**Measuring motivation and drive switching in rodents – why and how?**

*\*\*\* Dear reader, please note that this is a ResearchEquals ‘Idea’ manuscript, meant to elucidate the ideas behind a behavioural recording approach our lab is developing. This represents work in progress, and all feedback is welcome at* *m.m.karnani@vu.nl* *\*\*\**

**Summary**

To maximize survival, animals should switch between motivated behaviours, like drinking, feeding or social interaction, in accordance with environmental availability, internal needs, and species-typical ethological needs. *Drives* are the neural mechanisms giving rise to motivated behaviours, and should involve a switching mechanism producing motivational transitions which enhance survival and fitness. Lack of drive switching can lead to inflexible, repetitive behaviours, which are a hallmark of many psychiatric disorders, like obsessive compulsive disorder. In order to study drive switching, it would be helpful to directly measure motivational switching in genetically tractable rodent model systems. Here, a potentially useful motivational switching metric for rodent work is described and contrasted to similar concepts in the literature. It is proposed that this ethologically-grounded parameter could be a phenotypic unit relevant to behavioural compulsions in humans.

**Definitions**

*Drive* – a neural mechanism generating a motivated behaviour such as feeding.

*Motivated behaviour* – a set of behavioural actions generating attainment of a goal such as food intake.

*Behavioural cycle* – a cycle of one motivated behaviour from initiation through appetitive and consummatory phases to termination.

**Reasoning**

The drives for feeding, drinking and socializing generate a motivational scaffold upon which we build our daily lives. A drive switch is a neural phenomenon that changes the motivated behaviour of an animal, such as drinking a glass of water after a finishing a meal, or feeding when unexpectedly encountering a source of palatable food. Typically, drives switch on and off to meet internal needs like hunger and thirst, and are to some extent controlled by the availability of goal objects1 as well as conscious effort. On the other hand, key symptoms of feeding disorders, obsessive-compulsive disorder (OCD) and autism spectrum disorder include behavioural rigidity2, which is evident in abnormally frequent (or infrequent) motivations for food intake, exercise, social interaction, and self-care. These repetitive motivated behaviours are typically accompanied by inflexible and intrusive thought patterns, in particular in OCD2. One broad unifying cause of inflexible thoughts and behaviours could be an abnormality in drive switching.

A high or low rate of drive switching can be adaptive or maladaptive under different circumstances. Frequent switching is ideal under conditions of uncertainty, e.g., when exploring a new area with potentially high availability of many consummatory actions. Infrequent switching is ideal when exploiting a stable environment during a high need state. Although infrequent switching in the absence of consummation can also lead to suboptimal outcomes, like a shopping trolley full of drinks when shopping while thirsty, such scenarios are rare in the wild, as consummation is often possible as soon as the goal object is located. Continued hoarding of food after satiation3, however, could involve a highly adaptive attenuation of drive switching. Similarly, displacement behaviours4 and vacuum activities5 may be seen as adaptive facilitation of drive switching, i.e., in the absence of the intended goal object, a previously started behavioural cycle is brought to a close through a vacuum consummation behaviour or displacing to the ending of another behavioural cycle. Thus, control of drive switching can provide adaptive benefits.

To study the neural activity in flexible/stable drives, the degree of switching between motivated behaviours should be analysed. In addition, recording many standardized repetitions of motivational transition epochs during neural recordings could reveal the circuit mechanisms of drive switching. However, drive transitions have mostly been isolated during *approach/avoid decisions*6,7, while studies of competing appetitive drives tend to focus on cumulative amounts of each behaviour8–11. Only rarely, have studies in the absence of threat included drive switching12–14.

Focusing explicitly on drive switching would benefit fundamental research for at least two reasons. Firstly, the switching of a motivation typically leads to a stereotypical completion of a behavioural cycle15. This occurs in the face of aversive stimuli, suggesting positive feedback in the drive switching mechanism16,17. The drive switch would therefore be, to some extent, a ‘point of no return’ when two goals are equally available. Secondly, if motivational switching is structured repetitively, this could be used by competitors as predictive information in order to capture prey or hidden resources. Therefore, when drive switching generates behavioural variability/stochasticity that can elude competitors18,19, this would constitute a form of behavioural camouflage. Therefore, the neural control of drive switching merits investigation.

Hypothalamic neuronal populations are critical for activating motivated behaviours like feeding or aggression20. Manipulation and recording studies have shown that combinations of hypothalamic neurons can initiate the drives of these and other motivations20,21, suggesting that drive switching would entail some coordination of activity patterns across these populations. To explore this further, it will be necessary to set up a behavioural paradigm for monitoring multiple motivations in discretized, repeatable behavioural cycles so that repeated motivational switches can be observed.

Motivational switching is by no means a new concept (e.g., see Figure 3 and references in 22), and behavioural transition likelihoods are a well-known metric in behavioural ecology23,24. However, it is seldom measured in rodents12,13,25 (e.g., compared to invertebrates26–29), and has not been formalized as a common metric. This could be because the usefulness of such a metric is not obvious, and it may be seen as an overly elaborate way of expressing the same results as the standard metrics: overall duration of a motivated behaviour, behavioural bout frequency and length (measured as duration or amount consumed). Consider three situations (Figure 1A) where the overall intensity of a motivation (e.g., total duration through a recording) stays the same and *motivation* *switching, M,* is defined as the ratio of short and long bouts: if *M* increases, bout length should decrease and bout frequency should increase. If *M* decreases, average bout length is expected to increase and bout frequency should decrease. If frequency and average bout length do not change, while the bout length distribution becomes bimodal and heavily skewed to many short bouts and a few very long ones, increased *M* would alert the investigator to explore the other metrics. Thus, *M* is a more concise metric than bout length and frequency. To make it even more useful, *M* can be defined to capture the spontaneous probe epochs characteristic of rodent behaviour (Figure 1B). During consistent performance of a given motivated behaviour (such as feeding), rodents typically intersperse single trials of another behaviour (such as drinking), as if to probe other alternatives11,30,31. Thus, a ratio of single trials to continuous runs simultaneously captures rodent-typical motivational switching as well as hidden and correlated bout length and frequency changes.



Figure 1, Ad libitum feeding and drinking bouts are recorded. A, Across experiments, the total duration feeding/drinking does not change, while frequency and mean length of feeding/drinking bouts change (green and yellow) – motivation switching (M) would adequately summarize these changes (green and yellow). If total duration, frequency and mean bout length do not change (dark and light purple), there might still be a significant alteration in behaviour, captured readily by M, arising from asymmetric bout length distributions (inset). B, As mice perform blocks consisting of multiple sequential choices, they perform many spontaneous probe trials where a motivation is switched on only for one trial and then switched again (Singles, s). The prevalence of singles can be summarized by M, defined as the ratio of singles to runs of any length.

Previous studies have measured parameters similar to motivation switching. A probabilistic behavioural satiety sequence of feeding-grooming-resting, occurring over the course of an hour has been described in rodents32. However, quantification of these phases is not straight-forward as the sequence is highly noisy. Rapid switching of motivated behaviours on a sub-second timescale should be simpler to quantify with modern methods, and could act as a proxy of behavioural flexibility/rigidity. A recent study focused on sub-second transitions between body movement syllables, using transition matrix correlations to find a reinforcement learning model that reproduces natural movement sequences14. Transition matrices of motivated behaviours across need states have been used to identify overall behavioural pattern differences using cosine distance12, and to identify changed and unchanged behavioural transition types13. Motivation switching could be useful as a more intuitive summary metric than cosine distance. Strategy switching and set-shifting are ‘classical’ switching phenomena33 distinct from motivational switching. Set-shifting is often impaired in neuropsychiatric disorders34,35 and this is seen as a proxy of behavioural rigidity. In set-shifting, the time taken to change a behavioural strategy after a hidden rule change is measured. However, the reward for the correct choice remains the same. Therefore, although a behavioural switch of the action is involved30,36–39, the objective of the action does not change. Similarly, the goal was not changed in studies of ‘behaviour switching’40–43 – which therefore could perhaps be more appropriately called ‘strategy switching’. Motivational switching, therefore, is previously understudied and separate from strategy switching and set-shifting. In addition, while healthy humans make minimal errors in set-shifting tasks44, rodents typically require hundreds of trials to reach criterion31,39, suggesting limited use as a translational proxy of behavioural rigidity. Thus, motivation switching could be highly useful in translational neuroscience.

The translational usefulness of motivation switching as a phenotypic unit relevant to behavioural rigidity should be considered in terms of its validity45,46. Although outcome variables are sometimes considered primarily from the perspective of convergent/discriminant validity47, it seems useful to also discuss the other aspects of validity. It has clear face validity, and high potential for convergent validity, in the sense that the repetitive motivated behaviours and intrusive thoughts in many psychiatric disorders (OCD, feeding disorders, autism) likely have an underlying drive switching anomaly that can be captured by motivation switching. As the metric (*M*) is derived from ethological behaviour of rodents, and similar patterns have been seen in many laboratories11,30,31, it has internal validity and potential for external validity. Motivational switching has high potential for construct validity, in particular for feeding disorders that consist of maladaptive switching of the feeding drive (anorexia nervosa, binge eating disorder, bulimia nervosa) and repetitive exercise (anorexia nervosa). Construct validity should be tested with neural manipulations, which could lead to testing predictive validity using a neural substrate.

In summary, motivation switching may be a useful measure of behavioural flexibility in rodents, building on the behavioural satiety sequence, set-shifting, strategy switching and approach/avoidance conflict. Drive switching may be a unifying process gone awry in several mental disorders. Switching metrics (Figure 1) summarizing shifting between distinct drives could be quantified in some existing datasets, and new measurement systems for assessing this would be useful.

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