Perspectives

Sur base des données présentées dans les chapitres précédents, il serait intéressant d'examiner plus en détails le phénomène de renforcement. De fait, plusieurs autres procédures que celle du CPP existent, comme par exemple, celle de l'auto-administration (Thomsen & Caine, 2007 pour une synthèse de la littérature).

Même si elle est plus coûteuse en temps et plus invasive pour les animaux, vu qu'elle requiert le placement d'un cathéter au niveau de la jugulaire, la technique d'auto-administration possède l'avantage de pouvoir mesurer le renforcement chez des animaux qui sont libres de s'auto-administrer la drogue, en comparaison avec le CPP, où les animaux sont drogués de force. On parle alors d'administration passive (Stefanski *et al.*, 2007; Thomsen & Caine, 2007; Tzenchke, 2003). De plus, l'absence ou la présence de renforcement dans le CPP n'est pas prédictive du renforcement éventuellement obtenus dans un paradigme d'auto-administration (Bardo & Bevins, 2000; Sanchis-Segura & Spanagel, 2006; Tzschentke, 2007). Par exemple, une récente étude utilisant des souris mutantes a mis en évidence que les WT et les KO A_{2A} adénosine sont renforcées dans le CPP sous cocaïne dans les mêmes proportions, mais se distinguent largement dans un paradigme d'auto-administration (Soria *et al.*, 2006).

Concernant les souris WT et KO MCHR1, il serait donc intéressant de tenter de reproduire les résultats de Chung et collègues (2009) sur l'auto-administration à la cocaïne (Figure 57). Dans cette étude, l'auto-administration de cocaïne chez le rat est bloquée par l'administration d'un antagoniste MCHR1.

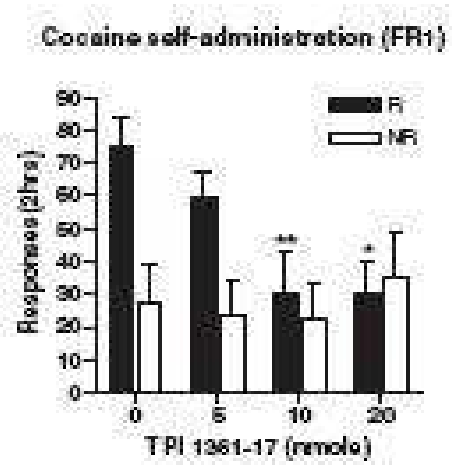

Figure 57. Effet inhibiteur d'un antagoniste MCHR1 sur l'auto-administration de cocaïne selon le nombre d'infusions de cocaïne obtenues (barres noires) et de réponses inactives (barres blanches). Différence significative à $P<0.05$ (*) ou $P<0.01$ (**) (Chung *et al.*, 2009, fig. 5, p. 4).

De plus, la rechute mesurées par différentes procédures, à savoir l'exposition aux stimuli contextuels précédemment associés à l'auto-administration de cocaïne, l'exposition à un faible choc électrique ou encore l'injection d'une faible dose de cocaïne, est également bloquée par l'administration de l'antagoniste MCHR1 (Figure 58) (Chung *et al.*, 2009).

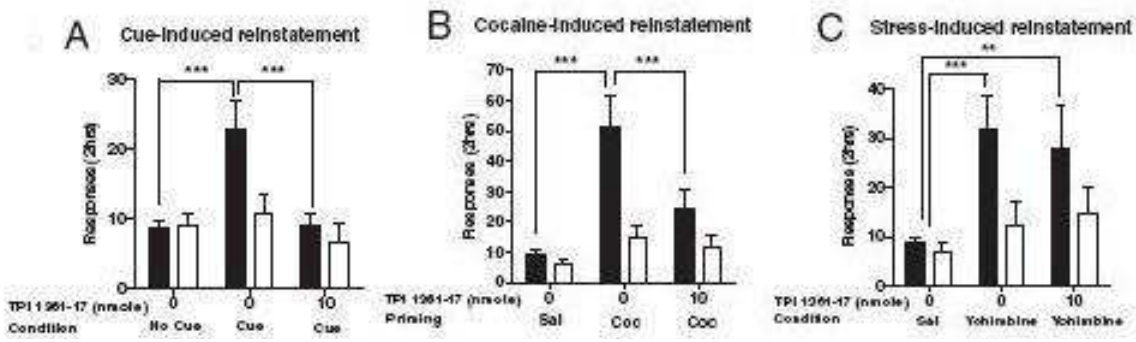

Figure 58. Effet inhibiteur d'un antagoniste MCHR1 sur la rechute mesurée par (A) l'exposition à des stimuli précédemment associés à l'auto-administration de cocaïne, (B) une injection préalable de cocaïne (10 mg/kg) ou (C) de yohimbine (2.5 mg/kg) avant le commencement de la session dans l'appareil d'auto-administration. La mesure effectuée est le nombre d'infusions de cocaïne obtenues (barres noires) et de réponses inactives (barres blanches). Différence significative à P<0.01 (**) ou P<0.001 (***) (Chung *et al.*, 2009, fig. 6, p. 4).

En complément, le paradigme d'auto-administration permettrait également d'approfondir la thématique de l'impact d'une restriction alimentaire sur les propriétés renforçantes des drogues d'abus. De fait, cette méthode est préférentiellement utilisée dans ce type d'étude (Lu *et al.*, 2003b).

Enfin, il serait également intéressant d'effectuer des mesures neurophysiologiques identiques à celles rapportées dans les études de Smith et collègues (2005, 2008), dans la mesure où les mécanismes sous-tendant les réponses comportementales des KO MCHR1 pour les faibles doses d'amphétamine et l'absence de sensibilisation à la cocaïne ne sont pas encore totalement établis.

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