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Research Report

Neural correlates of pair-bonding in a monogamous primate

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ABSTRACT

The neurobiology of social bonding, despite its relevance to human mental health, has been studied primarily in rodents. In this study we used position emission tomography (PET), registered with structural magnetic resonance imaging (MRI) to investigate central glucose uptake in 17 males of a monogamous primate species, the titi monkey (*Callicebus cupreus*). Twelve pair-bonded males (including six with a lesion of the prefrontal cortex) and five lone males were scanned. The five lone males were re-scanned 48 h after pairing with a female. Significant differences in glucose uptake were found between males in long-term pair-bonds and lone males in areas including the nucleus accumbens, ventral pallidum, medial preoptic area, medial amygdala, and the supraoptic nucleus of the hypothalamus. In paired before and after comparisons, males showed significant changes following pairing in the right nucleus accumbens and ventral pallidum but not in other areas. Lesioned males showed significantly higher uptake in the posterior cingulate cortex than all other males. These results indicate some basic similarities between rodents and primates in the formation and maintenance of selective social bonds, but emphasize the importance of studying long-term maintenance in addition to short-term formation of social bonds.

1. Introduction

The neurobiology of pair-bonding has been well-studied in rodent models, particularly the monogamous prairie vole (Winslow et al., 1993; Williams et al., 1994; Carter, 1998; Insel et al., 1998; Cho et al., 1999; Lim et al., 2001; Young et al., 2001a; Aragona and Wang, 2004). This work in rodents has identified a neural circuit beginning with sensory input into the olfactory system, and involving both the "reward circuit" (ventral pallidum, nucleus accumbens, ventral tegmental area) and the "social recognition" circuits in the medial amygdala and lateral septum (Liu et al., 2001; Young et al., 2001b, 2005; Lim et al., 2004a). The critical areas for the formation of pair-bonds are hypothesized to be the nucleus accumbens in females (Aragona et al., 2005) and the ventral pallidum in males (Lim et al., 2001, 2004b; Lim and Young, 2004). A recent model of affiliation in humans also concentrated on the μ-opioid receptors in the nucleus accumbens as mediators of the experience of affiliative reward (Depue and Morrone-Strupinsky, 2005).

The neurobiological basis of social bonds in humans has become an important topic in recent years, particularly with the increasing incidence of disorders in social bonding such as autism (Insel et al., 1999; Lim et al., 2005). Some very interesting human studies have used fMRI to investigate areas activated or deactivated while viewing objects of attachment

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(Bartels and Zeki, 2000, 2004; Aron et al., 2005; Fisher et al., 2005, 2006). These studies have identified some of the same brain regions of importance noted in the animal studies, including areas in the hypothalamus and the reward circuit. Animal studies have the advantage, of course, of offering a simpler, perhaps less variable model system. In studying titi monkeys, we can manipulate the exact time and conditions of the formation of a pair-bond. There is also the potential to administer experimental treatments which may affect the quality of the pair-bond, or the speed of its formation.

It is worth noting, however, that almost all previous research on the neurobiology of pair-bonds in animals has been done on rodents, and almost exclusively on the *formation* rather than on the *maintenance* of the bond. In the classic partner preference paradigm (Williams et al., 1992), a vole or other rodent chooses between a cage containing a partner, a cage containing a stranger, or an empty cage. This is almost always carried out in the context of giving a treatment followed by a short cohabitation period, and then a test for presence of a bond. It has rarely been carried out on established pairs.

Research on the neurobiology of either formation or maintenance of pair-bonds in non-human primates, the mammals most closely related to humans, is relatively meager. Partly this is because the common laboratory biomedical primate model, the rhesus macaque (*Macaca mulatta*) does not form pair-bonds. Rhesus monkey sexual consortships have been used as a model of sexual jealousy (Rilling et al., 2004), but these are temporary associations. Monogamous primates represent relatively few species, including the lesser apes (such as gibbons and siamangs), and New World monkeys such as marmosets, tamarins, saki monkeys, owl monkeys, and titi monkeys (Kleiman, 1977).

In the present research, we used monogamous titi monkeys (*Callicebus cupreus*). These small, arboreal South American monkeys form strong emotional bonds between pair-mates (Mendoza and Mason, 1997). In the wild and in captivity, this bond is reflected in the close coordination of travel between

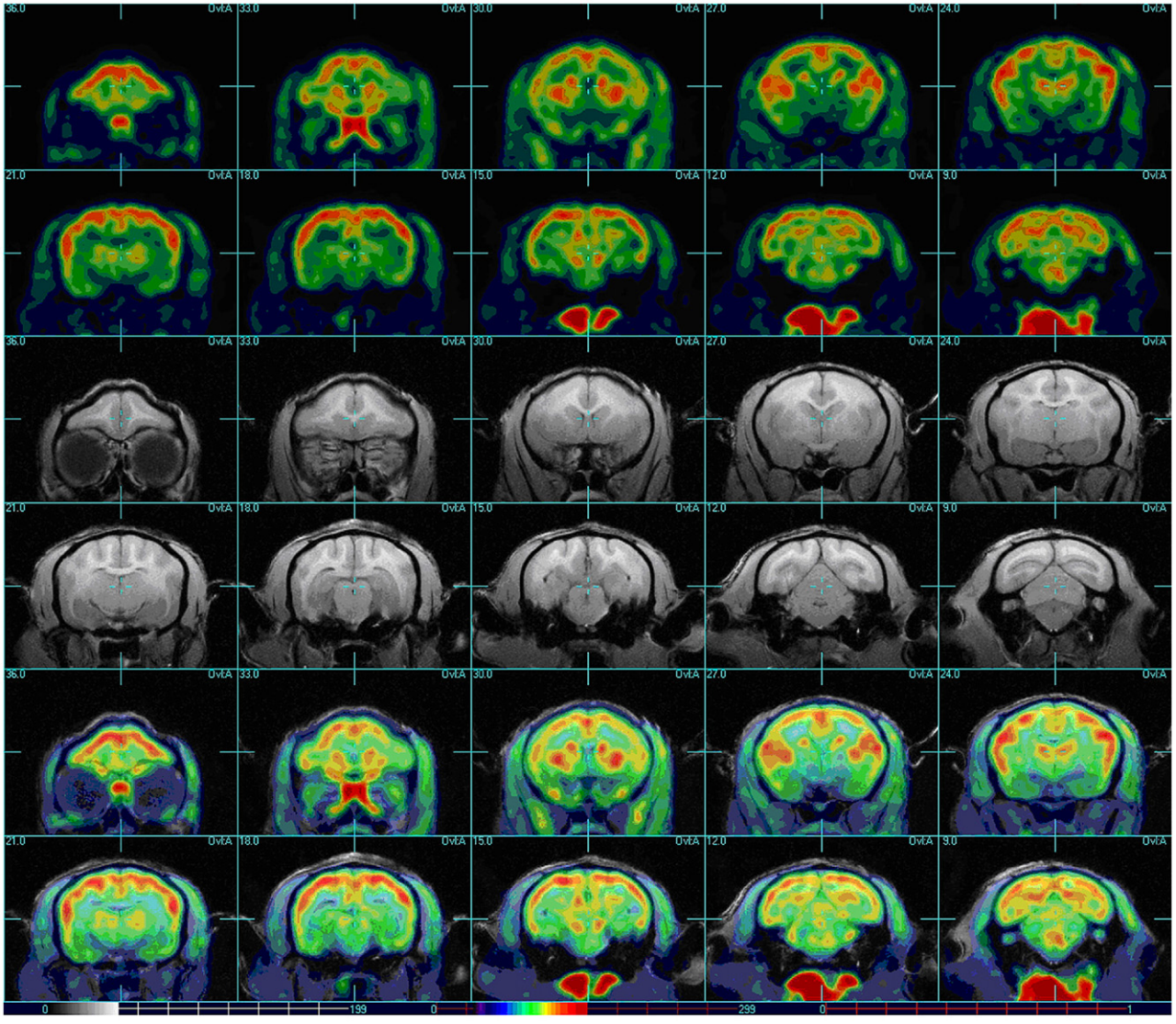

Fig. 1 – Series of images rostral (from upper left) to caudal in the titi monkey brain. Rows 1 and 2 are PET images, Rows 3 and 4 are corresponding structural MRI images, and Rows 5 and 6 are the two sets of images overlaid.