group will be composed of a group of individuals whose brain damages are as similar as possible in location, extent, and, in some cases, cause; if the latter, a good experimental group will be composed of a group of individuals whose behavioral symptoms are as similar as possible.

A particularly powerful method research method, **double dissociation**, allows one to determine whether two cognitive functions are independent of one another. A double dissociation occurs when lesions have converse effects on two distinct cognitive functions; that is, the sets of cognitive deficits produced by lesions in different areas are disjoint.

A classic example is the dissociation between Broca’s and area and Wernicke’s area; a lesion of the former impairs speech production but not speech comprehension and leaves the patient able to understand verbal commands and yet unable give a normal verbal response, while a lesion of the latter abolishes speech comprehension but not speech production and causes the individual to produce fluent and grammatical yet nonsensical sentences in conversation.

**Difficulties with the Lesion Method** Although lesions experiments with animals can benefit from homogeneous populations and lesions, experiments with humans rely on a population of subjects that can exhibit
a great deal of variability. The exact location and extent of a lesion are unlikely to be consistent across a group of human subjects, as can age, education, gender, upbringing, and so on; two individuals that have sustained identically sized lesions in the same location of their brains may exhibit different degrees of deficits. Furthermore, lesions in humans can have occurred different ways, such as epilepsy as compared to a gun wound or a stroke, each of which can yield different types of damage.

A second limitation of the lesion method is that the function of the lesioned area is not necessarily known; one must observe how the brain functions without use of the lesioned area. Though sound conclusions can nevertheless be drawn, only regions critical to a given cognitive function can be identified and not the entire set of brain regions that participate in a certain behavior. Second, as mentioned above, cognitive impairment may occur because a lesion disrupts communication between two still functional areas of the brain, resulting in what is called disconnection syndrome. Lastly, an impairment in cognitive function may be “silent” if another part of the brain can perform the same tasks as the one lesioned. Similarly, the importance of a lesioned area may be underestimated due to compensatory mechanisms.

**Single-Case Versus Group Studies** Single-case studies, where a single subject is extensively studied, are of limited utility because one data point is little to work with. However, group studies, where a group of individuals with similar traumas are studied, can obscure important subtleties when, for example, when a group’s average performance levels are calculated. For these reasons, multiple-case studies, where a series of individuals with similar traumas are each extensively studied, can yield more conclusive results than either of the previous two methods on its own.

### 1.2.2 Neurologically Intact Individuals

Any experimental group must be compared to a control group. The choice of a proper control group may be difficult as each subject in an experimental group must be matched with an individual of the control group with a similar background. For example, consider a case in which performance on a reasoning task is measured in a neurologically intact high school dropout as compared to a college-educated brain damaged individual: the two individuals may perform identically on that task, but it is not known whether the college educated individual would have normally outperformed the control individual.
Neurologically intact individuals are also important as participants in research conducted through brain imaging techniques, as will be discussed shortly.

1.2.3 Nonhuman Animals

Nonhuman animal groups can provide much more homogeneous experimental groups because one can choose a group of individuals that are genetically very similar, that have been raised in identical environments, and that have been administered identical brain damage (the ethics of administering lesions are outside the scope of the current discussion).

1.3 Techniques for Assessing Brain Anatomy

The ability to determine the exact location of brain damage in living individuals instead of in postmortem studies has been developing greatly since the 1970s with the advent of improved or new brain imaging techniques and has become fundamental to modern research. The development and improvement of brain imaging techniques is a field of its own; the basics, however, should be understood.

1.3.1 Computerized Axial Tomography (CAT)

Computerized axial tomography (CAT) elucidates the density of brain structures with the use of x-rays. Cerebrospinal fluid (CSF) is less dense than brain tissue, which is less dense than blood, which is less dense than bone; in CAT scans, denser matter appears lighter and less dense matter appears darker. In CAT scans, regions of the brain that have been damaged appear darker than the surrounding tissue because they have become filled with less dense CSF, while areas in which a hemorrhage has recently occurred appear lighter than normal due to the presence of blood. The “brain slice” images created by CAT scans are typically oblique slices through the brain due to the position of the subject’s head during scanning.

CAT scans are relatively inexpensive and widespread and can be performed on all individuals, unlike some other methods.

1.3.2 Magnetic Resonance Imaging (MRI)

CAT scanning has been largely superceded by magnetic resonance imaging (MRI). MRI relies on three magnetic fields. The static field, a constant magnetic field, generally varies from 0.5 to 1.5 Tesla (T), up to 2 or 4 T
in “high-field” imaging. Compare this to the strength of the magnetic field of the earth, which is approximately 0.0001 T. The static field aligns all magnetically sensitive particles in the same direction. The **pulse sequence** is an oscillating magnetic field that is tuned to a resonant frequency so as to perturb only one class of substances at a time. Typically, the pulse sequence is set to the resonance frequency of hydrogen atoms. The time it takes for the hydrogen atoms in a perturbed substance to return to normal, the *relaxation time*, is recorded by a **receiver coil**, which is positioned near around or near a portion of the individual’s head.

Relaxation times for hydrogen atoms vary according to the compound in which the hydrogen atoms are present. Thus, by modulating the pulse sequence, one can obtain information about the density and location of a particular type of substance, such as fat or brain tissue. The intensity of the signal released by a hydrogen atom relaxing from an excited state is measure by the receiver coil and its location is determined by a **gradient field**, a magnetic field that varies in intensity over the field being imaged. The combination of these observations enables the construction of a three dimensional image of the brain to be reconstructed.

MRI does not use potentially harmful x-rays, unlike CAT scanning. Furthermore, the spatial resolution made possible by MRI is superior to that that can be attained by CAT scanning. However, not every individual can be subjected to MRI; for example, the magnetic fields involved in MRI can disrupt the activity of a pacemaker. Furthermore, the strong magnetic fields involved in MRI can dislodge metal in the body that is not connected to hard tissue, such as a clip on an artery.

### 1.4 Techniques for Assessing Physiological Function

The imaging techniques described thus far construct images of the anatomi- cal structure of the brain but reveal nothing about brain function. There exist methods that measure brain function.

#### 1.4.1 Functional Brain Imaging Methods

Functional brain imaging methods are often used on subjects with known or suspected brain damage. However, such methods can also reveal much about brain function when used to study neurologically intact individuals.

**Positron Emission Tomography (PET)** In positron emission tomog- raphy (PET), radioactively labeled molecules are introduced into an indi-
individual’s bloodstream to be carried to the brain. The radioactive compounds used decay by the production of a positron, which collides with an electron, annihilates, and emits two photons that propagate in opposite directions. A ring of photocells around the patient detect such photon emission. Increased brain function is associated with increased metabolism; thus, the areas of the brain that emit the most photons are the areas in which brain function is highest.

Careful choice of the radioactive compound used allows PET to localize specific substances. For example, water containing oxygen-15 atoms will accumulate in the brain in direct proportion to local blood flow and be a marker for increased neural activity. Choice of a different radioactive compound that binds to dopamine receptors allows PET to determine the distribution of dopamine receptors in the brain.

PET uses ionizing radiation and so a single individual can undergo at most two to five PET scans per year. Another drawback is that the half-life of the radioactive isotope used determines the time period required to obtain a precise image of brain activity and PET scans can be time-consuming, making temporally precise imaging of brain function difficult. Furthermore, the precision of PET imagine is limited. Despite these limitations, PET can be an effective technique for identifying the multiplicity of brain structures involved in a cognitive brain function and is uniquely suited to examining the brain’s processing of certain substances, such as neurotransmitters.

**Functional Magnetic Resonance Imagine (fMRI)** As mentioned previously, increased brain function is associated with increased metabolism at the site of neural activity. This increased metabolism involved the deoxygenation of blood; as blood contains iron, this deoxygenation alters the sensitivity of blood to a magnetic field. An adaption of MRI that is attuned to measure the relative concentrations of oxygenated versus deoxygenated blood on the scale of seconds is used to accurately determine sites of increased brain function on a time scale that is shorter than that allowed by CAT scanning. fMRI does not involve ionizing radiation and thus one individual can undergo many fMRI scans, an advantage that PET scanning does not share. Multiple scans allow changes in an individual’s brain function to be tracked over time. Furthermore, fMRI produces very precise images, allowing stronger links between neuroanatomy and cognitive function to be observed.