Fig. 6 — An example of an lateral prefrontal cortex (LPFC) neuron showing differential activity depending on the reward block, not only during the instruction and delay periods, but also during the pre-instruction period. The task situation is the same as in Figure 3A. For this neuron, the activity is shown from 9 sec before the Instruction presentation to 3 sec after the Go signal presentation. The first and the second vertical dotted lines indicate the onset and offset of the 1-sec Instruction presentation, and the third vertical line indicates the time of the Go signal presentation. Other conventions are the same as Figure 3 (From Watanabe et al., 2002, with kind permission from the Journal of Neuroscience).

receive task-related cognitive and motivational information from the LPFC (Kawagoe et al., 1998; Platt and Glimcher, 1999; Sugrue et al., 2004). Indeed, anatomical studies indicate that the LPFC receives highly processed cognitive information from the posterior-association cortices, as well as motivational information from the OFC (Barbas, 1993). In a recent paper, in which neuronal activity was recorded from both the OFC and LPFC in the same monkey (Wallis and Miller, 2003), reward selectivity arose more rapidly in the former region than in the latter. Furthermore, LPFC neurons more often encoded both reward and WM-related information while OFC neurons more often encoded reward information alone. Thus, reward information might initially enter the OFC before being passed to the LPFC, where it is integrated with cognitive information. The LPFC could therefore play important roles in modulating eye movement-related neuronal activity in the LIP and caudate nucleus by sending integrated cognitive and motivational information to these areas.

Representation of "Cognitive" and "Affective" Goals in the Primate PFC

We propose here that the PFC is involved in representing both the goal of the behaviour (by the reward/omission-of-reward expectancy-related neuronal activity) and the way in which the goal could be attained (by the WM-related neuronal activity). We also propose that the LPFC is involved in the integration of cognitive and motivational operations for goal-directed behaviour. Similar ideas have previously been put forward suggesting that the PFC represents both goals and the means to achieve them (Miller and Cohen, 2001). However, it should be noted that there is a critical difference regarding the meaning of the term "goal" in these proposals; by "goal" we mean "reward", whereas Miller and Cohen (2001) mean

"proper behaviour" or the "correct response in the task situation". Thus, when they say "the PFC provides bias signals throughout much of the rest of the brain, affecting sensory processes as well as systems responsible for response execution, memory retrieval etc., by active maintenance of patterns of activity that represent goals and the means to achieve them", the "goal" is not an affective or motivational (reward) goal, but rather a cognitive or behavioural (correct response) one. If the "ultimate goal" of the organism is the survival of the individual and its species, the affective goal might be the "immediate goal" in a given situation, while the cognitive goal might be the "intermediate goal" towards the affective goal. As Miller and Cohen (2001) argue, the representation of both (cognitive) goals and the means to achieve them are surely essential for accurate task performance. We would like to extend their proposal concerning the function of the PFC in the control of behaviour to include the concept of an "affective" goal. It appears that the representation of the cognitive goal in the PFC is essential for the animal to make correct choices, while the representation of the affective goal might instead work to modulate the WM-related neuronal activity that is concerned with the representation of the means by which the affective goal can be obtained.

Whereas WM-related neuronal activity is predominantly observed during the delay period, the representation of the goal in PFC neuronal activity is observed not only during the delay period but also during the pre-instruction baseline period. Figure 6 illustrates an example of an LPFC omission-of-reward expectancy neuron that showed differential activity depending on the difference of the affective goal (reward), not only during the delay period but also during the pre-instruction baseline period. Such neurons might be involved in representing the affective goal throughout the trials when a certain reward is used continuously.
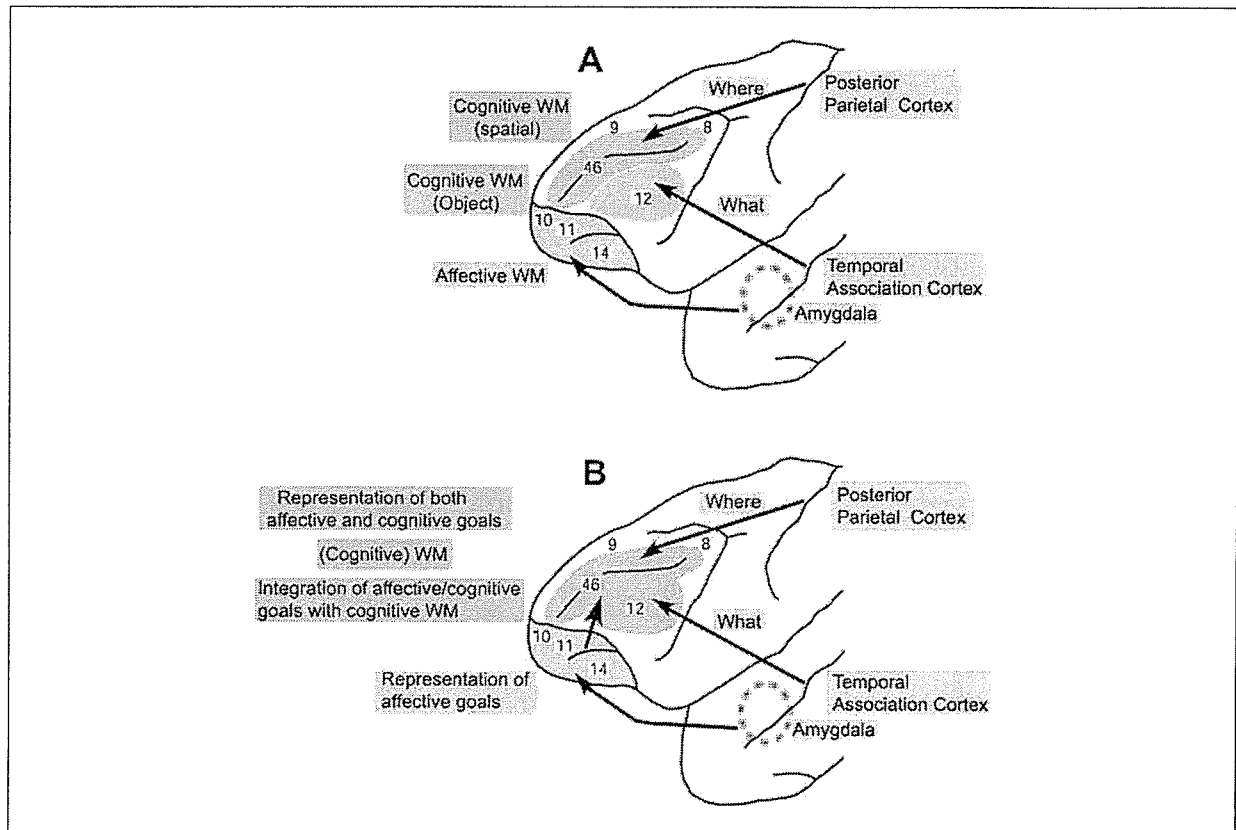
Fig. 7 – *(A) A model of functional differentiation in the monkey prefrontal cortex (PFC) in relation to the domain (affective and cognitive) of information held in working memory (WM). (B) Our model of functional differentiation in the monkey PFC in relation to cognitive and motivational operations. The numbers indicate areas in Walker's (1940) map of the monkey PFC.*

There are also neurons in the LPFC that appear to be involved in representing the cognitive goal in relation to the current task requirements during the pre-instruction baseline period (Sakagami and Niki, 1994; Asaad et al., 2000). Those LPFC neurons that show task- or rule-dependent sustained activity during the delay period might also be concerned with representing the cognitive goal (White and Wise, 1999; Wallis et al., 2001).

In addition, we reported pre-instruction baseline activities in the OFC reflecting the affective goal (Figure 4). Whereas reward/omission-of-reward expectancy-related neurons are relatively common, WM-related neurons are rarely observed in the primate OFC (Tremblay and Schultz, 2000), which supports an ablation study that indicated no clear WM deficit in OFC-ablated monkeys (Pribram and Bagshaw, 1953).

Thus, we propose that the OFC might be predominantly concerned with representing the "affective" goal, while the LPFC is involved in representing both "affective" and "cognitive" goals. The magnitude of neuronal activity representing the "affective" goal differs depending on whether the organism expects the delivery or omission of reward, and/or a difference in the type or magnitude of the reward. By contrast, there would be only one "cognitive" goal (for example, to respond according to the current task rule) in a

given task situation. The LPFC appears to play a critical role in (affective) goal-directed behaviour by representing not only cognitive but also affective goals, as well as representing the means to attain these goals in WM. While the affective goal representation modulated WM-related neuronal activity (Figure 2C), it will be interesting to examine whether the representation of the cognitive goal also modulates WM-related neuronal activity in the LPFC.

CONCLUSIONS

It has been suggested that the PFC is functionally differentiated with regard to the domain of WM information: the dorsolateral and ventrolateral PFC are concerned with representing spatial and object information in WM, respectively (Goldman-Rakic, 1996), while the OFC might be concerned with representing affective and motivational information in WM (Davidson and Irwin, 1999). Figure 7A illustrates a domain-specific differentiation model of WM in the monkey PFC, as proposed by Goldman-Rakic (1996) and Davidson (2002). Neurons in the ventrolateral PFC receive ventral "what" information and are more tuned to objects, while neurons in the dorsolateral PFC receive dorsal

"where" information and are more tuned to spatial stimuli (O'Scalaidhe et al., 1997). A recent study also indicated that the LPFC is functionally differentiated, with the ventral and dorsal sectors concerned with processing object information and the numerical position ('rank order') of objects, respectively, during a temporal-order memory task (Ninokura et al., 2004). Thus, there appears to be a domain-specific differentiation of the monkey LPFC with regard to the cognitive aspects of the stimulus, although it remains uncertain whether there is such a domain-specific differentiation of the LPFC with regard to WM.

Our model of the functional differentiation of the PFC is illustrated in Figure 7B. We follow the ideas put forward by Petrides (1996), D'Esposito et al. (1998) and Owen et al. (1998), and propose that the LPFC might be concerned with retaining and manipulating all types of "cognitive" information in WM without domain-specific differentiation. The OFC, which receives motivational information from the limbic system, particularly from the amygdala, is not directly concerned with WM (that is, the 'temporary storage and manipulation of information for complex cognitive tasks'), but rather is predominantly concerned with representing the affective goal. We propose that WM-related neuronal activities are concerned with representing which response should be performed to attain the affective goal and that reward/omission-of-reward expectancy-related activities represent the affective goal of the response. Representation of the affective goal by reward/omission-of-reward expectancy-related neuronal activities appears initially in the OFC and the information might then be sent to the LPFC (Wallis and Miller, 2003). In the LPFC, the representation of both affective and cognitive goals could be integrated with WM-related information to guide and control behaviour in order to obtain a reward more effectively, and thus leading to better survival.

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