Lesion Approaches
– Some Key Questions –

Lena Kästner

1 What is meant by the term "dissociation" in neuropsychology? What inferences can be made from the different forms?

Neuropsychologists refer to a patient's selective functional impairment on a particular cognitive task as "dissociation". If a lesion to a single brain structure impairs a patient's performance on multiple tasks demanding different cognitive abilities, *no dissociation* is said to be present. This latter claim points to potential problems with the logic behind dissociation arguments: they assume that we can identify and distinguish the structures composing our brains and single out the cognitive demands of a given task. That said, dissociation studies in neuropsychology may be characterised as an attempt to associate cognitive functions with brain regions; although, importantly, dissociations can generally be considered quite independently of the issue of localisation.

Most generally, there are two kinds of dissociations permitting different inferences. In a *single dissociation*, only performance on one particular task (task A) is impaired while performance on another (task B) is relatively spared. For example, consider two observed patients: P1 suffers from a lesion to structure X and her performance on both tasks A and B is impaired (no dissociation); P2 suffers from a lesion to structure Y but her performance is impaired only on task A, not on task B. In this case (assuming functional and architectural equivalence of P1 and P2), we infer that task A requires structure Y to be intact while task B does not.

Shallice (1988) usefully distinguishes three subtypes of such dissociations depending on the level of performance the patient reaches in tasks A and B, respectively. In a *classical dissociation*, performance on task A is well below the average range while performance on task B falls within the average range. In a *strong dissociation*, performance on both tasks is clearly impaired but it still is much worse for task A than task B. Finally, in a *trend dissociation*, both tasks are performed below mastery; performance on task B is still significantly better than on task A, though not "qualitatively dissimilar" (Shallice, 1988, p. 228).

From these cases we usually infer that performing task A, but not B, requires structure Y. However, task B could indeed recruit structure Y, only to a lesser extent than A. The observed impairment pattern would then be a *task-resource artefact* (Shallice, 1988). Alternatively, the patient may perform task A suboptimally, say due to misunderstanding the instructions, leading to a *task-demand artefact* (Ward, 2006).

Where two complementary single dissociations are found in two different patients, neuropsychologists speak of a *double dissociation*: if P1 in the above case was selectively impaired on task B but not A while the opposite was true for P2, and P1 performs task A better than P2 while the reverse holds for task B, neuropsychologists infer that performing task A requires structure Y while B requires X. This would falsify any model according to which tasks A and B are carried out by the same subsystem.

Using this logic, Mishkin *et al.* (1983) demonstrated separate "what" and "where" streams in visual processing in monkeys where inferior temporal lobe lesions resulted in shape discrimination but not landmark task impairment while the reverse was found after parietal cortex lesions.

More recently, studies in computational modelling have helped to identify and verify dissociations (e.g. Farah & McClelland, 1991; Lambon Ralph *et al.*, 2007; Plaut 1995) thereby helping us to develop better models of cognitive processing.

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2 Describe the main methods of lesion studies, together with the advantages and disadvantages of each.

Human Lesions. Studying lesions in humans relies on conditions relatively stable in nature allowing for multiple tests in the same subject with little risk of artifacts. Studies are relatively cheap, not usually ethically debatable, and bear a clear relationship to clinical practice. The risk of confirmation bias effects is reduced as lesions are not induced to test predictions. Finally, human lesion studies are powerful: a single case can easily challenge well established models.

They are, however, mostly limited to individual cases – like Phineas Gage, a railworker who survived a crowbar passing through his head and underwent dramatic personality change after the accident (cf. Macmillan, 2008) thus informing personality research. The availability of lesion cases depends on "luck of nature" and is almost impossible to plan ahead. As the pre-morbid state cannot be re-instantiated, the effects of human lesions are often difficult to estimate. Patients' conditions are poorly controlled and sometimes go along with severe impairments placing the patient in a personally / emotionally difficult situation that may affect neuropsychological study; another possible confound is cortical reorganisation. Their generaliseabiltiy is thus restricted.

Animal Lesions. There is a variety of ways to lesion model organisms. Aspiration and cauterisation techniques are rather crude, poorly localised methods removing parts of the animal's brain; collateral damage to neighbouring areas cannot be excluded. Knife cuts and cutting fibre bundles bear similar problems. Cooling specific brain areas to inactivate them (Galuske *et al.*, 2002) produces temporary damage but may affect nearby tissue as well. Neurotransmitter or ionchannel specific targeting is possible using neurotoxins, immunoleions (Shen, 1996), and genetic manipulations (e.g. *gene knockout*, *viral genetic targeting*, *optogenetic procedures*, and *pharmogenetic procedures*) permitting selective interventions on metabolic processes. Animal lesions are better controlled than human lesions, allow for group studies, and pre- and post-morbid and pre- and post-mortem comparisons, respectively. As in humans, animal lesions are relatively static allowing multiple tests in one subject.

The downside is that animals are purposefully lesioned. Besides the ethical concern, experimental manipulations may introduce sampling and confirmation biases. Furthermore, not all cognitive functions are available for study in animals. And if they are, animals may still be "overly simplistic" models not permitting inferences to humans.

Transmagenetic Stimulation (TMS). Externally applied strong electric fields can disrupt neural functioning *via* noise induction creating a reversible “virtual lesion”. Depending on the pulse sequence being applied, the effects can last microseconds or several minutes.

TMS is non-invasive and allows for repeated studies in the same subject/subject group without confounds of cortical reorganisation. It is the only lesion method that allows inferences about causal connections and can be used to investigate *when* particular brain areas become relevant in a given task.

However, TMS is limited to brain areas close to the cortical surface. Tissue inhomogeneities may cause inhomogenetic membrane potentials, and, as brains are “contaminated” by structure, intended and effective stimulation site may not coincide even if localisation takes individual subject differences into account. Finally, TMS pulses may induce muscle twitches, headaches, neck pains, or seizures thus bearing a possible attendant risk and/or yielding cross-modal effects.

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3 How, and why, are estimates of pre-morbid general intellectual functioning measured in human neuropsychology?

Assessing the extent of cognitive impairment in a neuropsychological patient requires comparing her current cognitive performance to her pre-morbid functioning, i.e. her cognitive functioning prior to the onset of her clinical condition. Knowledge about a patient's pre-morbid performance level enables the psychologist to evaluate her current (post-morbid) test performance against her individual background, i.e. what level of performance would have been expected of that very patient before the injury or disease.

Assuming a standardised population value, say average IQ, is insufficient; for even an individual currently functioning in the average range may have experienced significant deterioration of her cognitive abilities if she previously performed well above average. Problematically, however, most patients did not undergo pre-morbid neuropsychological testing. Pre-morbid abilities then have to be estimated to obtain a baseline that can serve for diagnosis. Two principal methods are considered.

An individual's general intellectual functioning has been found to significantly correlate with *demographic factors*, i.e. sex, age, level of education (years of education), occupation, and social status. Crawford *et al.* (1990) suggest a regression equation via which pre-morbid estimates can be directly obtained from these variables. The reliability of such procedures is subject to debate, however. While Crawford (1992) argues that administration of standardised reading tests is a more powerful tool to estimate pre-morbid functioning, (notably more recently) Adams *et al.* (2010) suggest demographic factors to be the more reliable measure.

Alternatively, *tests resistant to the effects of the patient's clinical condition* can be administered. The clinically employed standard measure for general intellectual pre-morbid functioning is a word reading test (either the National Adult Reading Test (NART) (Nelson, 1982; Nelson & Willison, 1994) standardised against the WAIS-R, or the Wechsler Test of Adult Reading (WTAR) (Wechsler, 2001) standardised against the WAIS-III; British and American samples exist for both). The patient is asked to read out a list of 50 short words with atypical grapheme-phoneme associations, i.e. irregular pronunciation, such as "simile", "heir", or "ache".

In order to perform well on this test, the patient has to have previously learned the words he is asked to read out. For applying standard pronunciation rules or will not yield the required phonological pattern.

Performance on NART and WTAR is relatively unaffected by cognitive deterioration due to aging, neurological, or psychiatric disorders, and correlates highly with IQ in the normal population (Crawford, 1989). Therefore, post-morbid NART / WTAR scores can thus serve estimates for pre-morbid IQ and be compared to WAIS-R / WAIS-III IQ obtained in post-morbid testing.

To ensure validity, obtained NART / WTAR IQs may be compared to estimates based on demographic factors; if NART / WTAR IQs are significantly worse, the test may have been invalid. In this case, demographic variables alone or a different test may be used to estimate pre-morbid functioning. For dyslexic patients, a lexical decision tasks (cf. Baddeley *et al.*, 1992) can be administered instead; for school-aged children, Wright *et al.* (2005) suggest using the third edition of the Cognitive Abilities Test (CAT-3) to estimate pre-morbid IQs.

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