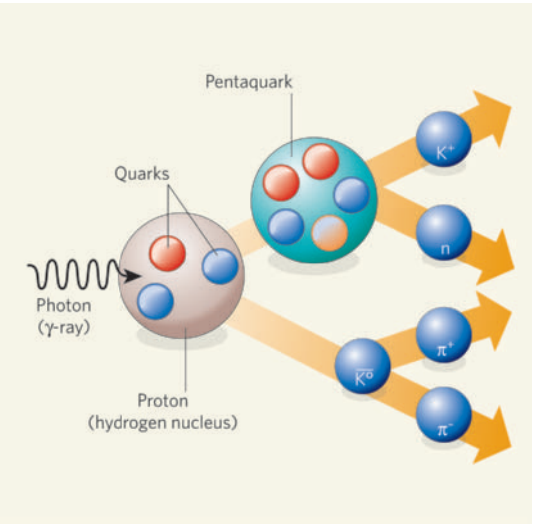

Figure 1 | Give me five. Representation of the reaction channel investigated by the CLAS experiment at the Jefferson Laboratory for evidence of a pentaquark state. An incident photon (γ-ray) initially interacts with a hydrogen nucleus, consisting of one proton. The main constituents of a proton are three 'valence quarks' of different types, or 'flavours': two 'up' (blue circles) and one 'down' (red). At sufficiently high interaction energies, the conservation laws of particle physics would allow a short-lived pentaquark (five-quark) resonance to be created — containing, in addition to up and down quarks, a 'strange' antiquark (yellow circle). This pentaquark does not live long enough to be observed directly; rather, its fleeting existence must be inferred from longer-lived products of this particular reaction — a K meson (also with strange-quark content), a neutron and two π mesons. From its reconstruction of such reactions, CLAS has failed to find any evidence for the existence of a pentaquark.

typically exceed 100 MeV.) No pentaquark had ever been seen with certainty, and their absence had been one of the planks upon which the standard quark model had been developed.

A surprising feature of the 1997 prediction was that the particle would have a width of the order of a few MeV and not the hundreds that might have been expected. Initially, the paper[1] received little attention, but the LEPS collaboration at the SPring-8 laboratory in Japan was encouraged to mount an experiment to look for the particle. The first pentaquark sighting was announced by them[2] in early 2003, exactly at the predicted mass and with a narrow width.

The experiment involved photon beams interacting with protons or neutrons in a carbon nucleus. There was some surprise that the first sighting of a particle with such a narrow width should have occurred in such a complex environment: the nuclear constituents are bound and have kinetic energy, which tends to smear any signals. However, this stimulated experimentalists elsewhere to look again at their data from earlier experiments to see if these contained evidence for the pentaquark.

Within a few months, teams from the Jefferson Lab, from Russia and from the SAPHIR collaboration at the Electron Stretcher Accelerator (ELSA) in Bonn, Germany, all announced that they, too, had spotted tantalizing hints of the particle in data taken in other experiments. For instance, the SAPHIR team's evidence of the pentaquark[3] came from data they had obtained in 1997–98 and confirmed its mass of 1,540 MeV. None of these experiments on their own was very significant, but the broad agreement among them created huge excitement.

By the end of 2003, more than ten experiments worldwide had reported evidence for the pentaquark (see ref. 4 and references therein), mostly produced by photons interacting with protons or neutrons ('photoproduction'). The pentaquark particle then decayed into a K meson and a proton or neutron. The targets included protons, and deuterium and heavier nuclei; the kinematics covered both low and high energy; and the narrow peak invariably occurred around 1,540 MeV. Hints of sibling pentaquarks also emerged, for example one with a positive value of another quantum number, charm, rather than strangeness. Well over 1,000 theoretical papers have addressed such phenomena.

In 2004 a series of theoretical criticisms emerged, centred around some anomalies. On closer inspection there seemed to be small but systematic differences in the mass, and in the width of the signals[4]; also, it was unclear how such a narrow width state was apparently produced so readily. Moreover, reports of negative experimental searches began to appear. The null results tended to come from experiments using nuclei, or hadrons such as π mesons or protons, rather than photons, and also included searches involving very-high-energy electron beams. Unlike some of the supposedly positive sightings, the common feature of the null results was that they tended to have rather large statistical samples.

One suggestion was that the pentaquark might have some unusual production mechanism, such that photoproduction at energies of a few GeV is especially favoured. This loophole could be closed by dedicated photoproduction experiments with high statistics, and two such experiments had already been designed at the Jefferson Lab.

The latest news from researchers in the Jefferson Lab's Large Acceptance Spectrometer (CLAS) collaboration, announced at the American Physical Society spring meeting on 16 April, adds to the concern about the reality of the pentaquark. The researchers have taken data from an experiment in which a photon beam hit a liquid-hydrogen target (Fig. 1), under conditions similar to those of the earlier experiment conducted by the SAPHIR collaboration. The CLAS team's data contain statistics that are improved by two orders of magnitude, and find no evidence of a pentaquark with mass 1,540 MeV.

The CLAS collaboration data show, at a level of precision at least 50 times higher than the published SAPHIR result, that this particular reaction produces no pentaquark. Researchers at the Jefferson Lab are currently undertaking dedicated hunts for the pentaquark, including an experiment that repeats their original pentaquark search with much higher statistics. Those data are being analysed, and the results are expected later this year. If they show a null result, the pentaquark story will probably have come to an end for physicists but will live on as a case-history for historians and philosophers of science. ■

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NEUROSCIENCE

Plasticity and its limits

Martin I. Sereno

How much can the adult brain compensate for injury to the senses of touch or vision, for example? The answer from the latest results on the visual system, involving damage to the retina, seems to be 'very little'.

Many sensory systems are characterized by connections from receptor surfaces, such as the retina or skin, in which the relationship between neighbouring inputs is preserved. The resulting 'topological maps' are also commonly maintained in subsequent projections between sensory areas within the brain. Early work showed that these map-like projections can adapt to the loss of input from part of the receptor sheet by rearranging input lines, with the silenced brain areas regaining responsiveness to remaining parts of the sheet.

In the somatosensory system, which among other things conveys the sensation of touch, this plasticity was unexpectedly found to persist into adulthood. Now, however, Smirnakis *et al.* (page 300 of this issue)[1] show that in the initial stages of the primate visual

system topological map-like projections are not plastic in the adult on a timescale of half a year.

The ability of the developing brain to adapt to damage is well documented. A striking example in humans is that children who have had their left cerebral hemisphere removed early in life often regain motor control of the right side of their bodies, and go on to develop almost normal language abilities using the right hemisphere[2,3]. As the brain matures, however, it becomes much less plastic. For example, even though adults may become proficient in a second language, they find it difficult to erase all traces of a foreign accent. Children, by contrast, can learn the fine vocal distinctions of a second language with native-speaker precision.

Given the reduction in plasticity with age, Merzenich and colleagues' demonstration in 1983, that the primary somatosensory cortex in monkeys remained plastic in the adult, came as a shock[4]. It had long been known that sensory maps in some vertebrates — such as that from the retina in frogs — remained plastic into adulthood[5]. But this was thought to be due to the fact that, in the frog, both the retina and the target brain area concerned — the optic tectum — add neurons throughout adult life.

In the experiment of Merzenich *et al.*, damage to nerves carrying touch information from several fingers in monkeys initially resulted in silencing of most of the corresponding finger maps in primary somatosensory cortical area 3b. After several weeks, however, the silenced region came to be activated by skin from the surrounding fingers — the representations of those fingers expanded to completely fill in the silent cortex. Although the body-map reconfigurations in the early experiments were measured in millimetres, much longer-term denervation of an entire arm resulted in reconfigurations of more than one centimetre[6] — a distance likely to have required sprouting by neurons rather than mere enabling of existing but formerly silent connections. The newfound cortical plasticity in adults was welcomed by cognitive neuroscientists, and had implications for recovery from brain damage and the role that sensory experience plays in it.

Equivalent experiments were soon performed in area V1, the primary visual cortex[7,8]. Initial reports showed that retinal lesions resulted, after several months, in the filling-in of the representation of the affected zone in V1 with input from the region of the retina directly surrounding the damage. It was also reported that cortical areas near the boundary of the region where the input was damaged showed changes within minutes of the lesion (for example, an increase in the size of the receptive fields there).

Over the years, however, the remapping picture in both somatosensory and visual cortex became more complicated. For example, in examining the hand representation in area 3b, Kaas and colleagues[9,10] found that the representations of the sensitive undersides of individual fingers were separated by narrow regions with reduced myelination, an indication of reduced within-cortical connections (Fig. 1). The locations of these septa, however, were not affected by the long-term loss of sensory input that resulted in somatosensory map reconfigurations in the same animals. That the septa appear at all suggests that somatosensory representations are normally quite stable despite variable experience; that they persist after peripheral damage suggests that some aspects of within-cortical connections are not plastic in the adult.

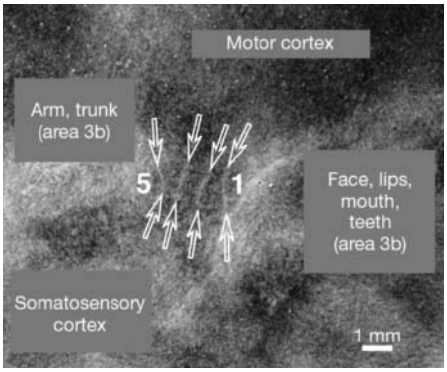

Figure 1 | Representation of fingers in the monkey somatosensory cortex. Somatosensory cortical area 3b contains a map of the entire body surface. In this myelin-stained section through the middle layers of the cortical sheet in owl monkey area 3b, thin septa (arrowed) are visible between the representation of each finger (1 is the thumb, 5 the little finger) where the density of myelin — and within-cortical connections — is reduced. These septa are not affected when peripheral nerve damage leads to reorganization of the finger maps, suggesting there are limits to cortical plasticity in the adult. (M. I. Sereno, unpublished material.)

In subsequent experiments with retinal lesions in cats, stages in the input pathway were examined to try to determine the main site of the plastic changes. The cortical filling-in of V1 occurred despite a persistent dead zone in the preceding stage, the dorsolateral geniculate nucleus, and basically unaltered projections from there to V1[11]. This suggested that horizontal within-cortical connections are the main plastic element. But the filled-in cortical region contained neurons with poorer contrast sensitivity[12], and in monkeys there was a long-term reduction in cytochrome oxidase staining[13] (an indication of reduced neuronal activity). Together, these features indicated that whatever reorganization had occurred was insufficient to support normal activity, even after a long recovery.

In their work, on monkeys, Smirnakis *et al.*[1] used both functional magnetic resonance imaging (fMRI) and microelectrode recording. To their own surprise, their results came down strongly against any substantial reconfiguration of the V1 map — their fMRI data showed that the 'hole' created in V1 by a retinal lesion was still there after more than seven months; and their microelectrode data suggested that the responses inside the hole were correspondingly weak.

How can the disparity with earlier results be explained? One possibility is that the previous microelectrode recordings may have been subject to 'single-unit' selection bias — with a microelectrode, it is difficult to estimate the proportion of neurons that *do not* respond to a stimulus. Although fMRI has relatively poor spatial and temporal resolution compared with single-unit recordings, like optical recording (and the anatomical cytochrome oxidase stain) it avoids the selection bias that may have resulted in an overestimate of the neurons that responded. Another advantage of fMRI is that it samples the whole brain. Subsequent reports using this method may uncover how higher visual areas react to the hole in V1 — a topic of great interest, because visual experience depends on those areas too.

Finally, these results[1] contrast with an account[14] of cortical reorganization in a human, assessed 20 years after retinal degeneration, which showed substantial filling-in of activity in what used to be the representation of the fovea in V1. In addition to the much longer recovery time, the lesion included the entire fovea instead of being situated to one side of it, and the subject was conscious. It remains to be seen what factor or factors can explain the difference.

The possibility of plasticity in the adult cortex plays on the hope that, if one only tries hard enough, it is possible to overcome neural adversity. But hope must not obscure the data — for now, it seems that one must try for a very long time indeed if the area in question is V1. ■

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