

人社院心智意識與腦科學研究所瑞士籍段克達（Christoph D Dahl）副教授， 分享特色研究：計算行為學、神經傳導物質系統、電生理紀錄

我在瑞士蘇黎世大學獲得碩士學位，有心理學和神經信息學背景，並在德國的圖賓根大學和馬克斯普朗克生物控制研究所的認知過程生理學系（尼可斯羅格特蒂斯教授）進行猴子神經生理學的博士研究。我在日本京都大學的靈長類研究所、臺灣大學心理學系及瑞士納沙泰爾大學比較認知學系接受博士後訓練。2019年，我成為臺北醫學大學心智意識與腦科學研究所副教授，並與雙和醫院合作。

所有的動物，包括人類，皆面臨在一個不斷變化的環境中求生存的挑戰。行為，也就是大腦的最終產物，成為應對環境中之不可預測與不規律現象最成功的策略。同時，行為有異於大自然篩選機制，會產生立即的效果。這也是神經科學對一般生物，尤其是大腦，如何產生行動最有興趣的著力點（卡喬波和德賽迪，2011）。在長遠的歷史中，行為缺陷已被觀察數千年之久，但在近期，我們才發展出建構在行為與大腦之下的結構功能關係的研究方法（甘迺迪和阿道夫斯，2012）。【右圖：段克達副教授開發以訂製的跑步機紀錄活體和行為自由的生物體的細胞外活動，使動物得以用自然的方式整合】



於是我相信，沒有比透過行為模式功能來研究大腦更貼切的方法了。因此，最根本的問題是，大腦與中樞神經系統如何將環境中的生物相關訊息，轉化為自然行為。這挑戰很明確：行為與大腦所具備的高度複雜性。行為在社交表現中更顯複雜，不只被隔離者的行為，其與團體之間互動的行為也會被研究。這些分析不只包括研究主體及其反應，也包括研究受體及其行為反應。整體而言，似乎不可能拿複雜的行為去比對更複雜的大腦神經相關系統（阿道夫斯，2010）。那麼，我們要如何處理這複雜的事物，以及從何開始我們的查驗？

行為學的傳統方法，就是行為科學，就是首次形成一個物種的行為戲目，所謂的人種圖，依不同的取樣圖譜編寫行為要素（阿爾特曼，1974）。然而如此會限制我們預測特定物種的系列性一般行為模式所能取得的研究結果，也會忽略了概略化後之行為模式的複雜性，而將他們歸類至某個類別。一個比較新的觀念是，動物和人類展現出的複雜行為是一系列連續性比較小型，一部分是刻板的活動。這種新的方法指引我們聚焦於從行為中抽取出最微小可測量且可辨識的元素，這些元素組成更大的行為模式，最終成為動物的「身體語言」（維爾奇科，2015）。為此，我採用電腦視覺技術及機器學習對空間與時間的高度解析，使用自動化程序來追蹤多種動物的身體活動及定位。

這種相對新穎的領域被稱為計算行為學，在傳統與現代主義之間架起了橋樑，並將傳統上是生物學子學科的行為學，引入了跨學科研究的領域（戴爾，費南度和祖伯布勒，2020；戴爾等人，2018）：這就為生物學家、神經科學家、計算機科學家、物理學家和醫師提供了一個協作框架。

這種方法產生的數據本身很有趣：例如，我們可以透過提出與生態相關的問題來了解動物物種。重要的是，透過這種方法，我們還可以推論到其他領域及相關的問題，例如上述行為與大腦之間的關聯。例如，我們知道，行為症狀經常重疊，並且主觀上會歸因於神經精神疾病，或者說是中樞神經系統的功能失效。神經傳導物質是可放大和調節大腦神經元之間電訊號的物質。當神經傳導物質的平衡功能發生變化時，中樞神經系統功能就會失效，最終導致行為改變。

因此，我研究的第二個方向，很自然地將目標鎖定在神經傳導物質系統，並確定由治療引起行為元素的調節。透過結合神經化學刺激及行為分析，我們可以研究針對特定受體類型，各種不同促效劑或拮抗劑如何選擇性地調節某些行為元素，而使其他不受影響。這促使了疾病模型的重新定義，例如社交焦慮、自閉症或社交溝通障礙，其特徵位在行為改變的最底層。第三項研究，在行為生物體中，我採用電生理紀錄（戴爾、羅格特帝蒂斯和凱瑟，2009、2010），以較直接的方式處理行為與大腦的關係。在這裡，我嘗試將在大腦不同解剖區域引發的神經活動與表現出的行為建立關聯性。透過對動物環境的虛擬操縱，我們可以檢驗複雜行為期間，解剖區域的功能劃分。

【下圖：段克達副教授（右 2）與洪君琳教授（左 1）及其研究助理在本校斑馬魚核心實驗室合影】



I have a background in psychology and neuroinformatics (equ. MSc at the University of Zurich, Switzerland) and I did my doctoral studies in monkey neurophysiology at the University of Tübingen and the Max Planck Institute for Biological Cybernetics, Department Physiology of Cognitive Processes (Prof Nikos K Logothetis), Germany. I received postdoctoral training at the Primate Research

Institute of Kyoto University, Japan, at the Psychology Department of National Taiwan University, Taiwan, and at the Department of Comparative Cognition of University of Neuchatel, Switzerland. In 2019, I came to join the faculty of Graduate Institute of Mind, Brain, and Consciousness (GIMBC) at Taipei Medical University as an associate professor. I also maintain an affiliation at Shuang Ho Hospital, New Taipei.

Animals, including humans, face the challenge of surviving in an ever-changing environment. Behaviour, the ultimate product of the brain, turned out to be the most successful strategy to deal with the environmental unpredictabilities and irregularities. At the same time, behaviour has an immediate effect, unlike natural selection. It is in the interest of neurosciences to address the question of how an organism in general and a brain in particular implement behaviour (Cacioppo & Decety, 2011). Historically, behavioural deficits have been observed for thousands of years, but only in recent times we have acquired the means to address the structure-function relationship underlying behaviour and the brain (Kennedy & Adolphs, 2012).

Consequently, I believe, there is no more essential way to study the brain via its functions in the context of behaviour. Thus, the essential question to ask is how the brain and the central nervous system translate biologically relevant information from the environment into natural behaviour. The challenges are apparent: Behaviour and the brain are highly complex. Behaviour becomes even more complex in its social manifestation, when not only the behaviour of an isolated individual is studied, but the behaviour of the individual and its group. Such analysis would encompass not only the subjected individual and its responses, but the recipient individuals and their behavioural responses. All together, it seems impossible to map complex behaviour acquired onto an even more complex neural correlate like the brain (Adolphs, 2010). Then, how can we account for the complexity and where do we start our examinations?

The classic approach in ethology, the sciences of behaviour, is that one first determines a species' behavioural repertoire, the so-called ethogram, to code behavioural elements according to different sampling regimes (Altmann, 1974). This, however, would limit our findings to a set of general behavioural patterns which we predicted to find in a given species. It would also disregard the complexity of behaviour by generalising across behavioural patterns and assigning them to classes. A more modern idea is that complex behavioural actions exhibited by animals and humans alike are series of concatenated smaller, partly stereotyped movements. These movements can be subjected to processes of quantification and, hence,

become measurable. This new approach dictates that we aim at extracting the smallest measurable and identifiable elements of behaviour, which constitute larger behavioural patterns and ultimately the animal's "body language" (Wiltschko et al., 2015) . To this end, I use automated procedures that track positions and body movements of multiple animals at high temporal and spatial resolutions using computer vision technology and machine learning.

This relative novel domain referred to as computational ethology bridges traditions and modernism and leads ethology, traditionally a subdiscipline of biology, into an interdisciplinary research domain (Dahl, Ferrando & Zuberbühler, 2020; Dahl et al., 2018) : This offers a collaborative framework for biologists, neuroscientists, computer scientists, physicists and physicians.

This approach produces data which is interesting per se: e.g., we can learn about an animal species by asking ecologically relevant questions. Importantly, with this approach we can also extrapolate to other domains and related questions, such as the above mentioned linkage between behaviour and the brain: We know, for example, that behavioural symptoms are often overlapping and subjectively assigned to neuropsychiatric disorders or, in other words, to functional failures in the central nervous system. Neurotransmitters are substances that amplify and modulate electrical signals between neurons in the brain. When the functional balance of neurotransmitter is altered, failures of central nervous system function occur, ultimately leading to changes in behaviour.

Thus, in a second direction of my research I neurochemically target neurotransmitter systems and determine modulations of behavioural elements caused by the treatment. With this combination of neurochemical stimulation and behavioural analysis, we can then investigate how various agonists or antagonists, targeting particular receptor types, selectively modulate certain behavioural elements, while leaving others unaffected. This leads to a re-definition of disease models, such as social anxiety, autism spectrum or social communication disorders, characterised at the most elementary level of behavioural modifications. In a third line of research, I follow a more direct way of addressing the behaviour–brain relationship by employing electrophysiological recordings (Dahl, Logothetis & Kayser, 2009 - 2010) in the behaving organism. Here, I try to correlate neural activity, elicited in distinct anatomical regions of the brain, with the exhibited behaviour. By virtual manipulations of the animal's environment we can then examine functional divisions of anatomical regions during complex behaviours.

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