Single case studies are a powerful tool for developing, testing and extending theories

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Abstract

Psychology embraces a diverse range of methodologies. However, the majority rely on averaging group data to draw conclusions. In this Perspective we argue that single case methodology is a valuable tool for developing and extending psychological theories. We stress the importance of single case and case series research, drawing on classic and contemporary cases where neuropsychological deficits provide insights into typical cognitive processes in domains including memory, delusions, reading and face perception. We unpack the key features of single case methodology, describe its strengths, its value in adjudicating between theories, and outline applied benefits for understanding deficits and interventions. The unique insights single case studies have provided illustrate the value of in-depth investigation within an individual. Single case methodology has an important place in the psychologist's toolkit and it should be valued as a primary research tool.

[H1] Introduction

Henry Molaison (HM) was 27 years old in 1953 when he had experimental brain surgery that attempted to control epilepsy so severe that he was unable participate in normal life[1]. His surgery was successful in so far as his seizure frequency was radically reduced. However, as psychology students worldwide have learned[2–4], the surgery also had the unanticipated consequence that HM was no longer able to form new memories. This unexpected consequence has been transformational for how psychologists and neuroscientists think about memory. Such single cases continue to inform cognitive theory today.

HM's case influenced understanding of the role specific brain regions (medial temporal lobes and hippocampus) play in the formation of enduring memories. But this just scratches the surface of his contribution. Until his death at the age of 82, HM participated in decades of experimental studies that advanced understanding of memory[5]. For example, despite his profound memory problems, HM could understand a joke and carry on a conversation[6]. This suggests that the cognitive processes underlying memory are distinct from those underlying language.

Even though the tools of psychology have advanced since 1953 with, for example, the development of functional neuroimaging techniques, single cases continue to contribute novel insights to psychological theories. For example, in 2020 a case of a 60-year-old geologist, RFS, who was diagnosed with progressive brain disease (corticobasal syndrome) was reported[7]. When shown the written digits 2 to 9, RFS reported seeing a tangle of black lines (Figure 1A). Strikingly, he had little difficulty recognising other visual stimuli, like alphabetic letters or faces, and the digits 1 or 0. This incredibly specific and surprising pattern of retained and impaired can broadly be described as a dissociation between impaired digit perception and intact perception of other visual objects. There has been much debate about whether selective impairments in visual processing relate to category, or rather reflect differences in the kinds of low level visual features necessary for identifying different kinds of [8–12] . RFS' dissociations between digits and letters favours the former account: it is difficult to see how the precise nature of this category-selective deficit could arise from differences in low-level feature processing.

Interestingly, visual distortion from digits impaired RFS's ability to recognise stimuli that he could easily recognize under other viewing conditions. For example, he could recognise when there was a drawing of a face embedded in a letter but not when it was embedded in a digit (Figure 1B) This phenomenon enabled investigation of the nature of conscious awareness of visual stimuli.

In this Perspective, we argue that the study of individuals who do not show typical performance is a critical part of the psychologist's toolkit that can provide unique and converging evidence for developing and testing theoretical accounts. First we discuss the benefits of studying deficits. Next, we describe what is gained from studying people as individuals rather than averaging across groups of people. We then provide further examples of what has been learned across domains from such single case studies of individuals, as well as the applied benefits of this approach.

[H1] The value of studying deficits

Psychology has a long and illustrious history of studying individuals who do not show typical development, or who no longer perform typically as a result of brain damage or psychiatric disorders across diverse fields[13,14,15,16,17,18]. One goal of studying such individuals is to understand the relationship between behaviour and its neural substrates (that is, localisation of cognitive function). A second goal is to better understand the 'deficits' themselves, often with a view to improving treatment outcomes[19]. Here we focus on a third goal: the use of deficits as windows into typical perceptual and/or cognitive processes.

Studying individuals with impairments to inform understanding of the unimpaired, neurotypical, cognitive system is an invaluable methodological tool for psychologists[20–25]. Indeed, the use of rare or abnormal events to inform the norm is an accepted methodology across scientificfields[26]. For example, research into genetic mutations advanced understanding of normal genetic mechanisms and rare volcanic eruptions enabled researchers to study the earth’s interior and test theories of the forces at work[26].

The strength of any method lies in what it can uniquely add to a field in order to provide novel or converging evidence. This is also true of the single case approach. Like any other experimental method, it is possible to apply a hypothesis testing, pre-registered experimental design approach to single case studies. However, studying single cases also provides the opportunity for accidental discovery. That is, the behaviour of these individuals will occasionally yield results not expected under current psychological theories, as in the case of HM or RFS, thereby inspiring new theories which can then be tested. Although accidental discoveries are possible with other experimental methods, single case methods are particularly well-suited to uncovering unexpected results and probing their underlying causes.

For example, in the 1950s the dominant view was that there was just one kind of memory, with debate focused on whether these memory traces (or engrams) could be separated from the neural systems responsible for perception or other cognitive processes. Consequently, it was unclear whether amnesia (selective deficits in memory without additional perceptual or cognitive impairments) should ever occur, and if it did, the prediction was that it should influence all kinds of learning[27]. Thus, HM’s selective loss in the ability to create new memories, without other perceptual impairments, challenged the status quo of memory research at the time. Furthermore, his ability to create certain kinds of new memories (he was able to learn new motor skills) but inability to create others (he could not learn new faces, words or the route through a maze)[6] forced a re-evaluation of theories of memory[28]. Thus, a revised theory of memory was developed that distinguished between ‘nondeclarative’ or ‘implicit’ memory and ‘declarative’ or ‘explicit’ memory[28]. This example illustrates a major contribution of the study of deficits in general: novel insights from an individual with cognitive impairments may lead to the, sometimes radical, revision of theories.

The study of deficits has also played a key role in adjudicating between rival plausible theories when this would not be possible using experiments with neurotypical participants or would require complex tasks that do not cleanly map on to cognitive processes. For example, consider the process of writing. People often have the perception that they are ‘saying’ the words in their heads as or before they write. This perception was encapsulated in the theory (the obligatory phonological mediation account) that written language skills are dependent on spoken language skills and it is not possible to directly write a word without first retrieving the spoken form[29,30]. However, following brain damage some individuals are able to correctly write words that they are unable to say[31]. This pattern of performance provides strong evidence against the obligatory phonological mediation hypothesis. Instead, the performance of these individuals supports a theory where written words can be directly accessed from meaning without having to rely on spoken forms[32,33]. To examine the same hypothesis in unimpaired, skilled writers is far more complex and consequently such studies are rare[31]. For example, a task (masked priming) has been used where the name of a picture has to be written just after a written stimulus is presented so briefly that the participant is not aware of what has been presented. This stimulus will sometimes sound similar to the word that is to be written (for example, ‘KAT’ presented briefly before the target ‘cat’)[34,35]. Although the lack of priming effect in this task has also been interpreted as evidence against the phonological mediation account, these claims require additional assumptions about, for example, the mechanism by which the prime would be expected to influence written naming.

Furthermore, the study of deficits and neuroscience methods (e.g., electroencephalography, EEG; functional magnetic resonance imaging, fMRI) can complement each other. Indeed, there are many instances where these methods have been combined, including in the study of RFS[7]. For example, the N170 is a scalp recorded voltage fluctuation (event-related potential; ERP) that is larger in response to faces than other stimuli, including faces where the features (eyes, nose and mouth) are in scrambled positions [36,37] . When RFS was shown faces embedded in letters, he showed the expected pattern of a larger N170 response to faces vs scrambled faces. Surprisingly, RFS also showed an N170 response of the same magnitude for faces (vs scrambled faces) embedded in digits, despite the fact that he reported that he was not able to perceive the digits, let alone the faces embedded inside them[7]. Thus, RFS's brain responses distinguished between different kinds of visual stimuli, regardless of whether he was aware of what he was seeing. These results show that extensive processing of visual stimuli, including identification, can occur without reaching the level of visual awareness; cognitive and neural theories need to accommodate these facts.

As another example, a neurotypical participant in an experiment examining the time course of neural activity in picture naming[38], subsequently had a stroke resulting in an impairment in word retrieval (anomia). Behavioural investigation identified that the word retrieval impairment was caused by difficulty retrieving the stored form of the word (despite having successfully retrieved its meaning). When neural activity before and after the stroke was compared, there was a large change in the ERP components between 250–450ms after the picture was presented. This finding provided strong evidence that retrieval of the word form occurs in the 250-450ms time window in typical processing (as this was the process that was impaired in this individual).

By contrast, drawing conclusions regarding the time course of word retrieval from neurotypical participants requires greater inference[39]. For example, some word properties (such as word frequency) are hypothesised to be associated with a particular process (such as lexical retrieval). The point in time that the process occurs can be inferred from observations of when effects of the relevant properties occur (for example, inferring lexical retrieval from when high-frequency and low-frequency words show different neural signatures)[40]. Clearly the strength of the inference relies on the strength of the underlying assumptions; in this case, regarding the stage of word processing at which the variable is. However, if the stage at which frequency influences processing is in doubt[41], then it can no longer be used as a marker for that particular stage, and this methodology is flawed.

In sum, the study of deficits provides psychologists with another tool for investigating whether different cognitive or neural processes are necessary to drive behaviour. Theories become stronger when more tools are available to test and develop them. Moreover, there are situations in which deficits can provide a clearer or easier test of theory than would be possible using data from neurotypical participants.

[H1] The value of single cases

So far, we have emphasised the important role that studying individuals who do not show typical cognition can play in psychological research. Notably, the examples provided have all been case studies of individuals. In this section, we describe some of the practical and theoretical benefits of single case methodology relative to the use of large groups of individuals, as is more standard in many (but not all) fields of psychology (for example, psychophysical experiments[42] and deep imaging[43] rely on small groups or individual subjects) (see also refs[20–24,44,45]). We explicitly focus on the strengths of the single case approach in relation to homogeneity of participants, depth of investigation and requirements for replication. Potential criticisms have been discussed and refuted at length in the literature (see refs[20–24,44,45] and Box 1).

Although single case methods by definition focus on the level of the individual, there is also value in examining performance across multiple cases (a case series[46–49]). Case series are distinct from group studies as individual performance is not averaged to reduce variability. Instead, the variability is used to test theoretically-driven associations. For example, the hypothesis that written naming is parasitic on spoken naming leads to the prediction that as spoken naming becomes more severely impaired, so should written naming. In other words, there should be a correlation between spoken and written naming across a case series of individuals. Evidence for a lack of a correlation would falsify this theory. See Table 1 for a comparison of group, single case, and case series designs.

[H3] Homogeneity

In group studies, performance is averaged across individuals. However, this averaging will only produce meaningful results when the individuals within the group are homogeneous in the aspect of performance under investigation[20]. For example, if a researcher is interested in the mechanisms underpinning understanding of sentences, they would need to study individuals with 'normal' language skills. However, given that grammatical structures differ across languages, the participants might also need to be restricted to speakers of a single language. The cautious experimenter would also limit participants to native speakers of that language, on the grounds that individuals who are proficient in that language but learned it later in life might process sentences differently. This group of participants would then be considered homogeneous. Consequently, averaging would be thought to reduce noise in the data from 'uninteresting' sources like lapses in attention during the task [50].

If we consider the same experiment, but where the participants are individuals with acquired language impairment (aphasia), the research goals might remain the same albeit with additional questions relating to how aphasia influences sentence comprehension, and what the mechanisms underpinning such effects might be. The same criteria for participant selection should of course apply as with the neurotypical speakers. However, the researcher also needs to consider the impact of the language impairment on participant selection. The nature of the language impairment depends on the location and severity of the brain impairment and is highly variable across individuals. For example, one individual could have a problem in distinguishing speech sounds, a second in recognising words, a third in understanding what these words mean, and a fourth in disentangling grammatical structure. Each of these impairments would lead to difficulty understanding sentences, but the average performance of these individuals would not provide any meaningful insight into the mechanisms by which sentence comprehension is impaired. In this case, averaging serves to increase noise and conceal theoretically interesting patterns rather than decrease noise to reveal these patterns.

Given that it is impossible to know in advance exactly which aspects of impairment might be important for the task in question, it can be most appropriate to examine performance at the level of the individual.[21,24,45–47,51] It can be difficult (or impossible) to define any group so that it is sufficiently homogeneous to be theoretically meaningful; examining individual performance overcomes this issue.

Although our argument primarily focuses on the need to study non-neurotypical individuals as single cases, studying neurotypical populations at an individual level can also be a profitable exercise as obtaining a sufficiently homogeneous group can be difficult in some fields. To return to our previous example, if a researcher is examining the effects of bilingualism on sentence comprehension, group homogeneity is unlikely because there are many ways that bilinguals can differ[52] For example, bilingual speakers can differ in the age at which they acquired their second language, how proficient they are in that language, how often they use the second language and in which contexts, the extent to which they still use their first language, whether their proficiency in their first language has declined (language attrition), the extent to which they switch languages within a context, and which language they consider dominant. All of these features can lead to variable findings across studies and consequent problems achieving consensus on bilingual performance[52]. Even when the population is homogeneous in many ways (for example, a population of monolingual undergraduate students from Western universities that has informed the majority of research in psychology[53]) it is not clear that the sample of participants will necessarily be homogeneous with respect to the cognitive function under investigation[54–58]. In situations like this, the application of single case (or case series) methodology could be more informative than averaging findings across a potentially heterogeneous population. Single cases allow the individual patterns to be identified rather than obscured, and case series further allow the variability across individuals in the cognitive function of interest to be systematically explored and related to variation in other aspects of cognition Similar arguments can be made for other methods in psychology, like neuroimaging[59,60] where there is increasing attention to the relevance and importance of such individual analyses.

[H3] Depth and replication

There has been increasing emphasis on the need for robust and replicable data in psychology[65–68]. A highly influential experiment in the 1960s demonstrating effects of word frequency on picture naming in neurotypical participants included only 11 participants and 26 items, with no consideration of experimental power, nor representativeness of [69,70]. Researchers now accept that experiments must be sufficiently powered (that is, include enough data points) to increase the chances of finding 'real' effects and of rejecting spurious ones, and to improve the likelihood of replicability[71,72]. However, practical constraints mean that including a large number of participants results in limited testing time per participant. Consequently, only a single task or small range of tasks or a limited number of items are examined, resulting in 'shallow' data. By contrast, single case studies enable the possibility of 'deep' data.

Well-designed single case studies use in-depth analysis with sufficient stimuli (in analogy to sufficient participants in group-based approaches) across a number of experiments designed to provide converging evidence and replicated over time. The strength of the evidence will still depend on the statistical power and replicability of the effects across experiments, just as in the group approach, but within the same participant. In addition, the opportunity to examine phenomena in depth, allows for nuanced investigation. For example, had RFS been one of many participants in an investigation of visual processing that included a short task with letter and digit stimuli, it is unlikely that the selectivity of his visual impairment would have been detected. Even if his selective impairment for digits but not letters had been identified, it is unlikely that this approach would have been able to distinguish between RFS's deficit in perceiving the digits and that of other individuals who can see digit shapes but have lost the ability to associate them with their identities. Furthermore, it is difficult to see how a group level approach would have led to the investigation of how RFS' deficit for digits disrupted the visual perception of nearby objects, which allowed his case to be used to study visual awareness.

The question of what counts as a successful replication is an ongoing challenge for contemporary psychology with important [73,74]. For example, would the results of an experiment with readers of English only be considered valid if the results replicated across all scripts and languages, including, for example, with readers of Chinese?[75] The answer is clearly no: even if the result only generalizes to the specific context of English reading the result is still valid in that it contributes to a theory, albeit one constrained by the unique characteristics of English script, lexicon and grammar

Similarly, the validity of findings for theory-building from one single case do not rest on replication in another case, who might have a different underlying deficit that leads to different results. Instead, in the single case approach, the results must replicate within the participant. The use of different tasks (or types of stimuli) allows for strengthening of evidence, rejection of task-related artefacts as an explanation for the pattern of performance, and converging evidence for a theoretical hypothesis. For example, RFS's perceptual distortion for digits 2 to 9 resulted in impaired perception of embedded figures across different tasks: naming of embedded objects, discrimination of embedded objects, discrimination of embedded shapes, discrimination of embedded arrows, discrimination of embedded symbols, and discrimination of embedded. These experiments strengthened the evidence for an impairment specific to these digits rather than a general visual impairment, allowed the researchers to reject task-related artefacts because each had slightly different requirements, and thereby provided converging evidence about the nature of RFS's visual impairment across tasks[7].

In sum, the single case study approach allows for detailed testing within a participant, thereby avoiding the concern of 'averaging away' theoretically important differences. Crucially, data simulations have demonstrated that the extent of testing within a participant (number of items each participant is tested on) may have a greater benefit for reducing error detecting effects in a study (increasing hits and reducing false alarms) than including more participant with deficits but less data per participant[46].

[H1] Theoretical advances

The study of individuals with cognitive impairments has provided impactful theoretical insights across many fields[76] . Here we provide examples from three domains. Additional examples are provided in Table 2 (see also refs[76,77]). Common methods for building theories using single cases are described in Box 2.

[H3] Reading

Early research in the 1970s and 80s on acquired reading disorders (impaired reading in previously skilled readers following brain damage) led to the popularity of case study methodology[78,79] by illustrating how careful analysis of patterns of performance across different individuals could help develop and refine cognitive theories. For example, that one individual could read irregularly spelled words (words that cannot be correctly read by sounding out individual letters, such as 'yacht') but not nonwords (for example, 'slape'), while another individual showed the reverse pattern, suggested that there were two separate routes by which reading could be achieved[78]. This approach of examining dissociations across tasks and individuals has also informed developmental models of reading acquisition, as similar dissociations to those found in acquired reading disorders have been observed in this domain[80].

Importantly, novel theoretical insights continue to arise from case studies in this field. For example, a case series of one Hebrew reader with acquired dyslexia (impaired reading following brain damage in a previously skilled reader) and 22 Hebrew readers with developmental dyslexia (difficulty developing reading skills found a novel and highly specific pattern of difficulty in reading vowels relative to consonants[81]. The individual with acquired dyslexia described their problems as "The voweling is completely gone" [81]. Through a careful series of tasks, the researchers developed the argument that these cases provide evidence for a vowel-specific deficit in the part of the reading system that is used to read novel words (known as the sublexical, grapheme-phoneme or 'sounding-out' route)[81]. This led to a novel theoretical claim that vowel and consonant letters are processed separately, which might also explain observed differences between consonant and vowel processing in unimpaired readers[82].

This case series also contributes to another ongoing debate about the extent to which the processes and representations used for reading are also those used for spelling[30,83]. Although vowels were particularly difficult for participants with dyslexia to read, many of them did not have more problems with vowels than consonants when spelling words[81]. This suggests distinct processes for reading and spelling because one was impaired but the other was not in these participants. Other researchers have also used dissociations between reading and spelling abilities in developmental cases to further understanding of this relationship[83,84].

[H3] Visual processing

Visual processing has benefited from insights from single cases beyond reading[85]. We have already discussed how RFS's selective visual distortions informed understanding of mechanisms of visual perception and attention[7]. Selective visual deficits have also contributed substantially to establishing that separate, specialised cognitive and neural mechanisms process visual attributes such as colour, shape, and motion in early and mid-level vision[25]. For example, individuals might be able to perceive shape and motion but not colour (cerebral achromatopsia)[86], implying that colour perception relies on separate cognitive and neural mechanisms to shape and motion. Similarly, individuals might be able to perceive colour and shape but not motion (motion blindness)[87], implying that shape and motion must also be processed separately. The fact that RFS's impairment was specific to digits provides evidence that number processing is distinct from letter processing despite digits and letters being very similar visually[7,88–90].

[H3] Face perception and recognition

Single case studies of individuals with both acquired and developmental disorders have also had an impact on understanding face processing. Prosopagnosia refers to difficulty recognising familiar faces. Individuals with propsopagnosia often need to use cues such as facial hair, gait or voice to recognise people[91]. Dissociations between prosopagnosia and other cognitive disorders such as dyslexia[92] have been argued to provide evidence that face processing relies on different mechanisms from word or object recognition rather than a single processing system underlying all of these processes[93]. Intriguingly, although individuals with prosopagnosia fail to overtly recognise familiar faces, some individuals with prosopagnosia show 'covert' recognition—they can differentiate between familiar and unfamiliar faces despite not being aware of the difference. Just as RFS's ERP responses distinguished between real and scrambled faces, some individuals with prosopagnosia show different ERP responses to familiar (but unrecognised) faces and unfamiliar faces[94], or different autonomic responses such as increased skin conductance responses (indicating increased arousal to the familiar faces)[95] or behavioural responses (for example, faster learning of correct vs. incorrect occupations for unrecognised familiar faces)[96]. These results have provided support for a theory according to which partial, degraded, information can support covert recognition, but does not allow for explicit recognition[97].

Understanding how faces are processed has also been informed by individuals with delusions such as Capgras delusion (the belief that significant others have been replaced by imposters, robots or aliens who look identical or near identical[97]). Capgras delusion has been reported in both the context of psychiatric disorder[98] and acquired brain damage[99]. Individuals with Capgras delusion recognise familiar faces (for example, they know that the face looks like that of their spouse). However, they do not show the usual autonomic response (for example, increased skin conductance) to that person [98]. This leads to a conflict: the face looks like a familiar person but the expected affective response is not experienced. This has been hypothesised to lead to the rationalisation that despite looking the same it cannot really be the familiar person (and instead is an imposter). This is an important theoretical account of the nature of Capgras delusion and was introduced as a competitor to psychodynamic accounts (according to which negative feelings about the 'double' can be held without guilt, which allows conflicting feelings, for example love and hate, towards a significant other to be resolved[100]).

However, the pattern shown in Capgras delusion also provides evidence against the account of prosopagnosia described above, where overt and covert recognition rely on the same processes, but only covert recognition is possible with partial information alone. Under this account it should not be possible for overt recognition to occur in the absence of covert recognition—if there is enough information for overt recognition this information should be (more than) sufficient for covert recognition[101]. Yet, this is precisely what is seen in Capgras delusion. Consequently, these patterns of results necessitated the proposal of two processing routes for face recognition (at neural and cognitive levels), one for covert and the other for overt recognition. Individuals with Capgras delusion also provide insights into more detailed mechanisms of face processing. For example, abnormal eye movement scanpaths when looking at familiar faces have been associated with reduced autonomic responses, suggesting that the neural control of eye movements can be influenced 'top-down' by subcortical influences from the autonomic system.[102]

[H3] Belief formation

In addition to advancing theories of face processing, investigation of cases of Capgras (and other) delusions has been instrumental in developing theories of how beliefs are formed and maintained. The influential two-factor account of delusional belief[103] was built on such cases. The critical point in this account is that although a perceptual disorder underpins the delusion (for example, lack of affective response to familiar faces) this is not sufficient to maintain the delusional belief: It is not rational to believe that your spouse has been replaced by an imposter. A more typical reaction would be something like 'when I look at my spouse I no longer feel the same way, but it is not possible that there could be someone who looks and acts exactly like her, so there must be another explanation'. Indeed, there are some individuals who do not have normal autonomic responses to faces who do not have Capgras delusion[101]. Thus, the two-factor account proposes a second impairment to a belief evaluation system (proposed to be located in the right frontal lobe[104]).

Thus far we have focused on developmental or acquired neuropsychological impairments as the cause of the two factors underpinning delusions However, delusions can also be caused by psychiatric impairments, and the two-factor account has also been proposed as an account of delusional beliefs in, for example, schizophrenia[104]. The two-factor account has led to an explicit cognitive model of how people derive new beliefs from observations of unexpected events[105,106]. This cognitive model in turn provides a more precise account of the impairment in individuals with delusions. For example, individuals with Capgras delusion must have a face processing impairment and a belief maintenance impairment. This example illustrates the reciprocal and iterative nature of theorising and evidence from case studies.

[H1] Object orientation representation

The above examples illustrate the different ways that detailed investigation of individuals with developmental or acquired cognitive impairments (or psychiatric impairments) can inform, extend, guide or radically redirect psychological theories. In the above examples, the data supporting these theories largely comes from single case methods. However, the theoretical developments from single case studies can be used to develop new experimental questions that can then be tested with neurotypical individuals. For example, AH had a theoretically unexpected difficulty localizing objects from vision because of a developmental difference[107]. Careful examination of the kinds of mirror image confusion errors (where visual stimuli are confused with the mirror image of that item e.g., confusing b and d; or copying a flag with the pole on the left as one with the pole on the right) that AH made in simple tasks like directly copying a picture of an object led to the development of a novel theory of how object orientation is represented[108,109]. This theory was subsequently used to make sense of the different patterns of orientation impairments observed across a series of individuals with different processing deficits[108].

The theory developed from the case study observations made predictions about which kinds of mirror image confusion errors should be more likely in neurotypical adults. These predictions were tested and confirmed across a series of experiments that differed in stimulus exposure duration, memory load, retention interval, test type, and instructions[110]. A series of experiments with typically developing children also provided converging evidence for the theory, and used the theory to make sense of commonly observed developmental phenomena (for example children's difficulties learning to distinguish the lowercase 'b' and 'd' which differ only by mirror reflection)[111].

Not every cognitive scientist has the resources or opportunities to do single case studies. The trajectory of theory development in the domain of object orientation representation makes clear how theoretical insights developed from single case studies can be examined using other experimental approaches.

[H1] Applied benefits

The world does not turn on theory alone. Assessment of an individual, or a case series of individuals, enables detailed understanding of areas of processing strength and difficulty. Such research has led to clear theories of the nature of the impairment (for example, the two-factor theory of delusions above). These theories can then guide clinical assessment, diagnosis and intervention[112]. For example, an individual who presents with Capgras delusion following brain damage will need assessment of their face processing, and their belief formation and maintenance, and intervention that is appropriately targeted at both of these impairments. In addition, tasks that were initially developed for research purposes can also be used clinically to provide more accurate and nuanced diagnosis[113,114].

For example, in the case of aphasia (an acquired language disorder), batteries of tasks focusing on systematic assessment of a range of specific skills, such as sublexical processes in reading (nonword reading) and identification of the spoken word form (auditory lexical decision) enabled clinicians to move beyond traditional syndrome-based aphasia classification (for example, Broca's aphasia or Wernicke's aphasia to theoretically informed and more refined identification of the nature of deficits[114]. For example, the syndrome of Wernicke's aphasia is classified on the basis of poor understanding of speech, and fluent (but inaccurate) speech production. However, research has shown that the cause of comprehension problems can differ between individuals[115]. The type of comprehension impairment can be detected clinically using three different tasks that tap into different levels of cognitive processing: minimal pair discrimination task (speech sound discrimination), auditory lexical-decision (spoken word form identification), and auditory word-picture matching or auditory synonym judgements (accessing the meaning of spoken words). The pattern of performance across these tasks precisely identifies the nature of the comprehension impairment[115]. Thus, as theoretical models of language processing have evolved, they have informed the development of novel diagnostic tools [112, 116].

Similarly, Specific Language Impairment, where children have major problems learning to talk despite typical development in all other areas, was previously understood as a unitary disorder. Research aimed to elucidate the nature of this single entity or perhaps of sub-types[117] rather than to relate an individual child's processing strengths and difficulties to theoretical models of language processing. However, investigations that went beyond the group average[118] revealed variability in the patterns of impairment. There is now general consensus on an updated term, Developmental Language Disorder, which explicitly acknowledges that this is a heterogeneous disorder that encompasses a range of problems[119]. Because of this heterogeneity, treatment should be guided by assessments of the principal dimensions of language difficulty (for example, phonology, syntax, semantics, verbal learning and memory).

Refined understanding of the nature of cognitive impairment for a particular individual that is afforded by in-depth, theoretically guided assessment leads to clearer foci for intervention. For example, the researchers studying RFS[7] were able to construct a new system for visually representing numbers that RFS quickly learned, enabling him to continue working in his numerically intensive profession despite his profound visual impairment. Such an impressive outcome would be unlikely had RFS been given more traditional treatments for number processing deficits, such as intensive practice comparing numerosity, as these treatments are based on addressing different underlying deficits than the difficulties that RFS had with numbers [120]. The specific intervention provided depended on a deep understanding of why RFS was having difficulties recognizing digits, and would not be expected to be a general solution for all individuals with numerical processing problems consequent to a neurodegenerative disease.

In sum, the single case approach provides a clear mapping between theoretical models and impairments, and in doing so provides clinicians with the tools for identifying the nature of the impairment in a particular individual. This theoretically grounded identification in turn enables the clinician to select a targeted treatment from a smaller set of theoretically sensible options, thereby increasing the likelihood that intervention will be successful[121].

[H1] Conclusions

A Google search of 'patient HM and memory' leads to over 100 million hits with over 730,000 hits in Google Scholar. These statistics alone indicate the potential power and influence single cases can have on scientific knowledge. This influence goes beyond curiosity value. The striking findings that someone can believe their wife is an imposter[97], be unable to recognise only a subset of numbers[7], or read consonants but not vowels[81], alter fundamental understanding of cognition. These fascinating phenomena stimulate the theoretician, and the depth in which such cases are examined allows for sophisticated and rigorous hypothesis testing.

In this Perspective, we summarized some of the valuable insights and theoretical advances from single cases and from the fractionation of 'unitary disorders'. We focused on the value of single case study methodology for the express goal of developing psychological theory. However, the arguments in favor of research that focuses on a deep understanding of individual cases, rather than data aggregated across a wider, potentially heterogeneous sample, holds for a wider set of scientific questions. For example, in many disciplines (such as medicine and allied health professions) systematic reviews of Randomised Controlled Trials (RCT), which treat all individuals who meet a set of inclusion criteria as homogenous, are the most highly regarded source of evidence[122]. However, the limitations of this design are becoming increasingly acknowledged. For example, statistically significant benefits in RCTs might be marginal in clinical practice[123]. Similarly, it might be (wrongly) assumed that the results of an RCT were true of all individuals in that study and will generalise to all others who meet inclusion criteria[124]. These limitations point to a need for individualised evidence for healthcare decisions. It is here that a well-designed study and analysis that goes beyond the group to investigate patterns for the individuals within that group (that is, across a series of individual cases) can shed further light on individual outcomes, thereby optimising the choice of intervention[125] . In medicine, there is increasing acceptance that trials where a series of treatment and no treatment phases are evaluated in an individual (N-of-1 trials) can provide high quality evidence on intervention effectiveness[126] . This view aligns with ours that single case research, and, in intervention, replication across a series of individual cases, are powerful and essential tools for both theoretical and applied research.

Cognition is complex, and scientists can select from a variety of methods to answer their research questions. Single case methodology can play an important role in the quest to develop theories of human cognition and is an essential part of the psychologist's palette. Despite the development of novel methodologies (that are appealing because of their novelty), single case studies continue to offer unique opportunities for advancing theories. In particular, identifying unusual patterns in single cases leads to leaps forward in directions that would not be predicted from current theoretical orientations. Going forward, we exhort researchers (and funders) to embrace single case methodology and integrate its results with those of other methodologies to maximise progress. Indeed, valuing and combining evidence from obtained using different methodologies will lead to the most rapid development of psychological theories, which provides optimal practical benefit for those with neurological difficulties.

Figure captions

Figure 1. RFS case study. A) RFS's attempt to copy an orange number 8. The original stimulus is on the left, and RFS's copy is on the right. RFS was given various pens and markers to choose from to complete the task. He began by drawing the black lines, and then added the orange background.

B) RFS was able to distinguish faces from scrambled faces when they were embedded in letters (left) but not digits (right).

Fig. 1 | RFS case study. a, RFS's attempt to copy an orange number 8. The original stimulus is on the left, and RFS's copy is on the right. RFS was given various pens and markers to choose from to complete the task. He began by drawing the black lines, and then added the orange background. **b**, RFS was able to distinguish faces from scrambled faces when they were embedded in letters (left) but not digits (right). Reprinted with permission from ref.[7], PNAS.

Table 1: Comparison of group, single case and case series designs

	Group	Single Case	Multiple single case studies	Case series
Participants	A large number of individuals	A single individual	Several individuals within a single paper or concatenated across papers	Several individuals within a single paper
Averaging of performance in data analysis	Carried out to reduce noise and reflect 'real' performance	Not used	Not used	Not used
Depth of data	Broad data sets, fewer measures, less depth.	In depth investigation	In depth investigation	Fewer measures, less depth.
Replication	With another group from the same population, or different experiment with the same group.	With different experiments within the same individual	With different experiments within the same individual or additional individuals	With another case series from the same population, or a different experiment with the same case series
Power	Number of participants	Number of items in a stimulus set Number of experiments conducted within a case.	Number of items in a stimulus set Number of experiments conducted within a case.	Number of participants Number of experiments conducted within a case.
Implications for intervention	Usually limited to 'one size fits all' according to outcome for group average.	Can be determined at an individual level	Can be determined at an individual level	Can be determined at an individual level Can provide indication of variety of different patterns of response to intervention observed
Scope of results to evaluate intervention	Results apply to the group on average and might not characterise any single individual	Results apply to the individual	Results apply to the individual with replication across individuals	Results apply to the individual with replication across individuals Results can be used to identify factors that influence outcome

Table 2: Examples case studies that have contributed to theory across the cognitive domains.

Domain	Reference	Case(s)	Etiology	Pattern of strengths and difficulties	Implications for theory and neurobiology
Object recognition	Holler, Behrmann & Snow (2019)[127]	DF, JW	Bilateral damage to ventral occipital lobe	Object Agnosia with poor recognition of images, but recognition of real-world objects was preserved when physical size matched real-world size	Separable coding of object size from object identity. Object size can be used along with a detailed representation of object shape to support identification. Object size coding is largely mediated by dorsal visual cortex.
Face perception and recognition	Duchaine et al., (2006)[128]	Edward	Developmental prosopagnosia	Prosopagnosia with severely impaired face recognition but performance within neurotypical range for a wide variety of matched visual recognition tasks with non-face stimuli.	For at least some individuals with developmental prosopagnosia, the deficit can be attributed to defective face-specific mechanisms, rather than a more general visual impairment that predominantly impacts face processing.
Spatial representation	Hartley et al. (2007)[129]	KC3, VC, RH, Jon, MH	Damage to the hippocampus	Spared processing of memory and perception for non-spatial aspects of visual scenes. Topographical perception varied across participants. A deficit in topographical memory in all cases.	Theories of declarative memory need refinement. The spatial and nonspatial tasks both depend on declarative memory, yet there was a dissociation in performance such that only processing of nonspatial information was preserved. The hippocampus is vital for short-term topographical memory.
Attention	Pishnamazi et al. (2016)[130]	SF	Selective bilateral amygdala damage due to Urbache-Wiethe disease	SF had low fear sensitivity and an impairment in classifying fearful facial expressions. Fearful faces were a strong exogenous cue to capture her spatial attention, though, unlike controls, her ability to disengage attention from fearful faces was no different than for other stimuli.	The mechanism by which fearful faces capture our attention is separable from the mechanism by which attention is disengaged from fearful faces, and the mechanism by which the fearful emotion of the face is recognized. The amygdala plays a role in evaluating the fearful emotion of faces, but not in biasing attention towards fearful faces
Consciousness	Schubert et al. (2020)[7]	RFS	Neurodegenerative disease	RFS was unable to perceive visually presented Arabic digits, with a distorted percept that impacted his awareness of embedded or nearby visual	Theories of consciousness need refinement. Theories must be able to account for how disruption in the perception of one category of

				stimuli. Event-related potentials that probed the neural processing of embedded face and word stimuli were the same whether or not awareness was impacted.	visual stimuli can result in a loss in awareness of objects that can be perceived in other contexts when those objects occur embedded in or nearby distorted objects. ERP components (like the N170 component associated with face perception and the P3b component associated with target detection) can be observed in the absence of visual awareness, and therefore are not appropriate neural markers of conscious experience of stimuli.
Lexical organisation	Khentov-Kraus & Friedmann, (2018)[81]	Case series (n = 23)	22 individuals with developmental dyslexia; 1 individual with acquired dyslexia following left internal capsule infarct	Vowel-letter migrations, omissions, and additions in reading, with significantly fewer errors on consonants. No vowel errors in speech production. Vowel errors occurred predominantly when the participants read via the sublexical route.route. For each case, 24 different assessments and the analysis of errors in reading 33,483 words ruled out deficits in orthographic-visual analysis, phonological-output, and visual, morphological, or auditory deficits. In spelling, vowels and consonants were equally accurate	The sublexical or grapheme-phoneme route of the reading system has separable components for processing consonants and vowels. There is a vowel-letter tier in this sublexical route. Spelling and reading use distinct processing components.
Morphology	Rapp et al. (2015)[131]	AES, DHY, KSR, PW, VBR	Left hemisphere stroke, including damage to the Inferior Frontal Gyrus	A double dissociation was reported, with four cases making more pure morphological errors with inflected forms in the written modality than the spoken modality, whereas one case made more morphological errors in the written modality than the spoken modality.	Morphological operations during language production are modality specific, with separable morpho-phonological and morpho-orthographic operations.
Reading	Yong et al. (2013)[132]	FOL, CLA	Bilateral posterior cortical atrophy (more marked on the right than the left)	Impaired on early visual, processing and visuo-perceptual and visuospatial tasks except for visual acuity. Word and letter reading was accurate and rapid with no difference in response latencies relative to age- and education-matched controls.	Direct access to visual word form representations are dissociable from other aspects of early visual processing. This direct access might rely on connections from the primary visual cortex to the Visual Word Form Area [133–135]

				Abnormal effects of word length were equivocal or absent MRI scans indicate relative preservation of the left fusiform gyrus (Visual Word Form Area).	
Spelling	Fischer-Baum et al. (2010)[136]	LSS, CM	Stroke with extensive cortical and subcortical damage in the distribution of the left middle cerebral artery[	Substantial letter perseverations when writing from dictation Analyses of large corpora of spelling errors indicated that letter perseveration errors tended to maintain position (defined by number of letters from either the beginning or the end of the word) between target and source responses.	Supports specific theories of serial order representation and processing in spelling that align with a more general class of computational theories of serial order behaviour across cognitive domains (for example, competitive cueing[137])
Spoken word production	Fieder et al. (2014)[138]	RAP	Left middle-cerebral artery infarct.	Impairment producing the correct determiners (the, a, or some) for mass nouns (for example, garlic). Systematic testing revealed that comprehension and production accuracy was influenced by how mass nouns were depicted (for example, a single bulb of garlic vs. many bulbs of garlic). Determiner difficulties emerged only when mass nouns and determiners were number incongruent.	Nouns are lexical–syntactically specified for mass/count status, but the derivation of countability can additionally be influenced by conceptual-semantics. Further research extended these findings, providing additional evidence for a semantic component in the representation of countability[139].
Sentence Processing	Schröder et al. (2015)[140]	Case series (n = 7; JT, UW, WE, JK, AF, RK, MP)	5 participants with left-hemisphere stroke, 1 (JK) with right-hemisphere stroke, 1 (AF) with left sided traumatic brain injury	Speech output was agrammatic (syntactically simplified with frequent omission or substitution of function words). All cases showed impairments in sentence production. Five cases showed impairments in sentence comprehension. There were dissociations between sentence structures (object who-questions vs object-relative clauses) and modalities (comprehension vs production) before treatment. Following treatment[141], the majority of participants did not show any improvements in sentence comprehension despite significant training effects in sentence production. In individuals with spared comprehension before treatment there was generalization across sentence	Evidence for modality-specific processes in comprehension and production of noncanonical sentences. These modality-specific processes have a unidirectional influence from comprehension to production.

				structures within production after treatment.	
Memory	Schapiro et al. (2014)[142]	LSJ	Complete bilateral hippocampal loss and additional medial temporal lobe damage	Anterograde amnesia. Inability to learn statistical regularities from sequences of shapes, syllables, tones, or scenes, despite no difficulties attending to the stimuli themselves.	Statistical learning is at least partially supported by a domain-general learning system that can be applied to multiple kinds of stimuli, rather than by modality-specific learning systems for different kinds of stimulus types. Previous neuroimaging research had shown that the medial temporal lobe learning and memory system is associated with rapid statistical learning[143], but the single case data indicates the system is necessary for this process.
Semantic memory	Baddeley et al (2001)[144]	Jon	Amnesia from early childhood owing to bilateral hippocampal atrophy (preterm birth, apnea requiring intubation; convulsive episode at age of 3).	Episodic memory shows impaired recall, but largely intact recognition. Semantic memory intact.	Semantic memory does not rely on recollective process of episodic memory for recognition or acquisition of semantic knowledge. Potential role of cortex in the parahippocampal region in memory
Time perception	Snyder & Chatterjee (2004)[145]	AF	Right temporal-parietal stroke	Lateralised deficit in spatial attention and poorer at judging the order of events in contralesional versus ipsilateral space. Temporal judgement improved for stimuli with more vertical separation.	Deficits in spatial processing are a known consequence of right temporal-parietal damage. This case demonstrates that damage to this region can also cause temporal processing deficits. Spatial and temporal processing interact, such that limitations in awareness of successive events closer in time can be compensated by greater distance in space. The right temporal cortex might be important in integrating spatial and temporal information.
Numerical cognition	Ashkenazi et al., (2008)[146]	AD	Infarct restricted to left intraparietal sulcus.	Acalculia Intact number comprehension and production. No major difficulty in retrieving arithmetic facts. Deficit in perception and manipulation of quantity (including atypical numerical comparisons, subitizing and calculation errors).	Findings support a model that dissociates processes for retrieval-based and quantity-manipulation-based arithmetic. Essential role of left intraparietal sulcus in numerical processing.
Music perception	Lebrun et al. (2012)[147]	AS	Congenital amusia	Unimpaired hearing, language, intellectual ability and attention.	Theories of pitch, rhythm and contour processing, need to

and recognition				Poor performance on melody discrimination, rhythm discrimination and music memory. Impaired fine-grain pitch discrimination.	account for severe and specific deficits in perceiving, memorizing, and producing music. Music depends on fine-grain pitch perception to a greater extent than other auditory functions.
Spatiomotor aspects of action	Vannuscorps et al. (2013)[148]	DC	Upper limb aplasia (DC was born without upper limbs)	Unimpaired in comprehending natural video and photographic presentations of actions involving hands (such as throwing) and other body parts (such as jumping). Impaired in identifying point-light animations of manual actions.	The results challenge motor theories of action comprehension[149–151]. No internal motor representation is required to identify actions. However, motor representations contribute to action comprehension when visual information is incomplete or ambiguous. Future research should interrogate how the motor system, visual and/or the conceptual system work together to achieve action comprehension.
Action planning	Forde et al. (2004)[152]	FK	Bilateral damage to superior and middle frontal gyri, superior and middle temporal gyri and lateral occipital gyri following carbon monoxide poisoning.	Action Disorganisation Syndrome. Performance on a range of everyday tasks was abnormally poor and characterized by numerous step omissions, sequence errors and perseverations. More errors at the end of a task than at the beginning.	Evidence for a temporal gradient: temporal order of selecting stored knowledge is determined by learned activation gradients imposed on knowledge representations (for example, using competitive cueing[137]).

6

BOX 1: Issues raised regarding single case methodology

The assumptions and methods of single case research have been extensively debated[20,24,26]. Major debates include whether a single model of the cognitive system holds for any individual with a 'normal' mind/brain (universality assumption)[20,22]; whether damaged cognitive systems represent the unimpaired cognitive system with one or more cognitive processes impaired (the subtractivity assumption)[20,24,44]; and whether there is continued need for case investigations with the advent of neuroimaging techniques[153–157].

Here we address three additional concerns.

[H1] How statistically sound is the evidence from an individual?

One basic premise of single case research is that an experiment with a single individual has the same status as a single experiment with neurotypical participants. The strength of this evidence depends on statistical power, appropriate and rigorous statistical analysis, and replicability of the effects across experiments. One misconception about single case studies is that they are underpowered because the number of participants is small. Rigorous and appropriate statistical methods have been developed to address the problem of comparing individuals to a control population[158,159]although there remains concern regarding the power of these statistical tests when comparing a single case to a control sample, especially when the control sample is small[160].

However, often the statistical inference for single case studies is based on a pattern of intact and impaired performance, across a large number of tasks, or a careful analysis of the distribution of errors produced. . In both of these cases,, the strength of evidence is improved by increasing the amount of data (for example, number of trials) collected from each participant[46]. Another basic premise of single case research is that two individuals cannot be assumed to have identical impairments. Just as no-one would expect an experiment in reading with English readers to only be accepted as valid for theory-building if replicated in Chinese readers, the validity of findings from a single case does not rest on replication in another case. Therefore, replicability in single cases is typically carried out via additional experiments with the same participant.

[H1] Is it problematic that the cases reported are rare?

Another potential concern is that the cases reported often show rare patterns, and so might be unusual or unrepresentative[24]. However, this is only an issue if one believes that this individual was unrepresentative of the population as a whole before their impairment[24]. This concern has also often been raised with respect to associations across case series of individuals.[46–49,161,162]. Cases who show a pattern that is significantly different to the trend could be statistical outliers (a result of 'noise') or theoretically informative rare cases—the cases that prove the rule[46–49]. Either position might be correct. What is critical is to investigate the source of the discrepancy from the trend to determine whether or not the individual pattern is theoretically informative[46–49]. By analogy, consider the hypothesis that all swans are white[48]. If a black swan is encountered as part of the series, further investigation is required to determine whether this is a white swan that is covered in soot, or a 'true' black swan that has not previously been encountered. The former is an uninteresting outlier, the latter is a theoretically critical 'rare' case.

[H1] Can single case studies be used for brain-behavior mapping?

There are many limitations that make it challenging to use single case studies to draw inferences about brain-behavior mappings. Brain-behavior relationships[60] and network-level properties of brain organization[64,163] are highly variable within neurotypical individuals. Lesion locations are rarely constrained to anatomical structures and damage disrupts both local cortical processing and connectivity between regions, further complicating brain-behavior inferences[164]. Moreover, neural plasticity occurs following brain damage; there remain many open questions about the nature of this reorganization (which is highly variable across individuals) and what consequences it might have for drawing inferences about structure-function mapping in the undamaged brain[165]. Finally, cognitive differences in single case studies are the result of a variety of etiologies, including acute brain damage, slowly progressing diseases, and developmental differences that have been with the individual since birth. The consequences of each of these etiologies on brain organization and reorganization are not well understood. In some cases, it might be possible to draw inferences about brain-behavior mappings from single cases[166,167], but for the most part claims about the neural underpinnings of a cognitive function from a single case should be considered with caution. Importantly, localization of function is not critical for single case studies to contribute to theory-building in cognitive science.

Box 2: Common methods for building theories using single cases

[H1] Dissociations

The Figure gives an example where dissociation is used to discriminate between rival theories. Neurotypical adults and children are able to recognise words and faces. Both types of visual stimuli could be recognised using a single processing routine (Theory A) or using separate processes (Theory B). Case 1 is able to recognise words but not faces (a dissociation between tasks). However, Theory A predicts that impairment to visual processing impacts on both word and face recognition. Thus, Theory B can better account for Case 1's pattern of performance—the two tasks use separate processing routes that can be independently impaired. However, it is possible that it is just easier to recognise faces than words, in which case mild impairment to Theory A's single processing route might result in Case A's data. Case 2 shows the reverse pattern—they can recognise faces but not words. Therefore, faces cannot simply be more difficult than words (or this pattern wouldn't exist). Thus, Theory B (but not Theory A) can account for both Case 1 and Case 2.

Thus, by using the reversed patterns across individuals (a double dissociation) strong evidence can be obtained to adjudicate between theories. Importantly, dissociations must be statistically verified. In particular, there should be a significant difference between the two tasks within an individual[168–170].

However, a double dissociation is not always required. For example, if the question is about the nature of the representation rather than about shared or separate processing routes then a single case that shows differences in processing of different types of stimuli could be sufficient (for example, digits versus letters in the case of RFS[7]).

[H1] Control data

Classically, dissociations required one task to show performance equivalent to neurotypical control participants and the other to show performance significantly poorer than controls[168]. However, some authors argue that a comparison to controls is not necessary, and a significant difference between tasks within the case is all that is required for a dissociation to be present [169,170]. In that case, it is particularly important that the difference between the two tasks for the single case is larger than the difference between the tasks in controls, which might only be apparent if control performance is off ceiling[171].

It is also important that the control data is of sufficient specificity: it is not sufficient for a single case to differ from control participants 'on average', but rather they must differ from a series of individual control participants. Hence, the measure needs to be sufficiently reliable that each control participant shows (or does not show) the pattern of interest. Without this demonstration, it is not possible to conclude that the individual with brain damage is truly showing an exceptional pattern. An effect that is reliable 'on average' might not be reliable at an individual level[54,62]. Thus, control data must be derived from paradigms that are sufficiently sensitive to distinguish signal from noise.

[H1] Analysis of critical variables

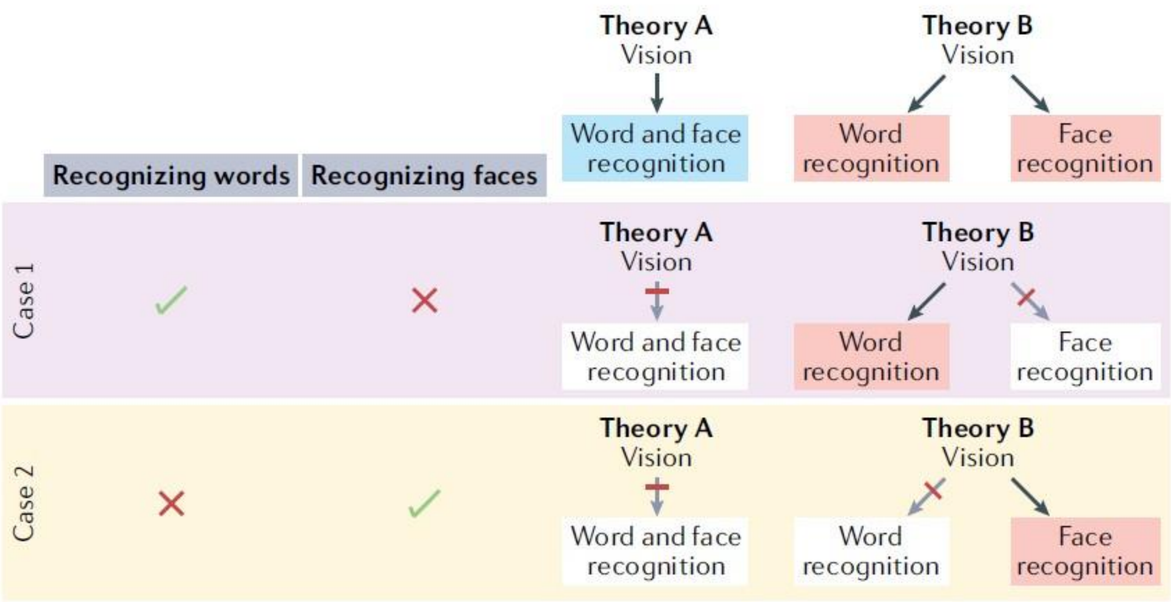
The factors that influence performance accuracy are also informative when using single case data to build theories (critical variable approach)[23]. For example, if word retrieval accuracy in aphasia is affected by how concrete or abstract a target word is in the absence of an impairment to word meanings, theories must be able to account for these effects[172].

[H1] Analysis of error patterns

The type of errors produced can also be used to guide investigation and build theories. For example, that errors in reading could be specific to vowels led to the theory that vowels and consonants are processed separately[81]. Similarly, the fact that some individuals make reading errors that are related in meaning to the target word (for example, ‘MARRIAGE’ read as ‘wedding’), rather than related in spelling (for example, ‘MARRIAGE’ read as ‘carriage’) suggests that reading can be proceeding via the store of word meanings (the semantic system)[173].

[H1] Intervention

Treatment of the cognitive impairment has also been used to test theoretical accounts[174], and is particularly powerful for testing causal relationships. For example, a causal association between impaired spoken naming and written naming might be consistent with a theory where written naming relies on spoken naming, but is also consistent with a third factor (poor access to word meaning) influencing both tasks. However, if treatment for spoken naming (that does not impact word meaning) fails to improve written naming, then the causal relationship between the two can be rejected.



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