

Time, action and psychosis: Using subjective time to investigate the effects of ketamine on sense of agency

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ABSTRACT

Sense of agency refers to the experience of initiating and controlling actions in order to influence events in the outside world. A disturbed sense of agency is found in certain psychiatric and neurological disorders, most notably schizophrenia. Sense of agency is associated with a *subjective compression of time*: actions and their outcomes are perceived as bound together in time. This is known as 'intentional binding' and, in healthy adults, depends partly on advance prediction of action outcomes. Notably, this predictive contribution is disrupted in patients with schizophrenia. In the present study we aimed to characterise the psychotomimetic effect of ketamine, a drug model for psychosis, on the predictive contribution to intentional binding. It was shown that ketamine produced a disruption that closely resembled previous data from patients in the early, prodromal, stage of schizophrenic illness. These results are discussed in terms of established models of delusion formation in schizophrenia. The link between time and agency, more generally, is also considered.

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1. Introduction

In humans, voluntary goal-directed action is accompanied by an experience of initiating and controlling the action, and through it, controlling the external world. This experience is referred to as the sense of agency. A disturbance in sense of agency may lie at the heart of psychotic symptoms such as delusions and hallucinations, which are characteristic of schizophrenia – a syndrome that also entails marked alterations in the perception of time.

Intriguingly, this sense of agency is associated with a *subjective compression of time*, such that actions and their effects are perceived as bound together across time (Haggard, Clark, & Kalogeras, 2002; Moore & Obhi, 2012). This effect is known as 'intentional binding' (Fig. 1A). In the standard version of the intentional binding paradigm, participants judge the onset of either voluntary actions (a key press) or the onset of a sensory event (a tone) presented 250 ms after the action. The perceived onset of the action is shifted later in time in comparison to the perceived onset of actions in a

baseline condition in which the action does not produce a tone. Furthermore, the perceived onset of the tone is shifted earlier in time relative to the perceived onset of tones in a baseline condition in which the tone is presented without action. In short, a causal action is experienced as occurring closer to the ensuing outcome while the experience of the outcome moves closer to its causal action. This binding effect is specific to *voluntary* action. When actions are *not* under voluntary control the reverse pattern of results is observed. It has therefore been proposed that intentional binding is a viable implicit measure of sense of agency (Haggard et al., 2002; Moore & Haggard, 2010; Moore & Obhi, 2012).

As noted, a disrupted sense of agency is characteristic of certain psychiatric disorders, most notably schizophrenia (Frith, 1992). Such would be the case, for example, in delusions of control, where the sufferer has a compelling sense of actions being controlled by an outside force. According to one influential model of sense of agency, the so-called 'Comparator Model' (CM), disordered experiences of agency in schizophrenia are produced by deficits in sensorimotor prediction. According to this view, the normal experience of agency is dependent on predictive motor control processes (Blakemore, Wolpert, & Frith, 2002; Frith, 2005). Specifically, an efference copy of motor commands is used to predict the likely sensory consequences of a voluntary action, and the comparison

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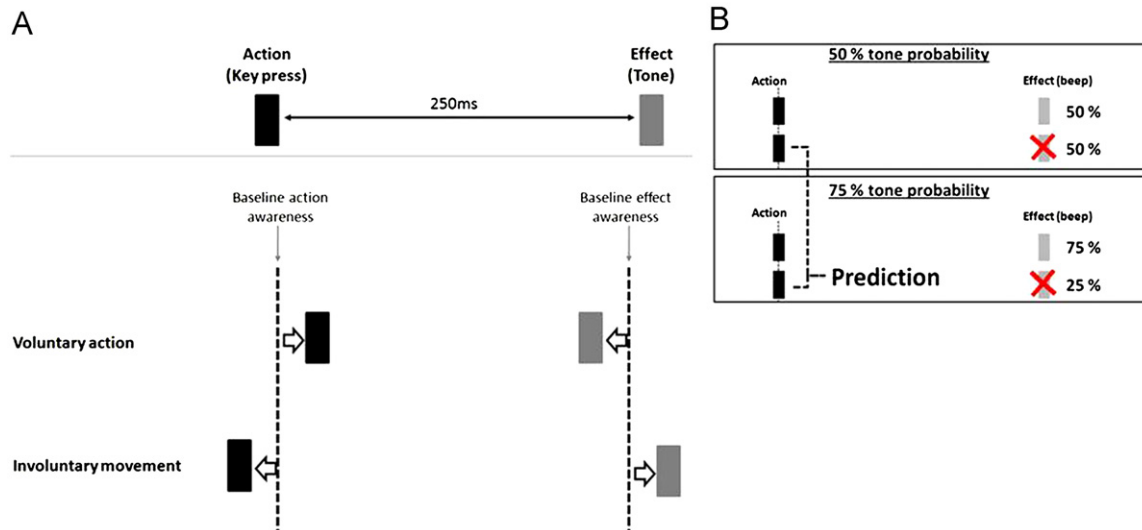


Fig. 1. (A) The intentional binding effect. Voluntary actions and outcomes are temporally bound together in experience, whereas involuntary movements and outcomes are separated in experience (see Haggard et al., 2002). (B) Operational definition of prediction in our study. A predictive contribution to action binding was derived from subtracting the shifts in the temporal experience of action on ‘action only’ trials in 50% effect probability condition, from shifts on action ‘only trials’ in the 75% effect probability condition.

between these predictions and the actual sensory consequences informs sense of agency. A match between predicted and actual sensory consequences of movement promotes the feeling of *self-agency*, whereas a mismatch reduces it. According to the CM, experiences of passivity in patients with schizophrenia can be explained by impaired sensorimotor prediction during voluntary action. This impairment would lead to a faulty mismatch between the actual and expected sensory consequences. As a result, patients experience a reduced feeling of self-agency for their movements.

In support of the CM, a number of studies on sense of agency in schizophrenia have shown that patients have deficits in sensorimotor prediction (Blakemore, Smith, Steel, Johnstone, & Frith, 2000; Shergill, Samson, Bays, Frith, & Wolpert, 2005; Synofzik, Thier, Leube, Schlotterbeck, & Lindner, 2009). Compelling evidence also comes from studies using the intentional binding paradigm. Moore and Haggard (2008) confirmed the contribution of prediction to sense of agency in healthy volunteers. When actions frequently produced an outcome, the shift in perceived time of action towards the (expected tone) occurred even on rare ‘action only’ trials, on which the outcome was omitted. This suggests that *predicting* the outcome was sufficient to generate the shift in perceived time of action. This was confirmed by the reduction in binding on ‘action only’ trials in a condition where the tone was unpredictable. This approach to exploring the predictive component of intentional binding is shown in Fig. 1B: The predictive contribution represents the *difference* in binding on ‘action only’ trials in the 75% condition (where 75% of trials are followed by tones) vs. the 50% condition (where 50% of the trials are followed by tones), and the more positive this difference the greater the predictive contribution.

Using this same procedure, deficits in sensorimotor prediction have been observed in patients with schizophrenia and in prodromal patients. However, the pattern of predictive deficits in these two groups is quite different (see Fig. 2). Patients with schizophrenia show an *absence* of predictive action binding (Voss et al., 2010), in direct support of the CM. On the other hand, prodromal patients, those who experience symptoms pointing towards a psychotic disorder but who do not yet meet diagnostic criteria, show much stronger predictive action binding relative to controls (Hauser et al., 2011).

In summary, the subjective perception of the timing of both a causal action and its ensuing outcome offers an implicit measure

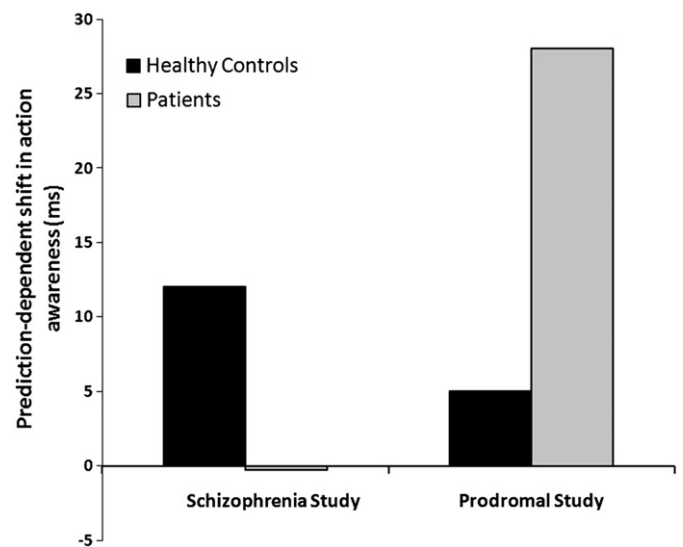


Fig. 2. Data from previous studies on patients with schizophrenia and patients in the psychotic prodrome. These data represent the predictive contribution to action binding (i.e., the difference in binding on ‘action only’ trials in the 75% vs. 50% condition). The greater this difference the stronger the predictive contribution). Both studies replicated the predictive contribution to binding in healthy volunteers found by Moore and Haggard (2008). However, the two groups of patients showed different deficits on this task. Patients with schizophrenia showed no significant predictive contribution (from Voss et al. (2010)), whereas prodromal patients showed an excessive predictive contribution (from Hauser et al. (2011)).

of SoA. Moreover, it is possible to develop this measure in order to determine the extent to which that sense emerges from a predictive relationship between an action and its consequences. This has been further refined to offer a novel way to explore the relationship between prediction, agency and timing in schizophrenia and the emerging results suggest that while, overall, disturbances in schizophrenia are compatible with disrupted SoA (as measured by altered experience of the temporal relationship between actions and outcomes), the precise nature of the disruption depends on the stage of illness and this interacts with the degree to which the action is more or less predictive of the outcome. In the current study, we sought to explore this further

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