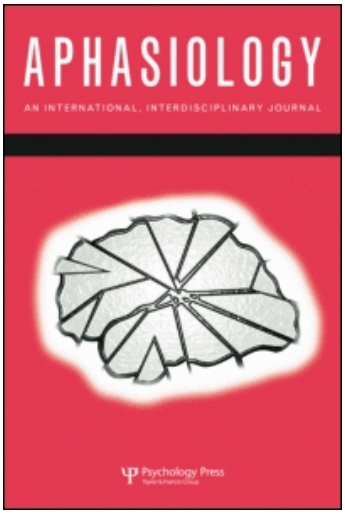

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Participation of the insula in language

Alfredo Ardila[a]; D. Frank Benson[a]; Frederick G. Flynn[b]
[a] Miami Institute of Psychology, Miami, USA [b] Madigan Army Medical Center, Tacoma, Washington, USA

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Participation of the insula in language

ALFREDO ARDILA†, D. FRANK BENSON* and FREDERICK G. FLYNN‡

† Miami Institute of Psychology, Miami, USA
‡ Madigan Army Medical Center, Tacoma, Washington, USA

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Abstract

Many investigators have suggested that damage to the left insula plays a role in aphasia. Among the various language disturbances associated with damage in the insula are Broca's aphasia, conduction aphasia, Wernicke's aphasia and subcortical aphasia. Although a wide variety of language disturbances have been related to insula damage, whether the damage to the insula was instrumental or merely based on its close anatomical juxtaposition to other language-significant neuroanatomical areas has never been clear. Recent studies of anatomical connections of the insula, point to an important viscero-limbic role and it can be suggested that the insula may influence verbal affect, a true language role.

Introduction

The insula, a complex and archaic brain structure, has never been understood. The basic anatomical parameters of the insula have been reported (Mesulam 1985). The anterior segment of the insula extends to and interfaces with Broca's area while its posterior elements adjoin Wernicke's area. The left insula is notably larger than the right in most humans (Mesulam and Mufson 1985). Both the asymmetry and the location in the epicentre of the human language area (Luria 1970, Benson 1979, Benson and Ardila 1996) suggest that the insula might be active in language. A role of the insula in language processing has long been suggested (Wernicke 1874, Freud 1891), but never substantiated. Electrical stimulation of the brain has supported the assumption that the insula is indeed a part of the language zone (Ojemann and Whitaker 1978).

Anterior insula

Involvement of the anterior part of the insula in Broca's aphasia was noted many years ago (Bernheim 1900, Dejerine 1914) and confirmed more recently by CT imaging and clinico-pathological studies (Mohr 1976, Kertesz *et al.* 1979, Kertesz 1991). In 20 cases of Broca's aphasia, using the CT scan as well as autopsy for localization, Mohr *et al.* (1978) found that lesions restricted to frontal operculum produced transient aphemia associated with mild word-finding difficulties but not

Address correspondence to: Dr Alfredo Ardila, Miami Institute of Psychology, 8180 NW 36 Street, Miami Florida 33166, USA.

* D. Frank Benson passed away on 12 October 1996.

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the classic clinical features of Broca's aphasia. Only with large lesions involving the entire operculum plus portions of the anterior insula and descending white matter was the full syndrome observed. Mazzocchi and Vignolo (1979) reported similar findings: the anterior insula was consistently damaged in patients who showed a persistent Broca's aphasia. In fact, while the frontal operculum and deep structures were usually damaged, the insula was always involved when the aphasia was permanent. Levine and Sweet (1983) examined different hypotheses regarding the site of damage in Broca's aphasia and conjectured that aphasia, like hemiplegia, has a focal area of primary importance surrounded by a fringe area of less consistent involvement. The nuclear area for Broca's aphasia was the inferior precentral gyrus; the insula was included in the fringe area. Murdoch *et al.* (Murdoch *et al.* 1986, Murdoch 1988) based on CT correlation studies, suggested that Broca's aphasia requires damage of the opercula, the insula, and the lenticular nucleus.

Signoret *et al.* (1984) conclusion, based on a review of Broca's original case, and Alexander *et al.* (1989), based on CT studies, insist that a permanent Broca's aphasia syndrome demands significant dominant hemisphere destruction involving frontal operculum, inferior and middle frontal gyri, periventricular and subcortical white matter, anterior parietal cortex and anterior-superior portions of the insula. While not every structure need be fully involved, it appears that most permanent cases of non-fluent Broca's aphasia will have structural damage involving the insula.

Impairment in motor organization of speech represents a central defect in Broca's aphasia (Benson and Ardila 1996). Dronkers (1996) pointed out that the left precentral gyrus of the insula is involved in motor planning of speech. Twenty-five stroke patients with a disorder in motor planning of articulatory movements were compared with 19 individuals without such deficits. A robust double dissociation was observed. All patients with articulatory planning impairments presented lesions including the anterior insula. This area was completely spared in all patients without these articulatory defects. Hence, anterior insula represents the crucial brain area in motor planning and organization of speech.

A growing consensus suggests that lesions restricted to F3 alone do not produce a permanent Broca's aphasia; on recovery, a mild defect in articulatory agility (dysprosody) produces the foreign accent syndrome (Monrad-Krohn 1974, Ardila *et al.* 1988). The syndrome of Broca's aphasia demands more extensive damage and CT scan studies systematically disclose that the anterior insula is involved when Broca's aphasia persists (Mohr *et al.* 1978, Henderson 1985).

Middle insula

Middle insula damage has been implicated in conduction aphasia. Wernicke (1874) originally proposed that the crucial location of damage in conduction aphasia was the insula, based on the mistaken belief that the pathways connecting posterior with anterior langauge areas coursed through the insula. Lichtheim's (1995) case of conduction aphasia with postmortem data confirmed Wernicke's assumption, and additional cases suggested that when language repetition was disordered the insula was damaged (Goldstein 1911). Others (Dejerine 1901, 1914), however, proposed the arcuate fasciculus as the main connection for sensory and motor language areas. Supramarginal and/or parietal operculum damage involving the arcuate fasciculus was proposed as crucial to the syndrome of conduction aphasia. Dejerine's topography has become accepted (Geschwind 1965, Damasio and Damasio 1983,

Benson and Ardila 1994, 1996) but Benson and colleagues (Benson *et al.* 1973, Mendez and Benson 1985) confirmed Kleist's (1934) earlier demonstration that conduction aphasia could result from damage in several different loci including regions above, behind or below the sylvian fissure (Hecaen *et al.* 1955). Conduction aphasia can be correlated with a broad range of localized brain damage (Kertesz 1979, 1985, Mendez and Benson 1985). Only suprasylvian location included insular damage.

Mazzocchi and Vignolo (1979) reported one case of conduction aphasia with damage centred in the rolandic operculum but with extension anterior and deep to the middle insula. The cases reported by Murdoch *et al.* (1986) involved postrolandic structures including subcortical structures under the middle insula. Ardila *et al.* (1989) reported six cases of conduction aphasia with insula damage. Lesion extension to the underlying structures was variable but in none was the cortex of the supramarginal gyrus, Broca's or Wernicke's areas involved. In all cases the insula and portions of the lenticular nucleus were affected.

Damasio and Damasio (1980, 1983) studied six cases of conduction aphasia; in four cases, the damage clearly involved the insula but in one no evidence of insular involvement was found. They proposed that the defects in repetition in their cases were based on disconnection of posterior sensory language areas from the anterior motor language areas and further suggested that the repetition deficit followed damage in a subinsular pathway, the classic arcuate fasciculus. Although the explanation of conduction aphasia as a disconnection syndrome has been challenged (Luria 1966, Brown 1972, Ardila and Rosselli 1990) considerable evidence is available to support this mechanism (Geschwind 1965, Mendez and Benson 1985).

Conduction aphasia has been associated with both pain asymbolia and pseudothalamic pain syndrome (Biemond 1956, Benson 1979). Some suggest that the pain disorder can be correlated with insular damage (Berthier *et al.* 1987); others suggest separation of thalamus and SII (parietal operculum) as the crucial feature (Biemond 1956).

Not all cases of conduction aphasia have insula involvement; it is possible that clinical differences (particularly a disorder in pain characterization) may occur in those cases of conduction aphasia in which the insula is damaged; however, to date this hypothesis has not been confirmed.

Posterior insula

The posterior insula and nearby temporal isthmus were associated with true Wernicke's aphasia by Marie (1906) but it is now more appropriate, however, to discuss Wernicke-type aphasias with recognizable subtypes (Lichtheim 1885, Luria 1966, Huber *et al.* 1975, Luria 1976, Benson 1979, Kertesz 1983, Lecours *et al.* 1983, Benson and Ardila 1996). Luria distinguished two sensory aphasias (acoustic-agnosic and acoustic-amnesic). Kertesz (1983) proposed four types of Wernicke's aphasia (Wernicke's aphasia with predominantly phonemic paraphasias, Wernicke's aphasia with predominantly semantic paraphasias, Wernicke's aphasia with predominantly neologistic jargon, and pure word deafness).

Variations in the syndrome of Wernicke's aphasia appear to reflect different localizations of tissue damage. Luria (1970) correlated the phonemic imperception of acoustic-agnosic aphasia with damage to the superior temporal lobe; unilateral lesions causing pure word-deafness consistently involve Heschl's gyrus and/or

pathways from the medial geniculate nucleus (Gazzaniga *et al.* 1973, Benson 1979, Yaqub *et al.* 1988). Liepmann and Storck's (1902) case of word-deafness had a left temporal subcortical lesion that included the posterior insula. A case of word-deafness with damage in the superior temporal gyrus and middle portions of the temporal operculum involving the posterior insula was reported by Kertesz (1983). Habib *et al.* (1995) reported a case of transient mutism and persistent auditory agnosia due to two successive inchemic infarcts mainly involving the insular cortex of both hemispheres. Neologistic jargon has been reported in cases with insula damage. Kertesz and Benson (1970), using isotope scan and/or autopsy localization in 10 cases with neologistic jargon, demonstrated damage in the posterior portion of the first temporal convolution, the supramarginal gyrus and the underlying white matter. Using a CT overlap technique, Kertesz (1981) found that the posterior insula was involved in aphasics with neologistic jargon; he eventually concluded (Kertesz 1983) that the anatomical structure invariably involved in neologistic jargon aphasia was the temporoparietal junction, combining the superior temporal lobe, supramarginal gyrus, posterior segments of the temporal and parietal opercula, and the posterior insula.

Modern CT scan studies (Kertesz 1983, Naeser 1983, Murdoch 1988, Kertesz 1994) consistently correlate the syndrome of Wernicke's aphasia with temporal lobe damage. Rather diverse areas of damage have been demonstrated, however, probably because Wernicke's aphasia is a heterogeneous clinical syndrome. Basso *et al.* (1985) found Wernicke's aphasia correlated with perisylvian lesions while Poeck *et al.* (1984) proposed that Wernicke's aphasia followed relatively circumscribed damage to the superior temporal gyrus. Mazzocchi and Vignolo (1979) monitored the evolution of the aphasia and found that in cases of Wernicke's aphasia that persisted for over 60 days the posterior insula had been significantly destroyed or involved. In all 13 patients with Wernicke's aphasia studied by Ardila *et al.* (1989), brain damage, as demonstrated by CT scan superimposition, involved the posterior insula and temporal isthmus. Lesion extension included the superior temporal gyrus and/or supramarginal gyrus. This latter study suggested that the critical areas for the full syndrome of Wernicke's aphasia included the posterior insula and temporal isthmus. When the findings of Wernicke's aphasia persist, insula involvement is almost invariably present.

The Wernicke's aphasia syndrome, however, includes a number of diverse symptoms (Benson and Ardila 1996). Studies suggest that cases with predominantly phonemic paraphasias plus verbal memory deficits show damage to the superior and middle temporal gyri (Cappa *et al.* 1981). A predominance of semantic paraphasias correlates better with temporo-occipital and angular damage (Benson 1979, Cappa *et al.* 1981, Kertesz 1983) while the aspect of phonemic imperception (word deafness) appears to be associated with Heschl's gyrus, medial geniculate-cortical pathways and/or posterior insula damage (Gazzaniga *et al.* 1973, Benson 1979, Kertesz 1983, Yaqub *et al.* 1988).

Electrical stimulation of the posterior insula has been associated with naming omission errors (Ojemann and Whitaker 1978).

Subinsular structures

A role of subinsular structures in aphasia received strong support from Marie (1906) who noted that the aphasic patients described by Broca suffered extensive

damage to tissues deep to the insula, an area subsequently known as Marie's quadrilateral space. Marie proposed that the major finding in Broca's patients was articulatory disturbance (anarthria) and suggested that damage in the quadrilateral space produced a motor speech defect, not an aphasia. Unfortunately, Marie's clinical descriptions did not include the disturbance, if any, that would result from pathology restricted to the quadrilateral space. The quadrilateral space was, at best, a vague entity including all or portions of the claustrum, the external capsule, extreme capsule, the internal capsule, putamen and insula. The area is large and rich with interconnections to significant neighbouring structures; a variety of clinical features could be anticipated. The most frequently reported pathology involving Marie's quadrilateral space is haemorrhage producing an acute, dense hemiplegia and mutism. With evolution, a severe verbal expression disorder with some degree of comprehension difficulty is observed. Often the comprehension deficit is sufficient to warrant the term global aphasia. Lesser degrees of destruction produce more specific disturbances with both aphasic and/or dysarthric elements.

CT scan investigations have more recently demonstrated communication disturbances resulting from lesser degrees of subcortical damage (Alexander *et al.* 1987, Metter and Hanson 1994, Naeser 1994). Most current reports emphasize two anatomical sites, the thalamus and the striato-capsular region (Alexander and Benson 1991, Kertesz 1991). The second will be stressed because of relations with the insula. Many studies have associated aphasia with striato-capsular damage (Alexander and LoVerme 1980, Damasio *et al.* 1982, Naeser *et al.* 1982, Cappa *et al.* 1983, Naeser 1983, Wallesch 1985, Alexander *et al.* 1987, Perani *et al.* 1987, Tanridag and Kirshner 1987), but whether the observed disturbances represented 'real aphasia' (Damasio *et al.* 1982) or dysarthria/aphemia (Schiff *et al.* 1983) remains controversial.

From review of their own cases and those reported in the literature, Alexander and colleagues (Alexander *et al.* 1987, Alexander and Benson 1991) proposed six striato-capsular language syndromes: (1) lesions limited to the putamen or the head of the caudate nucleus resulting in no language disturbance or only mild word-finding difficulty. If the putamen was extensively involved, hypophonia would be observed; (2) limited involvement of the anterior limb of the internal capsule producing no speech or language disturbance. Similarly, involvement of the paraventricular white matter produced no language or speech disturbance except a mild dysprosody; (3) involvement of the anterior superior paraventricular white matter caused reduction in language production without overt language abnormality; disconnection of the supplementary motor area from Broca's area is suggested as a cause; (4) a more extensive lesion involving striatum, posterior medial anterior limb of the internal capsule and anterior superior paraventricular white matter produced language abnormalities (word-finding difficulties, occasional phonemic paraphasias and mild disturbances in comprehension), plus a marked dysarthria; (5) posterior extension of the putaminal lesion to involve the temporal isthmus producing a fluent aphasia with neologistic output and impaired comprehension; and (6) damage lateral to the putamen (insular cortex, external capsule, claustrum and extreme capsule) producing a language disturbance characterized by phonemic paraphasias and resembling conduction aphasia. These studies suggest that the deep subcortical lesion of pattern 5 produced Wernicke's aphasia (damage at the temporal isthmus) while that of pattern 6 was associated with conduction aphasia (damage at the insular cortex).

Damage that involves the insula cortex and adjacent temporal isthmus appears to be the source of the language disturbances produced by pure subcortical lesions, at least in many instances. Subcortical structural lesions, however, may produce symptoms characteristic of a disturbance at some distance from the actual site of structural damage suggesting that dominant hemisphere language cortex may be functionally involved following separation from a deep structure (Benson 1979, Metter *et al.* 1981, Metter 1987, Metter and Hanson 1994).

Despite remarkable advances in brain image resolution over the past decade, the ability to identify damage to small subcortical structures such as the claustrum, the internal capsule and the insular cortex remains crude. Subinsular aphasia may be common and specific, or it may not exist at all.

Pure insula pathology

Pathology involving only the insula cortex and immediate subcortical structures is rarely reported. Alexander *et al.* (1987) reported two cases with CT evidence of pathology limited to the left insula and subjacent extreme/external capsules. An aphasia with mildly paraphasic production and agraphia was noted in both. Nielsen and Friedman (1942) reported several cases from the literature with autopsy-demonstrated left insula damage and mild aphasia. They noted, however, from their own cases and others in the literature, that a similar language syndrome followed isolated extreme capsule damage and postulated that insula damage without extreme capsule involvement would not produce aphasia. Starkstein *et al.* (1988) observed crossed aphemia associated with a right insular lesion. Fifer (1993) describes a patient with a lesion involving the right insula and adjacent white matter. The patient presented with an unilateral auditory processing disorder when presenting speech materials to the left ear. Habib *et al.* (1995) reported a case of bilateral insular damage, extending to a small part of the striatum on the left side, and to the temporal pole on the right. The patient presented mutism for about 1 month, did not respond to any auditory stimuli, and made no effort to communicate; on follow-up examinations, language competence had re-appeared almost intact, but a massive auditory agnosia for non-verbal sounds was observed. Shuren (1993) observed a patient who developed impaired speech initiation as the result of a left anterior insular infarct. The author proposed that dominant hemisphere anterior insular lesions impair the speech initiation loop. A possible role of the left insula in speech initiation and language motivation could be conjectured.

Overview of the participation of insula in language and communication

The insula occupies a central location in the brain area responsible for language and, based on this anatomical location alone, is frequently damaged in aphasia-producing brain lesions. Both the older autopsy-based studies and more recent brain image correlations suggest that anterior insula damage is often present in cases of moderate to severe Broca's aphasia, middle insula damage is frequently correlated with repetition defects (conduction aphasia), and posterior insula damage co-occurs with the word deaf features of Wernicke's aphasia. Damage to the lenticular area that extends externally to involve the insula, in addition to producing motor speech disorder, is often associated with language compre-

hension, repetition and word finding impairments. These observations suggest a possible role for the insula in language processing and indicate that damage to the insula may be a source of aphasia. They may, however, merely reflect contiguity. Whether the insula plays a role in language remains unsettled.

While the evidence of an insula aphasia remains circumstantial, review of the early anatomical/clinical correlation data, strongly confirmed by more recent brain image correlation studies, suggests that the insula is involved in selected varieties of aphasia. The word deaf component of Wernicke's aphasia, the repetition impairment of some cases of conduction aphasia, persistent Broca's aphasia, and defects in complex planning and organization of speech seem tied to involvement of the insula along with neighbouring structures and when the insula is not involved the clinical features are either less prominent or non-persistent. In addition, although the evidence is less robust, subcortical aphasia may be tied to insula damage. What is absent are behavioural observations following damage isolated to the insula.

In addition to the apparent role of the insula in aphasia syndromes, the possibility that the insula may play a specific role in more basic communication control deserves consideration. The cytoarchitectural division of the insula into anterior agranular, middle dysgranular (transitional) and posterior granular cortices, corresponds to similar, functionally significant divisions of the non-insular cortex. While the neurons of the insula have widespread and diverse connections, strong functional variation exists. The bulk of anterior insula pathways connect to hypothalamic-limbic structures. The bulk of posterior insular connections relate to sensory-motor cortex. Greater association of anterior insula with limbic functions contrasted with greater association of posterior insula with sensory-motor activity can be presumed.

All portions of the insula interconnect with all other portions but the degree of interconnection is not equal in all directions. A considerably greater number of connections traverse from anterior insula to posterior insula than in the opposite direction. When this anterior-posterior trend of insula conduction is correlated with the strong limbic input to the anterior insula, it can be proposed that the insula represents a major source of autonomic-visceral influence on the sensory-motor association cortex. Among the areas of dominant hemisphere sensory-motor cortex under this influence would be neuroanatomical structures crucial to language. From this it could be conjectured that the left insula would have a more direct influence on motivation and emotion as expressed in spoken/written language (verbal affect). The converse, a right insula influence on non-verbal affect, may also be considered. The insula may represent a crucial element participating in several distinct networks involved in verbal and non-verbal communication (Mesulam 1990). Habib *et al.* (1995) have proposed that the insula may represent one key component of a finely tuned attentional system whose function would be not only to select the relevant information from the continuous flow of auditory inputs, but also trigger the adequate interhemispheric balance according to the verbal or non-verbal nature of the current stimulus. Habib and coworkers have proposed that bilateral damage to the insula would disrupt the motivational mechanisms precluding to the motoric aspects of human communication, by depriving them of connections with various limbic structures.

Much of animal (including human) expression conveys emotional content. A number of 'types' of language are available to express emotion. Gestures and vocal

prosody are basic means, fully developed in advanced animals as well as man. Tail-wagging, raised ruff or tail-between-the-legs postures are readily recognized emotional expressions of a dog. Similarly, prosodic differences representing anger, fright and happiness are obvious in the vocal output of many species. While not fully proven, current evidence associates these basic means of emotional expression with operculum, basal ganglia and insula tissue (Ross 1981, Berthier *et al.* 1987, Darkins *et al.* 1988, Cancelliere and Kertesz 1990). The human has additional ways to express feelings. While prosodic qualities are crucial to spoken feelings, emotion can be expressed without either gesture or vocal inflection. Thus, one can laugh at what one reads, be frightened by a terror tale, or become sad based only on selected combination of words. Feelings are clearly expressed by word choice (morbid, happy, angry, etc.) and/or by the syntactical relationships of words (e.g. feeling blue versus blue sky). The emotional power of good poetry, the mood and social tone attained by a good novelist and the concern raised by a well-written editorial all express emotion through pure linguistic devices. Humour, use of irony or sarcasm, poetic metaphor, blasphemy, expressions of love, anger, concern, or disdain, can all portray emotion through word selection and combination alone. Humans routinely express emotion by gestures, by prosodic quality, by lexical selection, by semantic relationship and by combinations of any and all of these. Is there an anatomy of particular concern for emotional language?

Current studies of language and language impairments rarely isolate emotional language. None of the reports of insula damage and aphasia presented here have discussed emotional content. Only few studies support a separate emotional language system and, at best, these are tangential. Thus, patients with bilateral frontal (or fronto-pontine) damage producing pseudobulbar affect (Lieberman and Benson 1977) have appropriate emotional responses but cannot control the level of response. The language-emotion system operates but is no longer under frontal control. It has been reported that patients with bilateral occipito-temporal lesions no longer present emotional responses to visual stimuli, a visuo-limbic disconnection syndrome resembling visual agnosia (Bauer 1982). The paranoia of acquired deafness may represent a similar disconnection in which auditory stimuli no longer interact with limbic structures. In the above examples, non-insula areas (frontal, occipital, temporal) appear to influence input or control of emotional language; emotion is still expressed. The insula may be a central neural station crucial for language motivation and both comprehension and expression of emotion. That the left insula should be most important for the semantic and syntactic aspects of emotional language would follow logically. A strong case can be made for the insula as a major anatomical resource for the language of emotion. At best, however, this remains a conjecture. Both cases of damage isolated to the insula (difficult to demonstrate with current imaging techniques) and greatly improved techniques for measuring emotional qualities in language processing will be needed to prove that the insula has a role in human language.

In summary, participation of the insula in human language function has been suggested by students of aphasia for over a century and, in large part, has been confirmed by brain image correlation studies. The long-standing assumption that insula involvement in language dysfunction merely reflects contiguity, the immediate juxtaposition of the insula with neighbouring language cortex, needs rethinking. Anatomical studies suggest that the insula could well act as the cortical representation of the limbic (automonic) nervous system and, as such, may

provide a direct input from the limbic-emotion system that could influence the affective tone and the content of language output.

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