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EFFECTS OF COGNITIVE LOADING ON PILOTS AND AIR TRAFFIC CONTROLLER PERFORMANCE: IMPLICATIONS FOR NEURAL DYNAMICS AND COGNITIVE FLOW

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The digitized environment in aviation operations has seen marked growth and expansion as new technologies arrive and are implemented. The flight deck and air traffic control functions are two areas where growth is particularly robust. Previous work has identified the effects of compounded cognitive loading and SHELL interfaces in these work environments, and the potential consequences when relief or collaborative resource management is not employed effectively. This paper examines the relationship of cognitive loading in the context of cognitive flow to identify potential areas where neural metrics might aid in a better understanding of the dynamics to determine thresholds of overload. Application of the Triple-Network Model of neural regulation dynamics and Polyvagal Theory are explored for potential relationships to compromised situation awareness and working memory constraints. Conclusions indicate that when cognitive flow is disrupted, cognitive processing loads on working memory expand exponentially and rapidly reach a plateau that inhibits safe performance. Implications suggest a more focused effort in systems and training to address neural metrics and cognitive processing rates.

OVERVIEW

This paper assesses human factors issues contributing to cognitive load and potentially dysregulated cognitive processes arising from a disruption in cognitive flow. The growing proliferation of cognitive processing demands that affect operators engaged in aviation roles, including multi-crew flight deck and air traffic control (ATC) operations, often approach thresholds of overload. During nominal periods, operators typically function in a flow of cognitive processing that employs neural resources efficiently. At times, though, cognitive load demands can increase or expand to the extent that cognitive flow is disrupted. Consequently, constraints in working memory and other neural resources can result in a compromised cognitive system with potentially dangerous consequences. Variations affecting cognitive loading, and intrusion of novel situations or unanticipated events, can result in operator hesitation, confusion, or dysfunction (Gevins et al., 1998). Circumstances are then ripe for human error that can contribute to lapses, incidents, or accidents. Contributing elements include the brain and triple-network exchanges, coexisting with polyvagal system actions. Combined effects and neural metrics for elapsed time of responding are newer areas for more intensive investigation. By examining these processes within the aviation context, an increased understanding of the interaction and influences of cognitive loading, disrupted cognitive flow, and neural dynamics can be applied to operational contexts, training, and safety management programs in the industry.

COGNITIVE FLOW

Cognitive flow is conceptualized as a process that produces intense concentration that leads to integration and focus upon a particular goal. Flow describes a state of experience at or near peak capacity which can produce high

levels of performance, sometimes regarded as being “in the zone,” exemplified in the process of attention and dynamic engagement experienced by pilots on a digitized flight deck and ATC operators in tower and approach control settings. Cognitive flow can be a desirable and valued state for pilots and controllers. Achieving and sustaining cognitive flow supports optimal performance and extends neural processing capacity and resources. When disrupted, however, potentially dangerous consequences can ensue. For instance, where feedback is not clear or relatable, flow is disrupted. Beyond interrupting the positive state, disruption has the potential to influence cognitive awareness and task execution (Weber et al., 2009). A principal component in modulating and preserving cognitive flow is cognitive loading as experienced by the operator.

COGNITIVE LOADING

Task load (number of tasks performed) and cognitive workload are similar, yet differ in application. The concept of cognitive loading was introduced in 1988 and developed further by Chandler and Sweller (1991). As the term evolved to encompass attention and memory applications, an emphasis on information processing became prominent. Founded in instructional theory, these principles are observed when familiar situations or action sequences are presented to a pilot or controller and they process the data without delay and with minimal neural resources. Conversely, when a novel or unanticipated situation presents, working memory and long-term memory retrieval are slowed to facilitate comprehension. Neural resources are allocated first to task-relevant information and, depending on remaining capacity, to less relevant information (Giesbrecht et al., 2014). When tasks are performed in stages, neural resources are typically adequate to support mental processes, however, an operator’s cognitive capacity may be fully enveloped or exceeded when a single, large task becomes primary. For example, where deconfliction

decisions become the primary task, a less experienced pilot or controller may experience disrupted cognitive flow. In describing cognitive load, Taylor (2013) points out that two channels operate – one for visual information and another for auditory information. In recent advances in air traffic management, controllers have moved to increased verbal exchanges (e.g., Tower Team) and more complex visual information processing. Here, the dual channel issue becomes paramount with obvious overload potential in both channels. Pilots and air traffic controllers frequently execute dual-task coordination along with cognitive loading. The related behavioral strategies were evaluated by Johannsen et al. (2013) when studying motor movement and revealed that dual-task interference effects resulted in degraded timing and accuracy. While competing for neural resources, operator movements were affected negatively during attempts to correct for mistimed actions caused by information lag. For aviation operators, increased cognitive load and actions from lags in verbal or data display exchanges are relevant concerns.

It is becoming increasingly imperative in aviation contexts to synthesize and combine verified results and implications for cognitive loading and influences on cognitive flow. As Eurocontrol and the Federal Aviation Administration advance the implementation of several initiatives and system operations, the issue of cognitive capacity grows in relevance. Although efforts have approached the potential overload and contributing human factors problems from various directions, a more comprehensive and interactive perspective has been absent. It may be prudent, then, to highlight the relatedness and interconnectivity of what might appear as disparate functions into a systemic overview that can stimulate inquiries and approach solutions for some of the threats and challenges forthcoming, including approaches for more effective training.

COGNITIVE OVERLOAD AND MEMORY DEFICIT

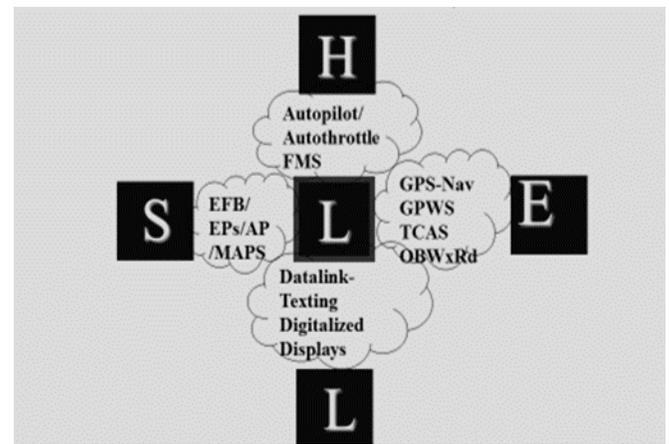
Capacity for information processing is finite according to cognitive load theory. Consequently, the presentation rate and complexity of information affects working memory capacity at a variable rate. Two factors involved are memory load and the nature of content. For example, a distractor adds to the working memory load and, by nature, interferes with flow processing. Causse et al. (2016) found that cognitive tunneling was induced when pilots encountered high working memory loads and, consequently, isolated themselves from auditory stimuli in order to intensify visual processing. The researchers concluded that high working memory load increased task difficulty and decreased accuracy, including missed data.

Consolidating efforts to better understand cognitive functions and effects for commercial pilots and air traffic controllers, it is useful to examine the progression of cognitive flow as a desirable state into demands on cognitive loading and the potential for overload which, consequently, can evoke or precipitate memory deficits that compromise work performance. Based on the original architecture developed by Hawkins (1987), an expanded concept shown in Figure 1

introduced SHELL Model 2017 (Miller and Holley, 2018) that illustrated an overlapping cognitive cloud connecting and creating an overlay among all five SHELL components (software (S), hardware (H), environment (E), liveware (L), and central liveware (L)). Analyzing and interpreting effects of the optical, aural, and digitized components on the flight deck are shared across all functions represented by the cognitive clouds and interact simultaneously in varying intensities. The conclusion indicated that cognitive resources would be depleted more rapidly due to compounding effects with consequent negative influences on other cognitive functions and related behaviors.

Figure 1

SHELL Model 2017 with Cognitive Cloud Overlay for Digitized Flight Deck



Note: Adapted from “SHELL Revisited: Cognitive Loading and Effects of Digitized Flight Deck Automation,” by M. Miller and S. Holley, 2018, in C. Baldwin (Ed.) *Advances in Neuroergonomics and Cognitive Engineering*, pp. 95-107 (https://doi.org/10.1007/978-3-319-60642-1_9). Copyright 2018 by Springer International. Reprinted with permission.

Advanced digitized flight decks and ATC locations require visual processing of multiple sources that must be attended to or monitored with operators remaining alert to changes or anomalies. When combined, these perceptual and cognitive processing demands can approach maximum processing capacity. As task load increases there is potential for increased cognitive loading and disrupted cognitive flow and loss of efficient neural resourcing. As a result, cognitive maps, continuity of processing, and situational awareness may be compromised (Miller et al., 2020).

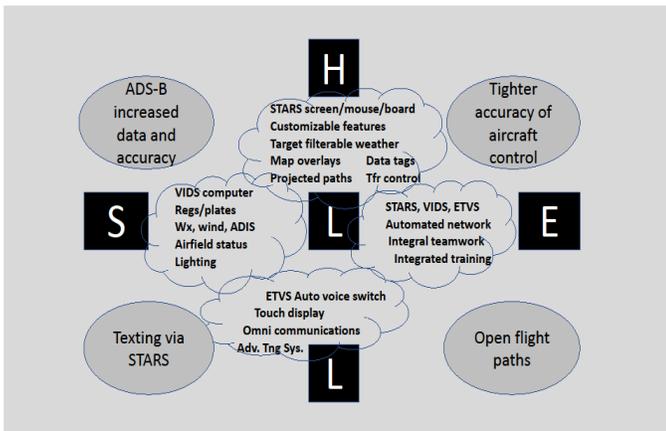
A review of pilot decision making (Endsley, 2015) confirmed that in low tempo operations extra cognitive resources are available, however, when uncommon or emergency events occur pilot time for reflection is substantially reduced. Identified in the study were several performance decrements in situation awareness that occur with cognitive overload: (1) delay in comprehending an event was

occurring, (2) fragmented scan of information sources, narrowed assessment, inability to commit to a course of action, and (3) failure to re-check new courses of action to assure implementation as intended. When aviation operators in advanced technology workplaces become loaded near maximum working memory capacity, during especially challenging flight maneuvers or unanticipated procedures, deferring critical actions could be catastrophic. When exceeded, neural capacities are stressed and, along with incipient cognitive error, mode confusion can result. This was demonstrated in the Australian study of pilots (Sherman et al., 1997) which also confirmed that workarounds highjacked cognitive resources.

A second version of a cognitive cloud is depicted for Standard Terminal Automation Replacement System (STARS) and Terminal Radar Approach Control (TRACON) operators as shown in Figure 2. While the functions are different from the flight deck, the principle of cognitive loading represents similar challenges and potential for ATC overload.

Figure 2

SHELL Model 2017 with Cognitive Cloud Overlay for STARS/TRACON Air Traffic Controllers



Note: Adapted from “A Change in the Dark Room: The Effects of Human Factors and Cognitive Loading Issues for NextGen TRACON Air Traffic Controllers, by M. Miller, S. Holley, B. Mrusek, and L. Weiland, 2020, in H. Ayaz (Ed.) *Advances in Neuroergonomics and Cognitive Engineering*, pp. 155-166 (https://doi.org/10.1007/978-3-030-20473-0_16). Copyright 2020 by Springer International. Reprinted with permission.

Efforts to study mental workload, and the origins of overload, have focused on situation awareness, information processing, and decision making where they occur simultaneously. When cognitive loading is too high or too low comparatively, the result can increase risk of human error. This is more likely when abrupt bursts of a large amount of information must be processed quickly (Gevins et al., 1998) and is more probable during unanticipated events and rapidly

changing information flow in the digitized cockpit or ATC environment. The outcome manifests as a potential cognitive overload challenge. Similar to the dual channel concerns, it has been established that the nature of a non-linear task environment stimulates operator concerns about future states of the system which, in turn, enlarges cognitive loading and the potential for overload.

NEURAL DYNAMICS OF COGNITIVE LOADING

Dietrich (2004) proposed a neurocognitive concept of flow by determining that inhibiting frontal lobe function (hypofrontality) is a prerequisite for implicit memory functions to activate fully. When manifested, cognitive flow could occur. The neurocognitive corollary is that the explicit system (top-down processing) reaches transient hypofrontality (rests) while the intrinsic system (bottom-up processing) predominates. This concept now is resident in the Triple-Network (TNM) model for domain functioning (Menon, 2010) that identifies specific constellations of brain structures with functional connectivity. The three components are (1) the Saliency Network (anchored in the cingulate and insula cortices) and active in attention or emotion processes and which actively modulates and mediates the other two networks, (2) The Central Executive Network (anchored in the dorsolateral prefrontal cortex and lateral posterior parietal cortex) and active during cognitively demanding tasks, and (3) the Default Mode Network (anchored in the posterior cingulate cortex, precuneus, and medial prefrontal cortex) which operates during reduced cognitive activity and mind wandering. When the Central Executive is active, the Default Mode activity is reduced, and vice versa. The implications are that as cognitive load increases the default mode deficits can result in weak connectivity and impaired thought processes. Similarly, when the default mode is overactive (rumination, e.g.) cognitive, task, and attentional functions may be impaired. For instance, if an unanticipated event or emergency occurs, the result could be cognitive tunneling due to elevated default mode activity focusing on negative possibilities.

Porges (2011) has advanced the Polyvagal Theory (PVT) which is interactive with the TNM structures and contributes an appreciation for the autonomic nervous system influences that bear on cognitive activity. When functioning nominally and operators are experiencing cognitive flow, the ventral vagal system is dominant, activated by the parasympathetic nervous system that promotes present-mindedness and a positive orientation to the environment. As concern, worry, frustration, or irritation occur, the sympathetic nervous system activates with accompanying rapid increases in physiology. Unless deactivated, this condition can elevate to the dorsal vagal system which reverts to parasympathetic nervous system functions and precipitates a sense of becoming overwhelmed or placing the body in an emergency state. Although the full effect likely would occur rarely in aviation contexts, less debilitating effects could readily occur with accompanying performance deficit. The combined results from the TNM and related responses by the PVT illustrate neural connectivity that

contributes an improved understanding to explain the loss of cognitive flow, burden of increasing cognitive load, and a potentially disrupted performance state. When neural processing capacities are exceeded, the prospect of degraded situation awareness and accompanying cognitive errors increase, which can further disrupt prospective memory (Touzani, et al., 2007). As indicated, multiple areas of the brain are active during cognitive flow and cognitive loading. Notably, actions originating in the cortical structures (TNM) differ from those originating in subcortical structures (PVT). Efforts to quantify neural metrics and interpreted activities among nervous system networks is advancing, and is necessary to determine loading and flow connectivity.

MEASURING COGNITIVE FUNCTION

Highlighting the human cognitive architecture, Paas and Sweller (2012) point out that working memory is more subject to maximum loading when acquiring novel information as compared with information previously processed. Absent an established schema, the duration and expenditure of neural resources to process the novel situation are extended. In particular, this occurs when skilled performance is needed and unanticipated circumstances arise. Typically, the metrics for task workload do not parallel those for cognitive load. Generalized concepts, as compared with domain-specific knowledge, influence cognitive load differently. For domain-specific information, the human brain has a processing capacity between 2 to 60 bits per second (bps) used for attention and decision-making, including perceptual and language processing. Comparatively, the auditory processing rate is about 10,000 bps. For sensory processing, the rate is as high as 10^6 bps (Fan, 2014). It is important to consider that conscious cognitive processing involves higher order information and is influenced by the limitations of working memory. The long-standing acceptance of the 7 ± 2 rule for chunking is not well suited to define neural processing rates. The conscious brain can process about 130 messages per second. There are about 86 billion neurons sending 5 to 50 messages per second and the brain has a capacity to process these at around 40 to 50 bits per second. In one of the early efforts to quantify the capacity of cognitive control, researchers manipulated the rate of information flow and determined for higher-level functions a relatively low processing rate of 3 to 4 bps for a given channel. When the rate exceeds capacity, error probability rates increase. Consequently, performance is likely to degrade. When information has been previously encoded, the conscious processing rate is far more efficient and requires less working memory capacity and reduced neuronal levels, such as during cognitive flow experiences. Various familiar mental algorithms can operate, then, with lower-level inputs (Wu et al., 2016). Exceeding the message capacity, as would occur during cognitive overload, means information is lost or misrouted. Since cognitive control acts as encoder and router of information flow, when cognitive processing involves uncertainty, the amount of information under cognitive control increases. Consequently, neural activation increases as

demands on cognitive control increase and will plateau when overloaded (Buschman et al., 2011).

Studying self control related to feedback processes, Woodward and Fairbrother (2020) determined that when under increased cognitive load operators will prioritize speed over accuracy. This is even more evident when dissimilar types of information are processed in tandem. Implications for pilots and controllers are that as cognitive loading accretes, the potential for missed or misinterpreted information is more likely. This potential was demonstrated in a program review (Miller et al., 2020) with eleven (11) air traffic controllers in a TRACON facility and twenty (20) controllers at a Tower Team control center. Their collective responses indicated notable occurrences of distraction, confusion, delay, and other influences that affected their situational and cognitive acuity. A majority (80.6%) reported needing extra time to re-establish scans, while 58% reported being distracted often or sometimes. Evidence for increased cognitive loading was implicit in responses indicating their attention was disrupted (70.9%) by atypical events or actions with accompanying confusion (61.2%) following the experience. When considering these results, the expanded and sustained activity represented in the cognitive cloud (depicted in Figure 2) would, consequently, result in more rapid consumption of available brain glucose essential for effective functioning. Similarly, protein that fuels working and prospective memory would be depleted rapidly (Touzani et al., 2007). As a result, it would be important to recognize that the changed situation compromises the cognitive system status. While some tasks can be deferred or relegated, this too requires cognitive resources and invariably involves activating schema or associated knowledge.

DISCUSSION

Adverse effects on flow need to be better understood to assess approaches for anticipating cognitive overload and disruption of flow. In the current digitized environment for aircraft operation and air traffic management, the number and complexity of tasks that operators perform is steadily increasing. It would follow, then, that cognitive loading from these tasks would likewise increase. Similarly, when a task is performed that has not been practiced regularly, performance may be affected adversely due to overloading a person's limited working memory capacity. This limitation also applies when the rate of information to be processed accelerates and exceeds cognitive loading potential (Wogalter & Usher, 1999). Consequently, pilots and controllers are likely to process information and tasks with relative efficiency depending on the nature of the demand. When several domain-specific tasks occur coincidentally, working memory capacity may be exceeded more readily as a result of the activity intensity. As a result, where an operator may be in an optimal performance zone and cognitive flow is disrupted, multi-tasking becomes more effortful and attention is split. Consequently, existing mental schemas are revised and cognitive architecture is restructured which reduces performance efficiency.

In the aviation sector, rapid and continuing advances in technology require complex cognitive effort and attention. Correspondingly, the field of neuroscience has progressively entered this domain with applications in neural and related systems that influence cognitive processing. With a principal responsibility to support and execute safe operations, aviation operators and the cognitive processes they employ must be thoroughly understood. While considerable research has been conducted in a myriad of contexts, bringing together the relevant subjects and results that influence cognitive flow and loading, along with accompanying memory deficits, has not been assessed or investigated to a suitable degree in aviation contexts. A more thorough understanding of the interactions and relationships among the components for the polyvagal system and the triple-network constellations would be useful to determine potential interventions for adaptive automation or programming for alternate levels in automated systems. Recent advances in measuring neural metrics for cognitive processing hold promise in determining thresholds for cognitive overload. The analysis and points raised in this paper focus precisely on these related structures, functions, and metrics and seeks to generate further discussion and disciplined inquiry.

REFERENCES

- Buschman, T. J., Siegel, M., Roy, J., & Miller, E. K. (2011). Neural substrates of cognitive capacity limitations. *PNAS* 108, 11252–11255. [https://doi:10.1073/pnas.1104666108](https://doi.org/10.1073/pnas.1104666108)
- Causse, M., Peysakhovich, V., & Fabre, E. (2016). High working memory load impairs language processing during a simulated piloting task: An ERP and pupillometry study. *Frontiers in Human Neuroscience*, 10, 1-14. [https://doi: 10.3389/fnhum.2016.00240](https://doi.org/10.3389/fnhum.2016.00240)
- Chandler, P., & Sweller, J. (1991) Cognitive load theory and the format of instruction. *Cognitive Instruction*, 8(4), 293-332.
- Dietrich, A. (2004). Neurocognitive mechanisms underlying the experience of flow. *Conscious Cognition*, 13, 746-761. [https://doi:10.1016/j.concog.2004.07.002](https://doi.org/10.1016/j.concog.2004.07.002)
- Endsley, M. (2015). Situation awareness misconceptions and misunderstandings. *Journal of Cognitive Engineering and Decision Making*, 9(1), 4-32. <https://doi.org/10.1177/1555343415572631>
- Fan, J. (2014). An information theory account of cognitive control. *Frontiers in Human Neuroscience*, 8, 680. <https://doi.org/10.3389/fnhum.2014.00680>
- Gevins, A., Smith, M., Leong, H., McEvoy, L., Whifield, S., Du, R., & Rush, G. (1998). Monitoring working memory load during computer-based tasks with eeg pattern recognition methods. *Human Factors*, 40(1), 79-91. [https://doi: 10.1518/001872098779480578](https://doi.org/10.1518/001872098779480578)
- Giesbrecht, B., Sy, J., Bundesen, C., & Kyllingsbaek, S. (2014). A new perspective on the perceptual selectivity of attention under load. *Annals of the New York Academy of Sciences*, 1316(1), 71–86. <https://doi.org/10.1177/154193129904300612>
- Hawkins, F. H. (1987). *Human factors in flight* (2nd ed.) Ashgate. <https://doi.org/10.1111/nys.12404>
- Johannsen, L., Li, K.Z., Chechlacz, M., Bibi, A., Kourtzi, Z., & Wing, A. (2013). Functional neuroimaging of the interference between working memory and the control of periodic ankle movement timing. *Neuropsychology*, 51(11), 2142-2153. [https://doi: 10.1016/j.neuropsychologia.2013.07.009](https://doi.org/10.1016/j.neuropsychologia.2013.07.009)
- Menon, V. (2010). Large-scale brain networks and psychopathology: A unifying triple network model. *Trends in Cognitive Sciences*, 15(10), 483-506. [https://doi:10.1016/j.tics.2011.08.003](https://doi.org/10.1016/j.tics.2011.08.003)
- Miller, M., Holley, S., Mrusek, B., & Weiland, L. (2020). Assessing cognitive processing and human factors challenges in NextGen air traffic control tower team operations. In: I. Nunes (Ed.), *Advances in Human Factors and Systems Interaction*, (pp. 289-295). Springer Nature. https://doi.org/10.1007/978-3-030-51369-6_39
- Miller, M., & Holley, S. (2018). SHELL revisited: Cognitive loading and effects of digitized flight deck automation. In: C. Baldwin (Ed.), *Advances in Neuroergonomics and Cognitive Engineering*, (pp. 95-107). Springer International. [https://doi:10.1007/978-3-319-60642-2_9](https://doi.org/10.1007/978-3-319-60642-2_9)
- Paas, F., & Sweller, J. (2012) An evolutionary upgrade of cognitive load theory: Using the human motor system and collaboration to support the learning of complex cognitive tasks. *Educational Psychology Review*, 24(1), 27-45. <https://doi.org/10.1007/s10648-011-9179-2>
- Porges, S. (2011). *The polyvagal theory: Neurophysiological foundations of emotions, attachment, communication, and self-regulation*. Norton.
- Sherman, P.J., Helmreich, R.L., & Merritt, A.C. (1997). National culture and flight deck automation: Results of a multinational survey. *International Journal of Aviation Psychology*, 7(4), 311-329. [https://doi:10.1207/s15327108ijap0704_4](https://doi.org/10.1207/s15327108ijap0704_4)
- Taylor, C. (2013). Cognitive load theory sometimes less is more. *i-manager's Journal on School Educational Technology*, 9(1), 61-68. [https://doi:10.26634/jsch.9.1.2402](https://doi.org/10.26634/jsch.9.1.2402)
- Touzani, K., Puthanveetil, S.V., & Kandel, E.R. (2007). Consolidation of learning strategies during spatial working memory task requires protein synthesis in the prefrontal cortex. *PNAS*, 104(13), 5632-5637. <https://doi.org/10.1073/pnas.0611554104>
- Weber, R., Tamborini, R., Westcott-Baker, A., & Kantor, B. (2009). Theorizing flow and media enjoyment as cognitive synchronization of attentional and reward networks. *Communication Theory*, 19(4), 397-422. [https://doi:10.1111/j.1468-2885.2009.01352.x](https://doi.org/10.1111/j.1468-2885.2009.01352.x)
- Wogalter, M. S., & Usher, M. O. (1999). Effects of concurrent cognitive task loading on warning compliance behavior. *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*, 43(6), 525–529. <https://doi.org/10.1177/154193129904300612>

Published in the Proceedings of the 2022 Human Factors and Ergonomics Society 66th International Annual Meeting, 2256-2260.
[https://doi: 10.1177/1071181322661544](https://doi.org/10.1177/1071181322661544)

Woodard, K. F., & Fairbrother, J. T. (2020). Cognitive loading during and after continuous task execution alters the effects of self-controlled knowledge of results. *Frontiers in Psychology, 11*(1046), 1-8.
[https://doi.10.3389/fpsyg.2020.01046](https://doi.org/10.3389/fpsyg.2020.01046)

Wu, T., Dufford, A., Mackie, M., Egan, L., & Fan, J. (2016). The capacity of cognitive control estimated from a perceptual decision making task. *Scientific Reports, 6*, 34025. [https://doi:10.1038/srep34025](https://doi.org/10.1038/srep34025)