CHAPTER 4

Age, cognition and emotion: the role of anatomical segregation in the frontal lobes

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Introduction

Phineas Gage (as described by Harlow, 1868) is the prototypical frontal lobe patient. The overall effects of Gage's frontal lobe lesion have been described as relatively intact cognitive functioning, but impaired social and emotional functioning (e.g. Damasio, Grabowski, Frank et al., 1994). Recently, theories of cognitive aging have converged on the idea that normal adult aging affects the frontal lobes of the brain more than other areas (e.g. Moscovitch and Winocur, 1995; West, 1996). Yet the typical picture of the effects of normal aging on psychological function do not seem to match those described for Gage - older adults tend to have many impairments of cognitive function but maintain social and emotional function relatively well. In this chapter we aim to reconcile this anomaly by considering the effects of adult aging on different regions of the frontal lobes. In particular, we propose that adult aging impacts the dorsolateral prefrontal areas of the frontal lobes earlier and more severely than the ventromedial prefrontal areas, and review the neuroimaging, cognitive and behavioral data relevant to this hypothesis.

The frontal lobe hypothesis of aging

Recent neuropsychological theories of normal adult aging have converged upon the idea that the frontal lobes of the brain are affected by the process of normal adult aging both earlier than other brain areas, and at a more rapid pace (Daigneault and Braun, 1993; Mittenberg, Seidenburg, O'Leary and DiGiulio, 1989; Moscovitch and Winocur, 1995; Parkin, 1997; Raz, 1996; Shimamura, 1994; West, 1996; Whelihan and Lesher, 1985). This 'frontal theory of aging' has been very influential on recent models of cognitive and neuropsychological change with age. The theory proposes that many age-related changes in cognition are attributable to deterioration of the frontal lobes, although obviously age also affects a number of other brain regions that impact cognition, such as the hippocampus. Two main strands of evidence support the frontal theory of aging: neurophysiological findings that brain changes with age are most prominent in the frontal lobes, and claims that age changes in cognition parallel those found in patients with focal frontal lobe damage. There is now substantial agreement that the frontal lobes are involved in executive processes of cognition (e.g. Baddeley and Della Sala, 1996; Grafman, 1994; Shallice, 1988), therefore age-related changes should be most evident in cognitive tasks demanding supervisory control.

In this chapter, we provide a brief review of the cognitive and neuroanatomical evidence for age changes in the frontal lobes, then utilize recent advances in understanding about different subregions within the frontal lobes to propose a more specific dorsolateral prefrontal theory of aging.

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Frontal lobe changes with age

The aging brain shows greater structural changes in the frontal lobes compared to other brain regions. Age decrements are evident in the size and number of neurons and cortical thickness (Albert, 1984; Haug and Eggers, 1991; Terry, De Teresa and Hansen, 1987). Earlier studies erroneously equated neuron density with neuron number therefore biasing the degree of age-related changes, and later interpretations suggest that the major age changes are in terms of the size of neurons in the frontal lobes (Coleman and Flood, 1987; Morrison and Hof, 1997). Age declines are also more prominent in the frontal lobes than other brain areas in terms of the density of presynaptic terminals (Masliah, Mallory, Hansen et al., 1993) as well as the quantity of normal tau protein (Mukaeova-Ladinska, Hurt and Wischik, 1995). Similarly, senile plaques, which reflect neuronal degeneration, are more numerous in the frontal lobes than elsewhere in the brain (Struble, Price, Cork and Price, 1985).

Moreover, neuroimaging studies show that the volume of the frontal lobes decreases more than that of other cerebral areas with age. For example, Coffey, Wilkinson, Parushos et al. (1992) report a frontal volume decrement equal to 0.55% per year, twice the rate of change in other areas of the brain. In a review of studies of magnetic resonance imaging (MRI), Raz (1996) found that the correlation between age and volume of cortical gray matter in the brain was more substantial for the frontal lobes than any other brain region. Studies which have examined age differences in the metabolic uptake of various regions of the brain using positron emission tomography (PET), indicate that blood flow to the frontal lobes is overwhelmingly reduced with age (Gur, Gur, Obrist et al., 1987; Shaw, Mortel, Stirling Meyer et al., 1984).

There is evidence that older adults perform poorly on cognitive tasks that are sensitive to frontal lobe damage. Mittenberg et al. (1989) examined age differences on a range of neuropsychological tests purported specifically to tap the functioning of right and left hemispheres of the brain in relation to temporal, parietal and frontal lobes. There was no age differentiation between right and left hemispheric functions. Frontal lobe measures showed stronger age-related declines than measures of temporal or parietal function. Mittenberg et al. concluded that “deleterious changes in frontal lobe efficiency are the pronounced and relatively specific sequelae of aging process” (p. 926).

Some neuropsychological tests, such as fluency and the Tower of London, are commonly used to assess frontal lobe function (Lezak, 1995). Age differences are usually found on these tests, e.g., fluency (Phillips, 1999; Whelihan and Lesher, 1992) and the Tower of London (Allamanno, Della Sala, Laitinen et al., 1987; Gilhooly, Phillips, Wynn et al. 1997). The Stroop test (Boone, Miller, Lesser et al., 1990; Daigneault, Braun and Whitaker, 1992), and WCST (Axelrod and Henry, 1992; Daigneault, 1992; Libon, Glosser, Malamut et al., 1994).

Age, memory and the frontal lobes

A major focus of interest in the study of the frontal lobe theory of aging has been the effect of frontal lobe damage on memory functions. Differences have been found on a range of memory measures identified as sensitive to frontal dysfunction. There is a large literature on age differences in the frontal lobes in relation to the frontal lobe theory of aging. For more thorough reviews of this area see Chao and Knight, 1997; Mayes and Daum, 1997; Moscovitch and Winocur, 1995; West, 1996. However, we describe only a few of the best-known findings.

Moscovitch and Winocur (1995) review a number of memory tasks that are impaired both in focal frontal lesions and adult aging. These tasks include remembering the temporal order of pre-material, remembering the source of inform working memory, and free recall of organizational: in essence any memory task which imposing strategic or inhibitory components. For example, Levine, Stuss and Milberg (1997) looked at the effects of normal adult aging and focal frontal damage on a test of conditional associative learning. In this task, there are fixed associations between elements of a set of stimuli, and the participant must attempt to learn the associations through trial and error. Participants with damage to the frontal lobes, and in particular, the dorsolateral regions of the prefrontal cortex, are impaired in associative learning, as were older...
Levine et al. (1997) argue that age-related changes in memory performance are attributable to frontal-lobe changes in the effectiveness of inhibition.

Age differences in memory may be influenced by both changes in the hippocampus and the frontal lobes (Moscovitch and Winocur, 1992). Gisky, Polster and Routieaux (1995) report a double dissociation between age-related deficits in item memory and source memory (remembering where a particular item was learnt). Individuals who performed poorly on ‘frontal lobe tests’ (e.g. WCST; verbal fluency, backwards digit span) were poor at remembering the source from which information was learnt but could accurately remember item information. In contrast, those who performed poorly on ‘temporal lobe tests’ such as subtests from the Weschler Memory Scales and delayed recall performed well on source memory but poorly on item memory.

**Age, problem-solving and the frontal lobes**

Much of the research into the relationship between age and frontal lobe functioning has concentrated on memory performance. However, it is also of interest to consider the effects of age on intelligence and problem-solving. Older adults are often reported to have impaired problem-solving ability (see reviews by Phillips and Forshaw, 1998; Salthouse, 1991), as also are patients with specific frontal lobe damage (Della Sala and Logie, 1998; McCarthy and Warrington, 1990; Shallice and Burgess, 1991).

Fifty years of research into the effects of age on intelligence and reasoning support the conclusion that increasing age results in preserved ‘wisdom’ or crystallized intelligence, but impaired ‘wit’ or fluid intelligence (e.g. Cattell, 1987). Fluid abilities involving abstract novel reasoning show relatively early and steep age-related declines (e.g. Phillips and Forshaw, 1998; Salthouse, 1993). Crystallized abilities reflecting acquired knowledge usually remain stable late into old age, particularly for socio-emotional material (e.g. Blanchard-Fields, 1996; Cornelius and Caspi, 1987).

The clinical picture presented by at least some patients with focal frontal lobe damage does not seem to match the effects of old age on fluid and crystallized intelligence. Consider the following description of the prototypical frontal lobe patient, Phineas Gage, in relation to the known pattern of age changes in cognition:

After the accident he showed no respect for social convention; ethics, in the broad sense of the term were violated... Another important aspect of Gage's story is the discrepancy between the degenerated character and the apparent intactness of the several instruments of mind — attention, perception, memory, language, and intelligence.

(Damasio, 1994, p. 11).

Other patients with substantial frontal lobe damage who show a similar dissociation between impaired wisdom and relatively spared intelligence have been described subsequently (Brazier, Colombo, Della Sala and Spinelli, 1994; Damasio and Van Hoesen, 1983; Eulinger and Damasio, 1985; Shallice and Burgess, 1991; Rolls, Hornak, Wade and McGrath, 1994). Reviews often emphasize the intact performance of patients with frontal lobe damage on intelligence and laboratory tests along with impaired social behavior, poor judgement, and inappropriate decisions taken in real-life (Benton, 1994; Damasio and Anderson, 1993; Milner, 1995; Parker and Crawford, 1992). This pattern suggests that precisely those problem-solving abilities which may be spared following frontal lobe lesions (e.g. abstract reasoning abilities, fluid intelligence) are most affected by aging; while the problem-solving abilities which are impaired after some frontal lobe lesions (e.g. social decision-making, using knowledge wisely) are least affected by aging. How can this discrepancy be addressed by a frontal lobe theory of cognitive changes with age?

One way of reconciling these apparent anomalies between performance of older adults and patients with frontal lobe damage is to consider the architecture of the frontal lobes in more detail. The frontal lobes occupy more than a third of the human cortex, and in order to make sense of such a large and diverse area many authors have proposed that the frontal lobes be subdivided. There has recently been much interest in the idea of localization of function within specific areas of the frontal lobes (see e.g. Beardsley, 1997; Darling, Della Sala, Gray and Trivelli, 1998; Eulinger, 1995; Sarazin, Pillon, Giannakopoulos et al., 1998). Relatively few studies of the frontal lobe theory of aging have explicitly...
examined the neuroanatomical and functional differences apparent within the prefrontal region. We will now outline in some detail the distinction between ventromedial and dorsolateral regions of prefrontal cortex, and the effects of age on these two regions, before returning to the implications that this has for cognitive function. We propose that adult aging differentially affects the dorsolateral prefrontal regions, in comparison to the ventromedial areas (see also Phillips and Della Sala, 1998).

**Ventromedial and dorsolateral regions of the prefrontal cortex**

Frontal theories of aging generally assume parallel decline across the various regions of the prefrontal cortex. However, the frontal lobes are a heterogeneous formation, and differentiable architectural and functional areas can be identified within this region. There is still considerable debate as to the number and function of distinct anatomical areas in the frontal lobes. For instance, there is some converging evidence of lateralization of function, at least in terms of left-frontal encoding and right-hemisphere retrieval mechanisms (e.g. Shallice, Fletcher, Frith et al., 1991; Tulving, Kapur, Craik et al., 1994), although this distinction may not apply to older adults (Cabeza, Grady, Nyberg et al., 1997). The distinction that might be particularly relevant to aging is between dorsolateral (DL) regions and ventromedial (VM) regions (see Fig. 1). The ventromedial region encompasses the lateral orbital gyrus, the middle orbital gyrus, the medial orbital gyrus and the gyrus rectus (Elingger, 1999), and is sometimes also referred to as the orbitofrontal region.

The cerebral cortex does not have a homogeneous cellular structure and organization. Several different codes have been proposed to designate the various cortical areas (Crosby, Humphrey and Lauer, 1962). The most generally recognized terminology applied to the different areas of the cortex is that of Brodmann (1909), who used numbers to indicate distinct regions, simply following the order in which he studied them on one single case (Rajkowska and Goldman-Rakic, 1995). Using Brodmann's terminology, the DL region is centered on areas 9 and 46, while the VM region encompasses areas 10, 11, 12, 13, 14 and 47. It is interesting to note that in Brodmann's

Fig. 1. Lateral, medial and ventral views of the brain specifying the location of the dorsolateral (light gray) and ventromedial (dark gray) prefrontal regions.
original map of the cerebral cortex the numbers 12, 13 and 14 are not mentioned (Braak, 1980; Gormann and Unutzer, 1993). Influenced by the work of his contemporary Vogt (1910), he later (Brodmann, 1910) inserted area 12 between area 10 and area 11 (Markowitsch, 1993). The location of areas 13 and 14, as currently agreed in the posterior orbitoventral surface of the human brain can be attributed to the work of Beck (1949) who mapped onto the human brain these two 'new' areas described by Walker (1940) in the orbital gyrus and gyrus rectus of the macaque brain. Several contemporary authors maintain that it would be more appropriate in humans to label Walker's (1940) area 12, which she described in the macaque, as area 47 (or 47/12). (For detailed discussions see: Barbas, 1995; Carmichael and Price, 1994; Eslinger, 1999; Pandya and Yeterian, 1996; Petrides and Pandya, 1994.)

The difference between the deficits following lesions in these two regions of the frontal lobes was recognized by early authors (here VM regions are referred to as basal, and DL regions as in the convexity of the frontal lobes). Cobb (1943, cited by Eslinger, 1999, p. 226) observed that "... the basal cortex represents more the emotional integration and the convexity of the frontal lobe the intellectual integration". Years later, in reviewing the topic, Luria (1969) was unequivocal: "the syndrome arising in patients with ... convexity and basal lesions of the frontal regions are different" (p. 749). The fractionation between DL and VM areas is also seen ontogenetically: the cytoarchitectonic development of the orbital areas precedes that of the dorsolateral areas both in non-human primates and in man (Orzhekovskaya, 1975, 1977). Indeed, studies carried out at the Moscow Brain Institute in the sixties (e.g. Kononova, 1962) showed that DL areas continue to develop after birth until the age of 12 years, and that their development finishes last in these regions compared to other areas of the brain, including orbital areas. Raz (1996) put forward the argument that those brain areas which are phylogenetically latest ('such as dorsolateral prefrontal and inferior parietal areas', p. 171) are also those which are most susceptible to the effects of aging: "the last to come (in evolution) is the first to go (in senium)" (p. 171).

VM and DL regions also differ in their cortico-subcortical connections (Petrides, 1994; Rolls, 1999a, b), indeed some authors clearly distinguish anatomical paths and functions of dorsolateral-subcortical and orbitofrontal-subcortical circuits (Fuster, 1996; Masterman and Cummings, 1997). Both VM and DL regions are richly connected to other parts of the brain (and each other). DL regions are intensely connected to primary sensory and motor regions, as well as the parietal cortex; while VM regions are heavily networked with the limbic system (Adolphs, Tranel, Bechara et al., 1996; Pandya and Yeterian, 1996; Rolls, 1996, 1999a, b). There is little doubt from studies of focal lesions in humans and monkeys, and from neuroimaging in normal adults, that these regions may have separable functions, although there is still debate as to what exactly these functions may be (Bechara, Damasio, Tranel and Anderson, 1998; Della Sala, Grey, Spinell and Trivelli, 1998; Goldman-Rakic, 1996; Petrides, 1994; Rolls, 1996). However, there is some agreement that DL regions are involved in cognitive processes classified as 'executive functions', such as monitoring multiple events (Cournay, Ungelerder, Kell and Haxby, 1997) and abstract problem-solving (e.g., Prabhakaran, Smith, Desmond et al., 1997); while VM regions are involved in emotional processing (Rolls, 1996) and the regulation of social behavior (Anderson, Bechara, Damasio et al., 1999).

There is increasing recent evidence of the different functional domains of these regions. For example Sarazin et al. (1998) report that in patients with frontal lobe lesions cerebral glucose metabolism at rest in DL regions (but not VM regions) relates to executive test performance, while metabolism in VM regions (but not DL regions) relates to behavioral and emotional abnormalities.

The VM region of the brains receives inputs from object-processing visual areas and somatosensory areas; it is also involved in the processing of taste olfaction and autonomic regulation. However, for the sake of clarity, we will limit our discussion on the frontal theory of aging to its prominent function, that of an emotion relay. Within the DL and VM areas there may be further differentiation (Goldman-Rakic, 1996; Petrides, 1994; Rolls, 1996, 1999a, b) which is beyond the scope of the present chapter to discuss. Barbas, Gashghaei, Rempel-Clower and Xiao (2002, this volume) and Miller and Asaad (2002, this vol-
ume) discuss the properties and functions of the DL and VM regions more comprehensively.

**Age effects on dorsolateral and ventromedial prefrontal regions**

The majority of published studies on changes in brain neuroanatomy with age do not clearly distinguish between different regions within the frontal lobes. However, West (1996) has made the suggestion of regional differences within the prefrontal cortex in the effects of aging in passing:

> Within the prefrontal cortex, there also is some evidence suggestive of regional differences in the effects of increasing age, with the dorsolateral prefrontal region demonstrating a linear decline throughout adulthood, and the orbital prefrontal region showing evidence of a decline only during the late 7th decade and beyond. (West, 1996, p. 276)

Moreover, there are a number of studies which report the effects of age on neuronal density and size in one specific region of the frontal lobes, but differences in the methodology and sampling used in these studies makes it somewhat difficult to compare across studies.

Haug and co-workers have intensively studied age-related neuronal changes in area 11 (part of the VM prefrontal cortex) in comparison to other areas of the brain. Their findings show that in area 11 large neurons do tend to shrink with age, but that this process occurs later (after 65 years), less massively and less rapidly than in other areas, including prefrontal area 6 (Haug, 1985; Haug and Eggers, 1991; Haug, Barrwater, Eggers et al., 1983). Terry et al. (1987) report the effects of age on neurons in area 46 (DL prefrontal cortex). There was a substantial decrease in the number of counted large neurons (correlation between age and number of large neurons = −0.63), and a corresponding increase in the number of small neurons and glia (correlations with age = 0.33 for small neurons and 0.51 for glia). Terry et al. conclude that increasing age causes substantial shrinkage in the neurons of area 46. This decline appears to be linear from age 30 to 100 years, in contrast to the later and slower decline in area 11 (Haug and Eggers, 1991). At odds with these findings, a recent well-controlled MRI study (Raz, Gunning, Head et al., 1998) reported very similar decrements in the volume of dorsolateral and orbital prefrontal regions from age 20 to 80 years (decrease = approximately 25%). However, these areas do not correspond well to our delineation of DL and VM regions: the area described as DL by Raz et al. (1998) includes Brodmann’s areas 8, 10 and 45, as well as 9 and 46. Further, the orbital prefrontal region defined by Raz et al. comprises areas 11 and 47, and not the more ventral and medial regions (12, 13, 14) which are critical in determining social behavior (Rolls, 1996).

There are a large number of in vivo studies of regional cerebral activity with aging, although relatively few clearly distinguish between DL and VM areas (as defined in Fig. 1). Some evidence can be gleaned from the literature of a differential decrement of glucose uptake within the different regions of the prefrontal cortex. For example, Duara, Margolin, Roberston-Tchabo and London (1983) incidentally report (see their Table 3, p. 768) that age correlates negatively with weighted regional cerebral metabolic rates in the dorsolateral, but not in the orbitofrontal gyri. More recently, De Santi, de Leon, Convit et al. (1995) in a PET study of glucose metabolism in young and old adults conclude that “there is a stronger relationship between age and dorsolateral frontal lobe metabolism than between age and orbitofrontal lobe metabolism” (p. 367). Correspondingly, Marchal, Rioux, Petit-Taboue, et al. (1992), examining the changes in cerebral metabolic rate of oxygen in volunteers aged from 20 to 68 years, found age-related effects in nearly all the cortical gyri they analyzed, including DL prefrontal gyri, but did not find age-related changes in VM prefrontal regions. Garmaux, Salmon, Degueldre et al. (1999) carried out a detailed study of frontal areas comparing PET activation during rest in 22 young and 21 old healthy adults. There were significant age effects on metabolism in dorsolateral areas 8, 9 and 46, and also other areas such as the anterior cingulate. There was no age effect on metabolism in ventral areas 10, 11 and 47. The more medial areas 12, 13, 14 were not reported.

Therefore, there are at least some hints from studies of brain structure that aging may differentially affect the DL as opposed to VM prefrontal cortex. We will turn now to consider the effect of age on some of the psychological tests taxing the DL or the VM regions.
Cognitive–behavioral tests of dorsolateral and ventromedial function

There are few tasks for which evidence exists to indicate that they specifically tap DL or VM prefrontal function. This is partly because there have been few theoretically driven attempts to design tasks specifically testing either DL or VM prefrontal functioning in humans. Also, it is likely that these areas will often act in concert to influence performance on many complex tasks. If the functioning of these areas is taken crudely to reflect strategy generation and monitoring (DL) versus emotion and motivation (VM), it is clear that both of these functions will be present in a great many cognitive tests.

However, from the literature there is some evidence that some tests reflect the function of one area much more than the other. This evidence will be reviewed below, along with any literature on age differences on the tasks. Tests are only considered if they meet two criteria: (1) supporting evidence from lesion studies and neuromaging of involvement of either DL or VM prefrontal regions in humans; and (2) some evidence to evaluate the effects of adult aging on the test. We do not discuss the considerable number of papers that indicate that the tests discussed below are generally sensitive to frontal lobe lesions but do not specify where in the frontal lobes such lesions occur. The prediction is that normal aging should cause poorer performance on tests sensitive to DL function but not on tests sensitive to VM functioning.

After this section, preliminary results from a study of aging and VM/DL functioning are reported looking at the effects of adult aging on six tasks for which the literature provides evidence to suggest involvement of either DL or VM prefrontal function.

Functions of the DL prefrontal cortex

A number of the classic ‘executive function tests’ have been well validated as dependent on the functioning of the DL prefrontal cortex through neuromaging experiments and studies of patients with focal lesions. Lesions localized to DL prefrontal regions are relatively rare, so there are comparatively few patient studies that clearly indicate the role of DL frontal regions. The tests considered here are the Wisconsin card sort task, letter fluency, Tower of London, delayed response, Stroop and recency judgement. Evidence for their selective dependence on DL rather than VM prefrontal areas is reviewed, followed by an evaluation of available evidence for the effects of adult aging on performance.

Wisconsin card sorting task

The WCST was developed to assess abstract reasoning, particularly the ability to identify abstract categories and shift cognitive set. The participant is presented with four stimulus cards with symbols that differ in shape, number and color and a pack of 128 response cards, and is asked to place each response card under one of the four stimulus cards. Only one of the dimensions is correct, color in the first instance. However, the participant is not told which dimension is correct and therefore must identify the matching card through trial and error, using the feedback provided. After 10 correct responses with color, the criterion is changed to shape without the participant’s knowledge. When the sorting dimension is changed the participant must shift cognitive set to identify and attend to the new dimension.

Evidence of DL and VM involvement. Milner (1963) compared 18 patients with DL prefrontal lesions and a control group of patients with lesions elsewhere in the brain, including the VM prefrontal region, on the WCST. Patients with lesions in the DL prefrontal cortex made significantly more errors and achieved fewer sorting categories than the control group whereas, patients with VM prefrontal lesions performed as well as the control group. Furthermore, Drewes (1974) examined the performance of patients with orbital, medial or DL frontal lesions performing the WCST and found that patients with orbital damage achieved better performance on the WCST than those with frontal damage outside this area. Ahola, Vilki and Servo (1996) did not find a significant difference in performance on the WCST between patients with frontal infarctions mainly involving the VM region and patients with nonfrontal lesions. However, group studies have indicated that DL damage does not necessarily affect WCST performance (e.g. Goldstein, Bernard, Fenwick et al., 1993). Anderson, Damsaio, Jones and Tranel (1991) argue that
and provide evidence that some patients with severe bilateral DL damage perform relatively well on the WCST. In a recent paper, Stuss, Levine, Alexander et al. (2000) argue that DL and VM lesions cause different patterns of deficits on the WCST, with DL lesions tending to cause a greater number of perseverative errors.

There is some support for the involvement of the DL prefrontal cortex in the WCST from neuroimaging studies. In a SPECT study, Rezzai, Andreasen, Alliger et al. (1993) found that there was a significant increase in blood flow to the DL prefrontal cortex but not the VM prefrontal cortex during performance on the WCST. Barceló, Sanz, Molina and Rubia (1997) examined healthy volunteers performing a computerized version of the WCST and found significant event-related potential (ERP) changes in DL prefrontal cortex while participants performed the task. However, another neuroimaging study by Cantor-Graae, Warkentin, Franzén and Risberg (1993) investigating activation during the WCST in normal participants did not find significant DL activation. Other studies suggest that there is involvement of both DL and VM prefrontal cortex in the WCST. Berman, Ostrem, Randolph et al. (1995) obtained rCBF PET scans during the WCST. They found related activation in the DL, mesial, orbital and polar frontal cortex during the task.

Overall, the evidence does suggest that DL regions are involved in the WCST, particularly in determining perseverative responses. The evidence also suggests that VM regions are likely to be involved in other aspects of the task. The WCST is a multicomponent task, likely to recruit a complex network of brain areas.

Age effects. There are many studies that have demonstrated age-related decline in performance on the WCST. For example, Daigleault et al. (1992) found significant age declines from 40 years onwards on the WCST. Fristoe, Salthouse and Woodard (1997) compared the performance of young and older adults on the WCST, and found that older adults were impaired on all performance measures, even when years of education and health variables were partialled out. Experimental studies suggest that age differences on the WCST are due partially to less efficient use of feedback to determine future choices, as well as to differences in working memory and processing speed (Fristoe et al., 1997). Nagahama, Fukuyama, Yamauchi et al. (1997) measured the rCBF activation in young and old participants while performing on the WCST. They found that both groups had significant activation in the left DL prefrontal cortex, however the activation in older participants was significantly lower than that of the younger participants. This supports the idea that any age-related deficit on the WCST may be linked to changes in the DL regions.

Letter fluency. Phonemic fluency tasks require the participant to generate words beginning with a particular letter in a short time period. Repeatedly retrieving words using a phonemic criterion is a relatively novel way of searching, so it has been argued that participants need to be able to generate and utilize effective retrieval strategies (e.g., Crowe, 1992).

Evidence of DL and VM involvement. There is evidence from neuroimaging and patient studies to support the involvement of DL prefrontal areas in letter fluency performance. Many neuroimaging studies such as those by Cantor-Graae et al. (1993); Frith et al. (1991) and Cuenod, Bookheimer, Hertz-Pannier et al. (1995); indicate significant activation in the left DL prefrontal cortex while normal volunteers perform letter fluency.

These findings are consistent with patient studies which suggest that there is a role for the DL prefrontal cortex in letter fluency. Stuss, Alexander, Hamer et al. (1998) compared the performance of a number of different patient groups on letter fluency. They found that patients with VM prefrontal damage were not impaired on letter fluency, but patients with left-sided DL prefrontal damage produced few words and made many task errors. Troyer, Moscovitch, Winocur et al. (1998) examined clustering and switching of word production on letter fluency in patients with focal brain lesions. They found that patients with left DL prefrontal lesions were impaired at switching from one retrieval strategy to another in comparison to healthy controls matched for age and gender. Evidence from patient studies suggests that lesions of VM regions do not substantially affect fluency performance (Hornak, Rolls and Wade, 1996;
Cicerone and Tanenbaum, 1997). Overall, there appears to be reasonably strong evidence of DL rather than VM frontal involvement in letter fluency tasks.

**Age effects.** Numerous studies have reported age deficits on tasks of letter fluency: older people tend to produce fewer words within the time limit (e.g., Daigneault et al., 1992; Torombaugh, Kozak and Rees, 1999). However, there are many different reasons to perform poorly on fluency tasks (Phillips, 1997), and other brain areas than DL prefrontal cortex are obviously involved in this task. Studies that have investigated qualitative production during fluency tasks indicate that age effects are not due to differences in switching strategies (Phillips, 1999; Troyer, Moscovitch and Winocur, 1997), unlike the production shown by patients with focal DL lesions. So, although there may be fluency deficits associated with DL frontal damage and age, these may not represent the qualitatively similar cognitive impairments.

**Tower of London**

The Tower of London task assesses the ability to plan the moves necessary to rearrange an array of colored disks on pegs from a starting position to match a predetermined position (Shallice, 1982). Some trials on the Tower of London involve making counterintuitive moves, which are necessary for solution, but do not place disks into their final goal position. Therefore, to perform the task successfully, the participant needs to look a few moves ahead and choose the appropriate sequence in which subgoals are to be reached (Gilhooly et al., 1999; Shallice, 1982; Ward and Allport, 1997).

**Evidence of DL and VM involvement.** There are many reports of the effects of frontal lobe damage on the Tower of London and related tasks (e.g., Shallice, 1982; Goel and Grafman, 1995). Morris, Miotta, Feigenbaum et al. (1997) report that patients with focal frontal lesions have particular difficulty in dealing with the first encounter of goal conflicts on planning tasks. Relatively few papers have reported in detail the lesions suffered by patients who perform poorly on the task. Owen, Downes, Sahakian et al. (1990) report the effects of frontal lobe lesions on planning in the TOL. They argue that there are no differences between inferior, lateral and medial sites of lesion in terms of planning deficits. However, it is not clear how these locations relate to our current distinction between DL and VM. Morris et al. (1997) found no evidence of differences between patients with DL and VM lesions in performing the Tower of Hanoi task. However, some patients with lesions affecting VM rather than DL areas have been reported to perform normally on the TOL task (Cicerone and Tanenbaum, 1997; Hornak et al., 1996).

PET studies of TOL performance consistently indicate DL prefrontal activation. Morris, Ahmed, Syed and Toone (1993) measured rCBF of normal volunteers performing a computerized version of the TOL and found significant activation in the left DL prefrontal region and not the VM prefrontal cortex. Similarly, Owen, Doyon, Petrides and Evans (1996) and Baker, Rogers, Owen et al. (1996) found significant activation in area 9 of DL frontal cortex during TOL performance, but no significant activation of VM areas.

Patient studies are therefore equivocal about the relative roles of DL and VM regions in TOL performance, while neuroimaging studies provide a consistent picture of DL rather than VM activation while carrying out the TOL.

**Age effects.** Allamanno et al. (1987) found a significant deterioration in performance on the Tower of London task due to normal aging. Robbins, James, Owen et al. (1998) examined 341 participants aged 21–79 years performing the Tower of London and they found that the oldest groups performed fewer trials in the minimum moves possible. Gilhooly et al. (1999) report evidence from protocol analysis that older adults are less able to make accurate mental plans than younger adults.

**The self-ordered pointing task**

Petrides and Milner (1982) devised a task in which the subject has to organize, carry out and monitor a sequence of responses rather than reproduce a sequence directed by the experimenter: the self-ordered pointing task. For an example of the type of stimuli used in this task, see Fig. 2. Poor performance on the self-ordered pointing task may be due to poor organizational strategies and/or poor monitoring of responses. Patients with frontal lobe lesions perform...
worse on the task than those with temporal lobe lesions (Petrides and Milner, 1982).

Evidence of DL and VM involvement. There have been relatively few studies in humans that have specifically examined the role of DL and/or VM areas in performing the SOPT. De Zubicaray, Chalk, Rose et al. (1997) reported a patient with a DL lesion who performed poorly on the SOPT compared to 10 healthy controls. Petrides and colleagues (Petrides, Alivisatos, Meyer and Evans, 1993b; Petrides, Alivisatos, Evans and Meyer, 1993a) examined rCBF in normals while they performed a series of self-ordered pointing tasks. Petrides et al. (1993b) observed significant increases in rCBF within the right mid-DL frontal cortex when participants performed a task requiring the monitoring of self-generated responses from a set of abstract designs. They also found bilateral activation within the mid-DL frontal cortex when participants performed a task requiring the monitoring of verbal self-generated responses (Petrides et al., 1993a). The available evidence therefore supports the idea that the SOPT involves the DL prefrontal regions, although there is little to rule out the involvement of VM regions also.

Age effects. A number of studies have found age effects on the SOPT (e.g. Daigneault et al., 1992; West, Ergris, Winocour and Saint-Cyr, 1998; Wiergersma and Meertse, 1990). There is evidence that age effects on the task begin quite early (before age 65 years, Daigneault and Braun, 1993) and are likely to be due to impaired monitoring of working memory (West et al., 1998).

Delayed response task. During the delayed response task, participants respond to a cue after a brief delay. The response is made on the basis of an internal representation maintained during the delay rather than directly in reaction to information present in the environment. The main neuropsychological processes examined by the delayed-response task are the representations of visuospatial stimuli, retention in short-term memory, retrieval and response selection.
Evidence of DL and VM involvement. Evidence from human patient populations supports the involvement of DL regions in the delayed response task, but also suggests that VM regions may be involved. Vérin, Parrot, Pillon et al. (1993) found that patients with DL prefrontal lesions had poor performance on delayed response tasks compared to patients with postcentral lesions and healthy controls. Freedman and Oscar-Berman (1986) found that patients with bilateral frontal lobe lesions of varying etiologies, including DL and VM were impaired on a delayed response task. Bechara et al. (1998), and Nies (1999) have also reported that patients with lesions involving only the VM prefrontal cortex are impaired on the delayed response task. Therefore, the involvement of the VM prefrontal cortex on the delayed response task cannot be excluded.

Neuroimaging studies in humans support the idea that DL prefrontal cortex is involved in the delayed response task. Goldberg, Berman, Randolph et al. (1996) and Honda, Barrett, Yoshimura et al. (1998) examined activation in the prefrontal cortex during delayed response tasks and found significant activation of the DL prefrontal cortex. Pasquale-Leone and Hallett (1994) using transcranial magnetic cortical stimulation (TMS) found that DL prefrontal cortex is important for performance on the delayed response task.

Oscar-Berman (1975) found that lesions in the DL prefrontal cortex of non-human primates significantly impaired performance on delayed response tasks compared to lesions in the VM prefrontal cortex. However, animals with lesions in the VM prefrontal cortex also showed significantly impaired performance compared to intact controls. Neuronal activity has been observed in both the DL and VM prefrontal cortex of non-human primates during delayed response tasks (Hikosaka and Watanabe, 2000; Watanabe, 1996). This evidence suggests that VM activity is related to reward expectancy, while DL activity relates to spatial working memory related in the delayed response task.

The evidence overall suggests a role for both DL and VM regions in delayed response tasks, although possibly for different aspects of task performance.

Age effects. We are not aware of any studies which have directly examined the role of adult aging in performance on delayed response tasks analogous to those used in patient populations. Some data relevant to this point are discussed below.

Stroop task. The aim of the Stroop task is to assess the performance of participants in a situation where stimuli can be classified according to conflicting categories. First, the participant is asked to read color names printed in black as quickly as possible. Then, the participant is asked to name the color of colored squares as quickly as possible. Finally, the color names are printed in an inconstant color of ink and the participant is asked to name the color of the ink rather than the color name. Longer latencies on the incompatible condition indicate inability to inhibit the habitual tendency to read the color name.

Evidence of DL and VM involvement. Perret (1974) found that patients with left frontal lesions demonstrated a greater progressive decrement in the Stroop test compared to the other patient groups and controls. There has subsequently been some disagreement in the literature as to whether DL or VM regions are most involved in the inhibitory functions necessary in the Stroop task. However, surprisingly, there has been little systematic attempt to look at the relationship between frontal lobe damage and Stroop test performance (Tranel, Anderson and Benton, 1994). Stuss, Benson, Kaplan et al. (1981) provide evidence that the VM prefrontal cortex is important for performance on the Stroop task. In an article describing the Northampton Veterans Administration study, Stuss et al. (1981) compared the performance of patients with schizophrenia who had been 'treated' with prefrontal leukotomies and normal controls on the Stroop task. They found that these patients whose lesions involved the lower VM area of the frontal lobes performed similarly to normal controls on the Stroop task. Stuss (1991) also showed that patients with large bilateral VM lesions perform similarly to normal controls on tasks that include factors of interference such as the Stroop task.

Cabeza and Nyberg (1997) reviewed the PET studies of Stroop task performance up to 1995, and
report rather mixed results: in some studies VM regions were activated during the color-ink naming, and in other studies DL regions were activated. Vendrell, Junqué, Pujol et al. (1995) investigated the areas of the brain involved in performance on the Stroop task using fMRI in patients with brain lesions. They found significant activation in the right DL region when participants performed on the Stroop task. Peterson, Skudlarski, Gatenby et al. (1999) carried out an fMRI study of Stroop performance and found substantial activation in very many brain areas, including both DL (areas 9, 45, 46) and VM (areas 10, 12) regions of the frontal lobes. Peterson et al. summarize their own along with a number of other Stroop activation studies, and conclude that the most consistent brain area activated is the anterior cingulate, with additional activation in dorsolateral area 46.

There are a number of methodological issues concerning how best to assess inhibition in the Stroop task, in particular, which baseline condition to compare to Stroop performance. Taylor, Kornblum, Lauber et al. (1997) compared PET activation during Stroop color-ink naming to a number of different baseline conditions, and found that the only region that consistently showed activation was the left inferior frontal gyrus (BA 44/45).

**Age effects.** A large number of studies have reported age differences in performance on the inhibition component of the Stroop task (e.g. Daigneau et al., 1992; Lepage, Stuss and Richer, 1999). However, there are problems in interpreting age-related slowing on this task, and some authors have argued that the major cause of age differences in performance is cognitive slowing rather than inhibitory failure (e.g. Boone et al., 1990; Uttl and Graf, 1997; Verhaeghen and De Meersman, 1998). Rabbitt (1997) outlines some of the problems associated with trying to assess ‘inhibition’ through tasks like the Stroop.

**Recency judgement**

In recency judgement tasks, participants are presented with a series of stimulus items and then have to judge which item of a pair was presented most recently. The participant is required to search back through memory for the previous occurrence of the items to compare their recency (Milner, Corsi and Leonard, 1991). Milner claimed that deficits on recency judgement may be the result of the inability to structure and segregate events in memory (Milner and Teuber, 1968). Shimamura, Janowsky and Squire (1990) found that patients with frontal lobe lesions are impaired at organizing information within a temporal context.

**Evidence for DL and VM involvement.** Milner et al. (1991) examined the areas of the frontal lobes important for making recency judgements. They found that patients with lesions involving the mid-DL prefrontal cortex were significantly impaired on verbal recency judgements, more so when the lesion involved the left hemisphere. In contrast, patients with lesions that did not encroach upon the DL prefrontal cortex were not impaired. More recently, Kopelman, Stanhope and Kingdon (1997) compared the performance of patients with focal frontal lesions on measures of temporal context memory. They found that patients with frontal lesions involving the DL region were significantly impaired on a recency task compared with patients with temporal lobe lesions. Patients with frontal lesions that did not involve DL regions did not show any impairment in recency judgement. However, Butters, Kasznia, Glisky et al. (1994) were unable to identify any specific relationship between temporal context memory deficits and the frontal lesion site. Zorrilla, Aguirre, Zarahn et al. (1996) examined the neural basis of recency judgement in healthy individuals, using fMRI. They found that there was significant activation in bilateral DL prefrontal cortex and not VM prefrontal cortex during a recency task. Therefore, neuroimaging provides further support for the claim that the DL prefrontal cortex is involved in making recency judgements.

**Age effects.** Mittenberg et al. (1989) found that both recency for words and recency for pictures were affected by age. Fabiani and Friedman (1997) also found that younger participants performed significantly better than the older participants on both word sequencing and picture sequencing judgements.

**Functions of the VM prefrontal cortex**

There are relatively few specific tests for which there is evidence from patient or lesion studies of involve-
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Deficits on recency tasks in VM frontal lesions indicated an inability to maintain gainful employment (e.g. Eslinger and Damasio, 1985) and personality change (e.g. Meyer and McLardy, 1948). The specific association between personality disorders and lesions in the VM regions of the frontal lobes was observed at the turn of the century by German neurologists (Knörrle, 1865; Jastrowitz, 1888; Oppenheim, 1890;Voegelin, 1897) and subsequently put to the test with large group studies (Kleist, 1934; Zhangwill, 1966). Welt (1888), quoted by Markowitsch (1992) reported the case of a patient who showed dramatic changes in his character after an injury confined to the VM aspects of the frontal lobes. She compared this case with several others taken from earlier literature, including the case of Phineas Gage. By comparing the available evidence she concluded that changes in character followed damage to the VM regions of the frontal lobes, in particular the right VM area. More recently, Rolls et al. (1994) reported a group of patients with VM lesions who show impaired social behavior, yet intact cognitive performance. In contrast, they report two patients with DL damage who show the opposite pattern of results: impaired cognitive performance but acceptable social behavior. The problem behaviors shown by VM patients included disinhibition, sexually inappropriate advances, boastfulness, mis-

interpretation of others’ mood states, impulsivity, and aggressive behavior. Duffy and Campbell (1994) reviewed the effects of lesions in specific regions of the frontal lobes and conclude that VM lesions result in impulsivity, aggressiveness, lewdness, and lack of empathy.

Behavior and personality change such as that described in VM patients is rarely associated with normal adult aging. There are no age changes in traits such as aggressiveness (Renaud and Murray, 1996), and age does not relate to either experimental or questionnaire measures of impulsivity (Phillips and Rabbitt, 1995). Furthermore, the incidence of personality disorders decreases in the course of normal aging (Amen and Molinari, 1994).

There are some tasks involving aspects of emotional functioning and social cognition for which there is evidence available to evaluate the role of VM and DL functioning, and these are now reviewed. The tasks described are the gambling task, emotion identification, and theory of mind.

The gambling task

Patients with VM lesions, but not those with DL damage, often make disastrous financial decisions in real life (Eslinger and Damasio, 1985). Bechara, Damasio, Damasio and Anderson (1994) therefore designed a laboratory task that aims to assess decision-making: the gambling task (see Fig. 3). The aim of the gambling task is to try to win as much money as possible. Participants are presented with four decks of cards and $2000 of fake money. The participant is asked to choose one card at a time from any of the four decks, and initially, the participant wins money no matter which pile is chosen. However, as the task continues, the participant will also pay penalties, which vary with the deck and the position of the card in the deck. Two of the decks of cards are considered high risk because they have both high rewards and high penalties, whereas two decks of cards are considered low risk because they have low rewards but even lower penalties. Picking cards from the low risk decks is more profitable in the long run. In order to perform well on the task, the participant must develop a hunch that the high paying decks are ‘bad’ and the low paying decks are ‘good’. 

The example of Welt gives of the preposterous character and outlandish personality of her patient is his lack of concern in among his fellow inmates by vividly complaining that in the hospital he was getting ‘burn stuff’ to drink rather than the smooth French wines he was used to (Markowitsch, 1992). Of course, this was well before the advent of the modern public health services.

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Evidence of DL and VM involvement. Bechara et al. (1994) found that patients with VM frontal damage select fewer cards from the good decks and choose more from the bad decks, whereas healthy controls and patients with lesions in the occipital, temporal and DL frontal regions select more cards from the good decks and tend to avoid the bad decks. In a later study Bechara et al. (1998) showed again that patients with VM damage are impaired on the gambling task and yet patients with DL damage perform normally on the task. Furthermore, Levine, Freedman, Dawson et al. (1999) describe a patient with a right ventral frontal lesion (areas 47, 10 and 45) who performed poorly on the gambling task.

Further support for the involvement of the VM prefrontal cortex on the gambling task is apparent in studies measuring the skin conductance responses (SCRs) of participants during the gambling task (Bechara, Tranel, Damasio and Damasio, 1996; Bechara, Damasio, Tranel and Damasio, 1997). Bechara et al. (1996) claimed that somatic state activation is necessary to make the distinction between good and bad decks in the gambling task, therefore participants should show somatic state activation when they are choosing between good and bad decks. Bechara et al. (1996) found that patients with VM prefrontal damage, as well as a healthy control group, generated reward and punishment SCRs. However, as the control group became experienced at the task, they also began to generate SCRs prior to choosing some cards, whereas the patient group did not. These anticipatory SCRs were generally higher in relation to the disadvantageous decks than the advantageous decks.

Overall, the findings suggest that performance on the gambling task depends upon the VM prefrontal cortex and not the DL prefrontal cortex.

Age effects. There is not yet any published work that we are aware of on the effects of age on the gambling task. However, on related topics, there are reported to be no age differences in efficacy of decisions on investing money (Walsh and Hershey, 1993) or decision-making in a task involving choice about which insurance policy to select (Hartley, 1989). Relevant data are also presented below.

Emotion identification tasks
In contrast to patients with DL lesions, patients with VM damage show lower affective responses to emo-
tionally loaded stimuli, have less control over their emotions, and poorer ability to interpret and empathize with the emotional states of others (Homak et al., 1996; Beech et al., 1996). In the facial expression version of the emotion identification task, the participant is presented with a photograph of a face, underneath which are a series of adjectives describing different emotions. The participant is instructed to choose the adjective that best describes the emotion displayed by the face in the photograph. In the vocal version of the emotion identification task, the participant is presented with a tape of emotional sounds and is instructed to choose from a list of emotions, the emotion that is best expressed by that sound.

Evidence of DL and VM involvement. Homak et al. (1996) compared the effects of VM prefrontal damage with lesions elsewhere in the brain on the identification of facial and vocal expressions of emotion. Homak et al. (1996) found that patients with lesions in the VM prefrontal cortex were significantly impaired on emotion identification tests compared with patients with lesions elsewhere in the brain. VM damage caused poorer ability to recognize emotional expressions, while damage to the DL prefrontal regions did not. Patients with VM lesions who performed poorly on emotion identification tasks also reported alterations in the experience of emotions.

Relatively few studies have looked at the performance of patients with focal frontal lobe lesions on emotion identification tasks, but there are a large number of neuroimaging studies. Most of these indicate activation related to emotion identification in a number of different brain regions including the frontal lobes. In a neuroimaging study using fMRI, George, Keiter, Gill et al. (1993) attempted to identify the areas of the brain involved in recognizing emotion in faces, and found highly significant activation in ventral areas of the prefrontal cortex during an emotion matching task, as well as less intense activation in DL areas. Other studies have found that both VM and DL areas of prefrontal cortex are involved in identifying facial and vocal expressions of emotion (Imai, Mori, Kirita et al., 1997; Sprengelmeyer, Rausch, Eysel and Pruzuntek, 1998). There is also evidence that VM prefrontal cortex may be differentially depending on which basic emotion is viewed (Blair, Morris, Frith et al., 1999; Phillips, Young, Senior et al., 1997). Blair et al. (1999) found that VM prefrontal regions are involved particularly in processing expressions of anger, rather than sadness.

Age effects. There has been relatively little research on changes in perceiving emotions with age (Carstensen, Isacowitz and Charles, 1999; Schaie and Willis, 1996; Weiner and Graham, 1989). Some theories suggest that increasing age should be associated with improvements, or at least stability, in the ability to interpret others emotions (e.g. Carstensen et al., 1999). Some studies suggest that increasing age may be associated with better ability to interpret and regulate emotion (Blanchard-Fields, Jahnke and Camp, 1995). Montepare, Koff, Zaitchik and Albert (1999) argue that age differences are generally not found in interpreting emotions from static pictures of faces, while age differences are more likely to be found in interpreting emotions from dynamic cues such as bodily movements.

Theory of mind

Theory of mind tests aim to assess the ability to accurately attribute mental states to other people (Premack and Woodruff, 1978). Impairments of 'theory of mind' have been argued to underlie the social and communicative difficulty experienced by individuals with autism (Baron-Cohen, Joliffe, Morris and Robertson, 1997). In most theory of mind tests, participants are given a story to read and have to assess the state of mind of a protagonist in the story. For example, in the 'Faux Pas' test (Stone, Baron-Cohen and Knight, 1998) participants must judge whether someone described in a story has done or said something socially inappropriate, whether the person making the faux pas is aware of their error, and whether the person hearing it would feel hurt or insulted by what was said.

Evidence of DL and VM involvement. Baron-Cohen and Ring (1994) claim that the VM cortex is involved in theory of mind. Stone et al. (1998) examined five patients with damage to the left lateral frontal cortex including the dorsal areas and more ventral areas performing on the Faux Pas task. They also tested
patients with bilateral damage to the VM prefrontal cortex from head trauma. Stone et al. (1998) found that both control participants and patients with DL prefrontal lesions detected and understood the faux pas. However, most of the patients with ventral prefrontal lesions made errors in detecting the faux pas.

Studies of neuroimaging provide further evidence that the frontal lobes are associated with theory of mind. A PET study by Fletcher, Happé, Frith et al. (1995) demonstrated that the left medial prefrontal cortex is activated when normal volunteers attempt to attribute mental states to others. In a later study, Happé, Ehlers, Fletcher et al. (1996) found VM activation in individuals with Asperger’s syndrome, a mild variant of autism, performing the same mental state attribution task. Baron-Cohen, Ring, Moriarty et al. (1994) found that there was significant activation in the VM, but not the DL, prefrontal cortex while normal participants performed a mental state recognition task. More recently, Gallagher, Happé, Brunswick et al. (2000) found activation in the medial prefrontal cortex when normal volunteers were presented with theory of mind stories and cartoons using fMRI.

Age effects. Few studies have looked at the effects of adult aging on theory of mind abilities. Happé, Winner and Brownell (1998) presented adults of various ages with a number of short passages then asked a question in which they had to attribute mental states to the protagonist of the story. They found that the older group actually performed better than the younger adults on the theory of mind stories, which would suggest that theory of mind ability is well-preserved in old age.

Summary of dorsolateral and ventromedial test findings

Tasks that are dependent on DL prefrontal cortex could generally be construed as assessing executive function. Such tests are in the main sensitive to normal adult aging. In contrast, tasks with high VM prefrontal involvement tend to require emotionally salient decision-making, and the sparse evidence that is available suggests that such tasks are little affected by age. We therefore propose that cognitive changes with age are better described in terms of deterioration of DL prefrontal cortex than in terms of general frontal lobe decline (see also Phillips and Della Sala, 1998). Next, we describe a pilot study to examine the effects of adult age on a selection of the tasks described above that are selectively sensitive to DL or VM prefrontal functioning.

The effect of adult aging on six tests of DL or VM prefrontal functioning: some preliminary data

To date, no studies have directly assessed the effects of adult aging on a range of DL and VM prefrontal tasks. We have some preliminary data to report on age differences on six of the tests outlined above for which there is some evidence for relatively specific involvement of either DL or VM frontal regions: (1) the Wisconsin card sort test (Grant and Berg, 1948); (2) a version of the self-ordered pointing task using abstract designs (Petrides and Milner, 1982); (3) a visuospatial delayed response task (Teixeira-Ferreira et al., 1998); (4) the gambling task (Bechara et al., 1994); (5) identifying facial expression of emotion identification using the color Ekman faces (Hornak et al., 1996); and (6) a faux-pas test of theory of mind (Stone et al., 1998). It is predicted that there will be age effects on the first three (DL) tests but not of the latter three (VM) tests.

Ninety participants were recruited: 30 aged between 20 and 39 years (mean age = 28.80, SD = 6.00, range = 20–38 years), 30 aged between 40 and 59 years (mean age = 50.27, SD = 5.65, range = 40–59 years) and 30 aged between 60 and 80 years (mean age = 69.93, SD = 5.47, range = 61–80 years). The groups were matched for vocabulary scores, and all participants met the WAIS-III UK and WMR-III UK selection criterion and did not have any history of medical or neurological problems. Graphs of the basic results are shown in Fig. 4.

A preliminary analysis of the data revealed significant age effects on all three tests sensitive to dorsolateral prefrontal dysfunction. There was a significant effect of age group on: the number of perseverative errors made on the WCST, \( F(2, 85) = 4.880, P < 0.05 \); the number of errors made during the self-ordered pointing task, \( F(2, 87) = 17.779, P < 0.05 \); and the number of errors made during the delayed response task \( F(2, 87) = 6.522, P < 0.05 \).
In contrast, there were no age effects found on two of the tests sensitive to ventromedial prefrontal dysfunction: number of cards chosen from risky decks in the gambling task $F(2, 87) = 0.916, \text{NS}$; and number of errors made in identifying socially inappropriate responses in the faux pas task $F(2, 86) = 0.961, \text{NS}$. However, there was an effect of age on overall accuracy on the emotion identification task $F(2, 87) = 3.414, P < 0.05$. Inspection of the effects of age on identifying particular types of emotion showed that out of the seven types of emotion portrayed, an age impairment was only found on labeling ‘sadness’, with no age differences in identifying the other six emotion states. This may be due to different interpretation of the verbal labels used for some of the emotions by young and old adults.

These results suggest that there may be a distinction that can be made in terms of the effects of normal adult aging on tests of DL and VM prefrontal function. More detailed analysis of test performance, and in particular an attempt to understand the reason underlying any age differences on a particular test, will allow a richer picture of the nature of age deficits on the tasks.

Fig. 4. Performance of young, middle and old participants on the six tests of dorsolateral and ventromedial prefrontal functioning. WCST = Wisconsin card sort test; SOPT = self-ordered pointing task.
Conclusions

The distinction between the effects of dorsolateral and ventromedial prefrontal lesions on human behavior has often been made in the clinical literature. However, this distinction has rarely been applied to the process of normal adult aging, despite intense interest in the effects of age on the frontal lobes. There are probably no tests which specifically tap only DL or VM functioning; the involvement of DL regions in cognitive control processes and VM regions in emotional and motivational processes mean that both are likely to be involved in a range of different cognitive tasks. Distinctions can, however, be made between some tests that are largely sensitive to DL but not VM damage (e.g., the self-ordered pointing test) and others that are largely sensitive to VM but not DL damage (e.g., the gambling task). Also, future analyses may help to distinguish qualitative patterns of performance indicative of VM or DL involvement in particular tasks (e.g., working memory versus reward anticipation in the delayed response task). Most 'frontal lobe tests' are multicompontental, and so it is only by detailed analysis of performance that underlying reasons for poor performance can be worked out (Phillips, 1997, 1999).

In the current chapter we argue that:

1. Neuroimaging and histological evidence supports the hypothesis that DL prefrontal regions are impacted by normal aging earlier, and more severely, than VM prefrontal regions.

2. The clinical picture seen in normal aging matches more closely the type of deficits seen in patients with DL lesions (i.e. executive and problem-solving dysfunction) rather than the deficits seen in VM patients (i.e. social and emotional dysfunction).

3. Evidence from the literature and the current reported pilot study indicates substantial age-related decline on most tasks sensitive to DL function, i.e. the Wisconsin card sort test, self-ordered pointing, Stroop, fluency, Tower of London, recency judgement. However, there must be some caution in interpreting these results because the reasons for age-related changes and DL frontal involvement may be different. All of these executive tests are relatively complex, involving a number of different information processing components, and there are correspondingly many different ways to fail these tests.

4. Evidence from the literature is much more scant on paradigms which might assess VM prefrontal functions, and the effects of age on such tests. The preliminary study reported here suggests that there are no age effects on tests of gambling, theory of mind (supporting a similar finding by Happé et al., 1998), and identification of all basic emotions with the exception of sadness. Further studies will explore in more detail the nature of such deficits in patients with VM lesions, and qualitative similarities or differences between the effects of VM lesions and the effects of normal aging.

From the current review, we conclude that there is growing empirical support for the differential functional roles of VM and DL prefrontal areas in cognition and emotion. There is also tentative support from brain imaging and behavioral studies for the hypothesis that normal adult aging affects primarily DL but not VM regions of the prefrontal cortex.

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