THE DREW REVIEW

Drew University
May 2022 | Volume 15

Artist Statement

In my recent work, I have been exploring a variety of mediums. Although I consider myself a primarily digital artist, during my time at Drew, I have been experimenting with traditional media, including watercolor, oil paint, and pencil. The pieces featured on the cover of this review are from a series of watercolor paintings I made that followed the decay of a bouquet of flowers. My work focuses on my emotions, both positive and negative. I express these through portraits, backgrounds, and semi-realistic drawings of objects.

Marion Riley
CLA 2023

The Drew Review

Drew University
The College of Liberal Arts
May 2022
Volume 15

Foreword

The Drew Review, Drew University's annual research journal for the undergraduates of the College of Liberal Arts (CLA), publishes undergraduate student research from the previous calendar year.

This year, we received a total of twenty-seven submissions and have published seven. Those interested in submitting their work in the future will require a faculty nomination, which must include the author's name, paper title, and a brief rationale for nomination.

As we are a double-blind, peer-reviewed journal, all submissions must be submitted without any identifiable information, such as the student's name or the name of the professor for whom the paper was originally written. All images will be published in black and white, and it is the author's responsibility to ensure that the images are permissible for reproduction under copyright law. All students who submit should expect requests for revisions prior to the board's final decisions for publication.

As always, we are beyond grateful for our faculty advisors, Dr. G. Scott Morgan of the Psychology Department and Dr. Jens Lloyd of the English Department. Their help and support is what ensures The Drew Review's success each year.

Editorial Board

Table of Contents

Fostering Self-Compassion Within School Communities

Kiersten Greiner

Abstract

During adolescence, drastic changes in physicality, social schemas and psychological health present emerging young adults with an array of challenges. Without effective coping strategies, they are more vulnerable to the development of various mental health disorders. Self-compassion has been shown to predict psychological health and overall well-being in the presence of adversity. Given this, the current study tested the effectiveness of an intervention at improving adolescents' self-compassion. Thirteen participants aged 13-19 attended an after-school self-compassion workshop that met for four sessions. The Self-Compassion for Youth Scale (SCS-Youth) was used to measure the students' pre-and post-intervention self-compassion scores. There was a significant main effect of time on participants' total self-compassion scores, indicating that the participants' scores increased significantly from before attending the workshop to after. This finding could have real potential value; because self-compassion is associated with a multitude of benefits, its incorporation could be one method to help students successfully navigate the challenges of adolescence and beyond.

Adolescence represents a critical period of significant growth and extensive change. This transitional phase between childhood and adulthood marks a period of rapid psychological, physical, and behavioral changes that expose adolescents to a multitude of challenges (Neff & McGehee, 2010). The commonly shared desire to "fit in" by being popular and attractive often leads to adolescents' feelings of inadequacy and makes them especially susceptible to developing negative self-image (Harter, 1993). Many of the emotional difficulties faced by adolescents arise from concerns with self-evaluation. Without knowledge of effective coping mechanisms to properly manage the difficulties of this period, adolescents are more vulnerable to the development of various psychological disorders (Bluth et al., 2018).

While being forced to navigate complex social situations, adolescents are also frequently faced with intense academic pressure. The structure of the American education system places an expectation on students to do well in middle and high school so they can attend a good college and ultimately land a successful career. While well-intended, this pressure is often counterproductive; it can provoke mental health struggles that ultimately hinder students' ability to thrive in school (Horowitz & Graf, 2019). Learning to practice self-compassion may help adolescents effectively manage the variety of stressors with which they are faced.

Self-compassion is the ability to extend kindness and understanding toward yourself during instances of

perceived failure and inadequacy, as well as to take care of yourself in times of suffering (Neff, 2021).
Self-compassion consists of three elements: self-kindness vs. self-judgment, common humanity vs. isolation, and mindfulness vs. over-identification. Leading self-compassion researcher Kristen Neff defines self-kindness vs. self-judgment as the ability to be warm and understanding toward oneself during moments of suffering, failure, or feelings of inadequacy, instead of diverting to self-criticism. Common humanity vs. isolation is the ability to recognize that suffering, failure, and feelings of inadequacy are part of the shared human experience; no one is alone in their struggles. The last component, mindfulness vs. over-identification, is the willingness to observe one's negative thoughts and emotions with openness, clarity, and balance, neither suppressing nor exaggerating them to either extreme (Dahm & Neff, 2015). Neff explains that having compassion for yourself is no different than having compassion for others. Just as compassion involves noticing the suffering of others and the desire to help relieve their pain, self-compassion entails extending the same support to yourself during your own struggles.

A significant amount of research has demonstrated the association between self-compassion and overall wellbeing (Barry et al., 2015; Bluth & Blanton, 2014; Neff & McGehee, 2010). Self-compassion opposes the approach of other responses to failure which characteristically promote self-degradation; it provides a non-judgmental environment for one to safely confront their weaknesses. The unique role of self-compassion in accepting personal shortcomings has been shown to be more effective at inspiring self-motivation. Because the embodiment of self-compassion welcomes mistakes, the individual is more likely to use failure as a learning opportunity for future growth (Breines & Chen, 2012).

Self-compassion also plays a key role in determining how concerned one is about others' perceptions of them. Those with higher levels of self-compassion were less fearful of being evaluated by others because it provides them an unwavering sense of belonging independent of external evaluations. Overall, their sense of self-worth is more stable because their competence is not contingent on social approval which is bound to fluctuate over time (Neff & Vonk, 2009). Self-compassion is associated with healthy, productive, and balanced conflict-resolution skills. Those with higher levels of self-compassion are more likely to value the needs and desires of both themselves and others, and respond to turmoil in a more peaceful manner. The ability to successfully solve interpersonal conflict enhances the quality and connection of their relationships (Neff & Yarnell, 2013).

Self-compassion can also predict one's psychological health. Self-compassion was positively correlated with happiness and life satisfaction and negatively correlated with anxiety, depression, and stress. That is, those with higher levels of self-compassion tend to be happier and more content with their lives, experience less stress, and are less susceptible to the development of anxiety and depression (MacBeth & Gumley, 2012).

The studied benefits of self-compassion are particularly applicable to the experiences of adolescents. The desire for them to be accepted and recognized as popular and attractive is especially strong during exposure to the middle school social environment. By establishing self-acceptance, they will be better prepared to overcome the feelings of inadequacy that are associated with concern for others' opinions. Additionally, the ability for one to rely on their own feelings of self-worth and acceptance has been linked to the growth of stronger adaptive communication skills (i.e. participation, asking questions, and seeking help). This is a skill that is highly beneficial for academic achievement and ultimately valuable in the workforce (Long & Neff, 2018).

Self-compassion is also likely to help adolescents cope with the inevitable mistakes that come along with the rapid psychological, physical, and behavioral changes they are undergoing. By accepting their failures with a loving heart, they will be better motivated to improve themselves in the future. They are also more likely to have healthy, genuine, and stable relationships with others (Neff & Yarnell, 2012). If adolescents learn how to show themselves compassion, they will be able to cope better with the challenges they are confronted with during this period of transition. With an improved ability to deal with the inevitable adversity of life, adolescents with high levels of self-compassion will be set up for success in young adulthood and beyond (Bluth et al., 2018).

With increased motivation, enhanced psychological resilience, improved self-worth, and greater life satisfaction being just some of the benefits associated with the embodiment of self-compassion (Neff & McGehee, 2010), it is clear that finding strategies for effectively cultivating one's capacity for self-compassion is extremely important. Self-compassion interventions have been one method shown to significantly improve self-compassion levels (Zeller et al., 2014). Participants were granted an improved understanding of self-compassion which allowed for increased awareness of their own self-deprecating habits. In recognizing these moments of negative self-talk, they were better equipped to offer themselves kindness instead (Neff & McGehee, 2010). Many interventions also introduced the concepts of mindfulness, common humanity, and self-kindness, all of which were successful at improving self-compassion levels (Binder et al., 2019; Bluth & Eisenlohr-Moul, 2017).

Although self-compassion interventions have been successful, they have primarily been studied among young adult/adult populations. Relevant research on adolescents has been focused on exploring the link between self-compassion and psychological well-being, as opposed to testing various interventions and their effectiveness in improving one's individual capacity for self-compassion (Blanton & Bluth, 2013; Galla, 2016; Klingle & Van Vliet, 2017). Current research suggests that the benefits of these interventions can potentially prove effective for adolescent participants as well (Neff & McGehee, 2010).

To the researchers' knowledge, only one study has been conducted to test the effectiveness of interventions on adolescent self-compassion growth in non-clinical populations. “Making Friends with Yourself” is a six-week intervention that included 34 participants between the ages of 14 and 17 (Gaylord et al., 2015). The information found in the study referenced above is valuable but limited and provided a good basis for the methodology used to conduct the current study. For example, the participants in the previous study expressed that they felt they could have learned more from their experience had they been more aware of the benefits and personal growth that was being cultivated through the program (Gaylord et al., 2015). It seems that the participants in this research are more likely to display an increase in measured self-compassion given they have a better understanding of the goal which they are working toward. The participants also preferred the activities that had more well-defined goals as opposed to ones that encouraged open-ended responses (Gaylord et al., 2015). The at-home components of the intervention were described by the participants as “inconvenient,” and “time-consuming” (Gaylord et al., 2015). The pre-existing pressure to complete academic responsibilities had an adverse effect on the participant’s motivation to engage in self-compassion work at home. With this information, the current study only consisted of components to be completed during the workshop.

Given the multitude of benefits associated with self-compassion, the success of interventions, and the lack of research within the adolescent population, the goal of the current study was to test the effectiveness of a self-compassion intervention for students in grades 6th through 12th. The program consisted of four sessions that took place after school. The participants completed a self-compassion questionnaire before and after the intervention in order to detect any changes in the students' self-compassion scores. It was hypothesized that students' self-compassion scores would increase after attending all four sessions of the program.

Method

Participants

One hundred and fifty students who attend a private K-12 school in central Pennsylvania were invited to participate in the study. The students in grades 6th through 12th were recruited by the school's guidance counselor during one of their weekly morning meetings. She informed them about the opportunity to attend an after-school workshop teaching them about the importance of self-compassion and methods to improve their own, as well as the data that was going to be collected. Twenty-four students between the ages of 13 and 18 signed up to participate in data collection and twenty students chose to also participate in the self-compassion workshop intervention. The control group consisted of the students who completed the online questionnaires but did not attend the workshop.

Procedure

Twenty-four students in grades 6th through 12th were asked to fill out an online questionnaire that measured their self-compassion. The survey began by asking the participant to enter a random four-digit number that was used to identify them while ensuring confidentiality. The participants were then asked to answer 17 questions that best describe how they act towards themselves in difficult times. The questionnaire was filled out by all participants two times; once before the start of the self-compassion workshop, and again after the completion of the program in order to detect a change in their self-compassion levels.

Intervention

The self-compassion workshop was a two-week course that met twice a week for a total of four sessions. The sessions were each an hour long and took place immediately after school at 3 p.m. Sessions were led by the school's guidance counselor who has over 10 years of experience working with adolescents within school environments.

During session one, the students learned about the definition of self-compassion and the potential benefits that come along with continued practice. They were introduced to a self-compassion building exercise titled "A Moment for Me," (Bluth et al., 2015) which encouraged them to think about a situation in their life that was difficult or causing them stress or discomfort. They were then asked to become aware of any sensations that arose in their body in response to the situation that came to mind. The exercise used the concepts of mindfulness and common humanity to inspire students to speak to themselves in a more gentle way.

During session two, the students began to become aware of their inner critical voice. They were given a checklist of 35 statements that reflect self-judgment and asked to mark the ones they have thought or said to themselves. The identification of these statements was meant to help them visualize the ways in which they were self-judgmental. After this, they were given a checklist of 36 statements that reflect self-kindness and asked to mark the ones they have thought or said to themselves. After completing both checklists, they were asked to reflect on the differences between the number of statements they marked for the judgmental versus kindness checklists. They were encouraged to engage in a group discussion regarding what they noticed from their participation in this exercise and to reflect on whether or not they tend to show themselves kindness.

During session three, students were asked to participate in two writing activities that were meant to help them foster a compassionate relationship with themselves. They were first asked to think about their younger self when they were around four or six years old and imagine that their feelings had just been hurt. They were instructed to write them a letter of comfort using self-compassion. They were reminded that both their younger self and their current self deserve to be treated with love and compassion.

The second activity introduced the definition of a mantra and encouraged them to create two of their own: one that can be used in the midst of a difficult situation, and the other for when they are feeling full of self-compassion and ready to take on the world. They were given a list of words for inspiration that helped them create their own statements of advice. After creating their mantras, they were asked to reflect on the statements they chose and how the words made them feel. They were encouraged to engage in conversation about how their mantras could be used to help them be more self-compassionate.

During session four, the students were given the opportunity to put their self-compassion knowledge into action. The session began by explaining how movement can be used as a form of self-compassion. The students were guided through a compassionate movement activity to help them step out of their minds and practice bringing attention to their physical bodies. They were guided to stand up, take a few deep breaths, and become aware of how their feet felt on the floor. They were then instructed to move various parts of their body and encouraged to recognize any tension releasing. Following the activity, they were asked to identify how it felt to give attention to their body, and what parts really needed it the most. They were encouraged to engage in conversation to reflect on their experience and to think of situations in their life where compassionate movement would be helpful. The program concluded with the “Here-and-Now Stone Activity” (Hurley & Rockman, 2015). Each student was handed a stone that was collected outside the school building. The students were reminded about the harsh conditions rocks sustain for millions of years. They were encouraged to think about themselves as strong and resilient just as the stone in their hand. They were asked to notice the stone's color, texture, size, imperfections, shape, etc., and to focus all their attention on the sensations of the stone. They were then encouraged to keep the stone nearby to touch whenever they feel overwhelmed with emotion to remind them of their strength and to help them stay grounded.

Measure

The Self-Compassion Scale for Youth (SCS-Youth) (Neff et al., 2021) consists of six subscales: Self-Kindness, Self-Judgment, Isolation, Common Humanity, Mindfulness, and Over-Identification and is composed of 17 items. Example items are: "I'm really hard on myself when I do something wrong," and "When I notice things about myself that I don't like, I get really frustrated." Participants indicated their responses to each item using a 5-point scale ranging from 1 = Almost never and 5 = Almost always. To compute a total self-compassion score, the negative items (Over-Identification, Self-Judgment, Isolation) were reverse-scored, and all 17 items were summed. The potential range in values was from 12 to 85, with higher scores indicating greater self-compassion.

Results

Twenty-eight students between the ages of 13–17 were enrolled in the study. Fourteen percent (n=4) of the participants were a part of the control group which only completed the measure but did not attend any of the sessions. One hundred percent (n=28) of the students attended the first workshop, but only 68% (n=19) attended all four workshop sessions. The data of the 32% (n=9) of participants who did not attend the entire program were excluded. Eighty-six percent (n=24) completed the pre-intervention survey, and 60% (n=17) completed the post-intervention survey. Due to the small sample size of both the control group (n=4) and intervention (n=13), the data from control group participants (n=4) was excluded due to the likelihood to undermine the ability to detect a change from the pre- to post-intervention scores.

The participants answered 17 questions each time they completed the Self-Compassion for Youth Questionnaire (SCS-Youth) both before and after attending the workshop. The questions were divided into six subscales: Self-Kindness, Self-Judgment, Isolation, Common Humanity, Mindfulness, and Over-Identification, all of which represent a different aspect of self-compassion. The 13 participants received a score in each of the six subscales which were calculated from the average score of the questions that make up each category. The highest possible score to obtain in each of the subscales was a 5, indicating the most possible self-compassion, and the lowest score, 1, indicating the least possible self-compassion. Because the Self-Judgment, Isolation, and Over-Identification subscales were reverse-scored, higher scores are indicative of greater self-compassion. The average of these six subscales was calculated to provide a single total self-compassion post-intervention score (M=3.3, SD=.751). Results displaying the mean and standard deviation of the six subscales scores pre-and post-intervention are summarized in Table 1.

Table 1

	Pre-Intervention		Post-Intervention	
	M	SD	M	SD
Total SCS-Youth Score	2.85	.898	3.31	.751
Self-Kindness	3.28	1.04	3.36	.958
*Self-Judgment	2.85	1.15	3.13	.788
Common Humanity	2.67	.981	3.41	.983
*Isolation	2.85	.728	3.39	.606
Mindfulness	2.97	.855	3.36	.845
*Over-Identification	2.54	.721	3.27	.880

*Reverse-scored

The experiment used a 2x6 repeated measures design and was conducted using a two-way repeated-measures ANOVA to investigate the effectiveness of the after-school workshop on participants' Self-Compassion for Youth (SCS-Youth) scores. The results of the two-way repeated-measures ANOVA revealed that there was no significant main effect of measure on participant's self-compassion scores F(5, 60) =1.044, p = .4, indicating that participants scored similarly on each of the six subscales when the pre- and post-scores were averaged. However, there was a significant main effect of time on participants' total self-compassion scores F(1, 12) =12.698, p=.004, indicating that the participants' scores increased statistically significantly from before attending the workshop to after.

There was a marginally significant interaction between time and measure F(5, 60) =2.339, p=.052, suggesting that the changes of the scores from pre- to post-intervention did not happen equally across all subscales. Figure 1 shows the interaction between time and measure on all six subscales. The significant increase of the scores on the Common Humanity, Isolation, Mindfulness, and Over-Identification subscales ($p < 0.05$) drove the overall effect of the intervention on the participants' self-compassion scores.

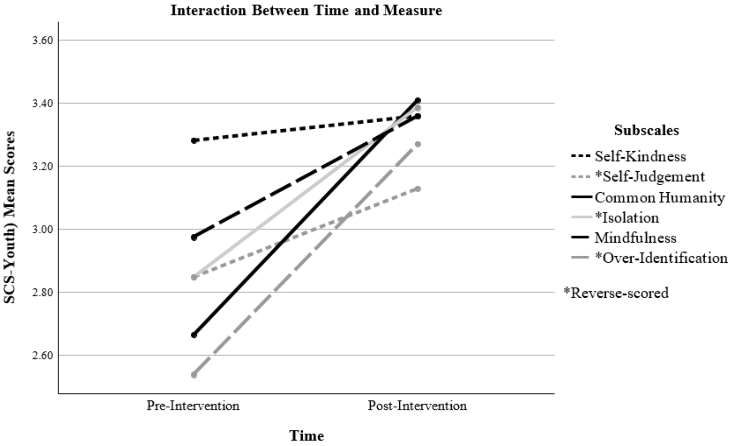

Figure 1

Discussion

The primary goal of the study was to evaluate the effectiveness of an after-school program at increasing the Self-Compassion Scale Youth (SCS-Youth) scores of the participants. The results provide evidence to support the hypothesis: students who attended the workshop showed an increase in their SCS-Youth scores. Furthermore, that effect was most prominent in the Common Humanity, Isolation, Mindfulness, and Over-Identification subscales of the SCS-Youth measure. The implications of these findings will be discussed below.

Common Humanity vs. Isolation

Both participants' Common Humanity and Isolation scores increased significantly from pre-intervention to post-intervention. Based upon the increase in Common Humanity scores, it suggests that the participants came away from the intervention with a greater understanding that suffering and inadequacy are part of the shared human experience. Because Isolation was reverse-scored, higher scores indicate that participants also felt less alone following the intervention. Anecdotal evidence from the guidance counselor running the intervention coincides/compliments with the increased scores on these subscales: “One of the most powerful parts of these workshops was the vulnerability of the participants. They shared experiences and thoughts with their peers in very real and raw ways. In turn, their peers responded with support, ideas, and encouragement. The connection among participants seemed tangible at times. This is not something I have seen many times over the course of my ten years of working with adolescents. Truly remarkable.” In the previously mentioned study, “Making Friends with Yourself,” several participants expressed that the common humanity component of the intervention was particularly helpful for them when learning to be more compassionate towards themselves (Gaylord et al., 2015). This, along with the data collected in the current study and observations from the guidance counselor, point to the potential value in teaching students about the collective human struggle.

Mindfulness vs. Over-Identification

Participants’ Mindfulness and Over-Identification scores increased statistically significantly from pre-intervention to post. The change in Mindfulness scores implies that, following the intervention, they were better able to observe their thoughts and feelings as they are, both positive and negative, without trying to deny them.

Given that the Over-Identification subscale was reverse-scored, higher scores indicate that participants held a more balanced approach to their emotions, neither suppressing nor exaggerating them to either extreme compared to before the self-compassion workshop.

Self-Kindness vs. Self-Judgment

There was no statistically significant difference in participants' pre- and post-intervention Self-Kindness and Self-Judgment scores. This indicates that participants did not report greater feelings of understanding towards themselves during moments of perceived failures and inadequacy after the intervention. It also suggests that there was no improvement in their own self-criticism. Given that the workshop was only two weeks long, a possible explanation for this finding could be that participants did not have enough time to improve deeply ingrained self-talk. Future studies should utilize an intervention longer in duration to detect any changes in Self-Kindness and Self-Judgment scores. Additionally, it would be helpful in subsequent studies to understand which specific activities within the intervention correlate to changes in each of the six subscales. Collecting qualitative data from participants about their experiences attending the workshop and perceptions of the effectiveness of the activities could potentially provide insight into understanding the subscale differences.

Even though there were only significant changes in four out of the six subscales, the participants' total self-compassion scores increased statistically significantly following the intervention. This suggests that participants reported an overall increase in their self-compassion levels compared to before attending the workshop. This finding could have real potential value; if middle and high school students are given the opportunity to attend a similar workshop, there is a possibility for the improvement of their self-compassion levels.

This program was successful at increasing self-compassion in the short term, but further research should be conducted to examine the long-term effects of the intervention and whether the initial increase in self-compassion levels remains stable over time. Previous research has suggested promising results; over a one-year interval, the sense of community derived from self-compassion interventions successfully protected against the negative effects of low self-esteem (Gaylord et al., 2015). However, subsequent studies should investigate this change over an even longer period of time and compare the differences between each of the six subscales in terms of their endurance and ability to withstand adversity.

This study has a number of limitations that are common in pilot studies. The sample size was small and all participants attended the same private school in central

Pennsylvania, limiting generalizability. Additionally, the researcher was only able to recruit four participants for the control group and a number of the participants failed to attend every session, resulting in their data being excluded from the final analyses. Consequently, data from only 46% (*n*=13) of the total participants was used. It would be important for future studies to utilize a larger, more diverse sample population to detect any differences in the effectiveness of the intervention across age and gender and to provide a control group. It would also be valuable to examine self-compassion interventions in adolescent populations from varying environments (i.e., public middle/high schools, religious-affiliated schools, boarding schools). Future studies should also strive to keep attendance stable throughout the entirety of the intervention.

Future research could help us understand if the skills learned in the workshops actually help students navigate the intense academic and social pressure of middle and high school. If this is the case, self-compassion workshops should be more widely available for students, as it is likely to provide them with invaluable skills to help navigate the challenges of adolescence and beyond.

References

Binder, P., Dundas, I., Hjelen, S., Hjeltnes, A., Woodfin, V., & Moltu, C. (2019). Becoming aware of inner self-critique and kinder toward self: a qualitative study of experiences of outcome after a brief self-compassion intervention for university level students. Frontiers in Psychology, 10.

Bluth, K., & Blanton, P. (2014). The influence of self-compassion on emotional well-being among early and older adolescent males and females. Journal of Positive Psychology.

Bluth, K., & Blanton, P. (2014). Mindfulness and self-compassion: exploring pathways to adolescent emotional well-being. Journal of Child Family Studies, 23, 1298–1309.

Bluth, K., & Eisenlohr-Moul, T. (2017). Response to a mindful self-compassion intervention in teens: A within-person association of mindfulness, self-compassion, and emotional well-being outcomes. Journal of Adolescence, 57, 108-118.

Bluth, K., Gaylord, S., Campol, R., Mullarkey, M., & Hobbs, L. (2015). Making friends with yourself: a mixed methods pilot study of a mindful self-compassion program for adolescents. Mindfulness, 6(6).

Bluth, K., Mullarkey, M., Lathren, C. (2018). Self-Compassion: A potential path to adolescent resilience and positive exploration. Journal of Child and Family Studies.

Breines, J., & Chen, S. (2012). Self-compassion increases self-improvement motivation. Personality and Social Psychology Bulletin, 38(9), 1133-1143.

Dahm, K., & Neff, K. (2015). Self-compassion: What is it, what it does, and how it relates

to mindfulness. Handbook of Mindfulness and Self-Regulation.

Galla, B. (2016). Within-person changes in mindfulness and self-compassion predict enhanced emotional well-being in healthy but stressed adolescents. Journal of Adolescence, 49, 204-217.

Harter, S. (1993). Causes and consequences of low self-esteem in children and adolescents. The Plenum Series in Social and Clinical Psychology.

Horowitz, J. M., & Graf, N. (2019). Most U.S. teens see anxiety and depression as a major problem among their peers. Pew Research Center.

Hurley, A., & Rockman, P. (2015). Self-compassion and mindfulness. Toronto, Ontario: The Centre for Mindfulness Studies.

Klingle, K., & Van Vliet, J. (2017). Self-compassion from the adolescent perspective: A Qualitative Study. Journal of Adolescent Research, 1(24).

Long, P., & Neff, K. (2018). Self-compassion is associated with reduced self-presentation concerns and increased student communication behavior. Journal of Learning and Individual Behavior, 67, 223-231.

Mcbeth, A., & Gumley., A. (2012). Exploring compassion: a meta-analysis of the association between self-compassion and psychopathology. Clinical Psychology Review.

Neff, K. (2021). The Definition of Self-Compassion. Self-Compassion. https://self-compassion.org/the-three-elements-of-self-compassion-2/.

Neff, K., Bluth, K., Tóth-Király, I., Davidson, O., Knox, M. C., Williamson, Z., & Costigan, A. (2021). Development and validation of the Self-Compassion Scale for Youth. Journal of personality assessment, 103(1), 92-105.

Neff, K., & McGehee, P. (2010). Self-compassion and psychological resilience among adolescents and young Adults. Self and Identity, 9(3), 225-240.

Neff, K., & Yarnell, L. (2013). Self-compassion, interpersonal conflict resolutions, and well-being. Self and Identity, 12(2), 146-159.

Zeller, M., Yuval, K., Nitzan-Assayag, Y., & Bernstein, A. (2014). Self-Compassion in recovery following potentially traumatic stress: a longitudinal study of at-risk youth. Journal of abnormal child psychology, 43(4), 645–653.

The Inescapable Burden of Reality

Riya Divekar

Preface

This paper was originally written for the class, “Sociology of Mental Health and Illness”. As such, **sensitive topics such as suicide, socioeconomic disparities, and mental health stigmas are discussed throughout the paper**. This paper will begin by explaining the benefit of viewing mental health through a sociological lens, then illustrate a case study highlighting the link between socioeconomic status and depression, examine theoretical perspectives explaining this phenomena, and end by briefly touching upon future actions. This paper does not serve to deny anyone’s personal emotions or mental illnesses that cause them turmoil. Rather, it serves to encourage looking outside of the minds of those affected by mental illnesses for solutions to combat the patterns that hurt countless individuals and families.

“Success is simply a matter of luck. Ask any failure.”[1]

This quote, by American journalist Earl Wilson, illustrates how American culture has traditionally valued success as a direct measure of individual effort and worth. It paints those who do not succeed as being inert individuals, who seek out some external element – ideally metaphysical and out of their control – in order to manufacture a discourse of reality that covers their shame and serves as an excuse for their lack of work-ethic and vigor. This outdated point of view causes harm and prevents much needed social change by ignoring the systemic issues that predetermine, or at least greatly influence, many elements of an individual’s life. To some extent, the first portion of Wilson’s quote is true. It is plausible that luck determines the family we are born into, the conditions that family has lived through, and the inequities that face the societies we live in. We do not actively control that. This “luck” may also affect an outcome graver than successes like income, class, and education, that we believe society values.[2] In 2018, 1.4 million Americans attempted and 48,344 completed suicide[3]. Some may attribute these deaths to an individual’s ability to cope with challenges and others may consider psychological differences to be the major factor behind them. However, it would be incomplete to ignore the extrapersonal, social factors behind pre-suicidal, depressive, or anxious psychological conditions. Socioeconomic disparities place certain disadvantaged subpopulations at a higher risk of suicide by reinforcing inescapable, circuitious conditions that hinder an individual's ability to control their fate. This perpetuates the psychological conditions that can manifest as mental health issues, life dissatisfaction and, ultimately, suicide.

Suicide is a major cause of death in America and the rest of the world.[3] No matter the socioeconomic status, age group, location, or time frame, mental health issues and suicide can hurt an individual, a family, and the greater community. There is substantial stigma against those suffering from mental health disorders: depression is perceived as just laziness, suicide as just cowardice. The stigma against mental health disorders is one reason why many do not receive adequate help to prevent its progression.[4] To aid those suffering with mental disorders, there must be a cultural shift in the perception of their validity and a desire to ensure more access to resources and medical care that can help those struggling. When analyzing mental health and illness, there are four interconnected fields (psychology, psychiatry, epidemiology, and sociology) that analyze the different aspects (psychological, social, environmental, and biological) of mental illness.[5] To promote the most comprehensive understanding of the issue, all these viewpoints should be considered and integrated. The real nature and impact of mental illnesses continue to transcend the disciplinary categories, so integrating the research will result in the best solutions. Apart from revealing greater insight into the roots of mental illness, sociological analysis could also result in the added benefit of reducing the stigma against mental illness. If there are more concrete, less abstract trends that can affect the mental healths of many people, suicide and mental illness will be viewed as less of a flaw within a person. Those who are affected by mental illness will not be viewed with as much stigma, since sociology focuses on the impact of interpersonal communication, institutions, and ideas that affect how people live and function. Since psychology focuses on the intrapersonal causes of suicide and provides personalized treatments, it can be easy to blame the person affected or view them as an abnormality, without creating extrapersonal changes that will prevent the same fate for posterity. This paper will provide an understanding of some recent suicide related trends through a theoretical sociological lens.

Research has shown that the suicide trends have changed over time. In “Deaths of Despair and the Future of Capitalism,” economists Case and Deaton explore how working class Americans face struggles in life that have caused increased rates of unhappiness and suicides among Americans without college degrees.[6] These trends have been most clearly seen in white people ages 45 to 54, but all racial groups have greater “deaths of despair” among groups that do not possess a Bachelor's degree. The suicide rates between White people aged 45 to 54 who have completed college and who have not began to diverge in the 1990’s and in the 2010’s. Those who possess a Bachelor’s degree have almost half the rate of suicide. This divergence is also seen in marriage rates, chronic pain, alcohol intake, and general unhappiness. All these measures can be reflections of life satisfaction, as mental illnesses, often dismissed due to their abstract, multifaceted nature, can impact these components of life.

Although the college experience itself could be one of the causes of this divide,[6] it is not possible to ignore the economic implications of obtaining a college education. From a conflict-theory sociological perspective, college serves as a way for the prevailing social order to sustain itself. Although many individuals are able to utilize a college education to improve their social standing and their economic fate, and recent efforts in Affirmative Action and scholarships from non-profit organizations may reduce the divide, generally, children from more affluent backgrounds are more able to go to college and receive opportunities that result in higher paying jobs. Sociologist Annete Laureu explores this in her book "Unequal Childhoods."[7] From a young age, middle class children are generally raised with the concerted cultivation model of child-rearing, which focuses on providing children with intellectual and skilled activities. Parents have enough money to cover the basic survival needs of their families, so the extra money is invested into their child's future. This allows them to develop skills that are valued in our workforce and economy – skills that are particularly beneficial during college applications. Poorer, working class families do not have the ability to provide their children with these experiences due to the more limited resources in their families and communities and the schedules of the parents. It is not just the mentality of the parents that affects the child's skills; there are economic restrictions that the child has no control over. This causes a generational continuance of income status or maintenance of lower income due to lack of class mobility. The resulting income (and subsequent lifestyle) divide can have great implications on the struggles of subsequent generations. Further evidence that the college experience is not the key factor limiting depression in people with a Bachelor's degree can be found by comparing the U.S. to other nations. The economies of nations other than the United States have drastically changed, affecting the jobs available, but they do not exhibit the same trend.[6] This could be due to less individual economic responsibility for basic survival needs. Thus, the capitalist economy of the United States and the economic result of education differences are a larger factor behind the increased suicide disparity.

The realities of life differ among different socioeconomic subsets of the American population. People progress through life and make different decisions based on the social structure, the preexisting rules of society, they are exposed to. There is a twofold effect of the conditions that people live through – the physical component and the mental components. Sociologist Barbara Ehrenriech explores the physical, economic realities of the inescapable conditions of poverty.[8] For a month, she lived life as if she was poor. She struggled to make ends meet, even though she started off with more “savings” than most impoverished people do. Living paycheck to paycheck hinders the ability to make “smart” economic decisions due to lack of investible money from unlivable wages and lack of support, excruciating labor, and family commitments. Having an initial amount of money that can help one get situated in their adult life can have dramatic results over time, but our government does not provide much of that. Additionally, statistics show the inequities in the physical dimension. There is a $578 difference between the national average monthly cost of rent in urban versus suburban areas.[9] Additionally, the costs of food, a necessity of sustaining life, are not uniform. A 2018 study conducted by the University of Minnesota confirmed that smaller food stores have higher prices for most staple foods compared to supermarkets.[10] In the suburbs, there is greater access to supermarkets and even wholesale food stores, especially when the prevalence of car ownership and its accompanying freedom are factored in, compared to cities that only have space for smaller cornershop food markets. Different environments make way for different experiences. Thus, the social structure in different environments associated with different income brackets has consequences that keep people in their own class.

Economic considerations also impact health outcomes.[6] The American healthcare system is very costly, partially due to private, high-cost insurance. Without the ability to regularly visit a doctor, small preventable problems go unnoticed until they become large enough to have severe impacts – both on an individual's life and a family's disposable income. Although some health disparities linked with low socioeconomic status may be a result of culture and variations in behavior, the implementation of interventions can change the trends; in fact, there is a positive correlation between width of health outcome disparity between classes and the number of medical innovations by disorder.[11] These economic restrictions keep people in poverty, increasing their stress and lowering their standard of living.

The mental implications of economic disparity are a bit more abstract, but George Herbert Mead's interpretation of the mind is a foundation for understanding how the individual is affected by their society. This interpretation is based on how we first learn language; images, concepts, and situations give meanings to words and the words then affect how we think.[12] The concept of the "mind" is used to describe the intangible essence of our personality and way of thinking. When thinking about the concept of self, Mead explains that there is a duality in our view of ourselves. The "me" portion involves understanding how we connect to our community and society by understanding the social environment, whereas the "I" portion describes the behavior we partake in based on our interpretation of "me". As we progress through the world, there is a loop where the "I" decides how to behave, the "me" integrates the environment in order to gain a more comprehensive understanding of the world, and the "I" thinks critically of that information, and then takes that information to dictate future behavior. Our own personality consists of our understanding of the world and how we judge it, and to a greater extent, where we find ourselves existing in it. In this instance, the actions and self understanding of the “I” is dependent on how one understands their place and role in the world, or their idea of “me,” leading to self comparison.

Jaques Lacan also discusses how our internal thoughts are greatly affected by our understanding of the external world.[13] Just like Mead explained our personality using the “I” and “me,” Lacan splits our unconscious and conscious thoughts into parts based on how we integrate information to develop an understanding of the world. The three categories that interact and affect each other to create our understanding of ourselves are the Real, the Imaginary, and the Symbolic. The Real represents how the world does not follow an orderly pattern and that there are limitations in how much we truly know about our existence. As the Real does not provide us with the clarity we need as a basis for higher functioning thought, we revert to the Symbolic. In the Symbolic, we take the thoughts of the Other, make them our own, to give our experiences meaning that we can build off of. The concept of the Other represents the external world, especially in terms of how other people, social institutions, and the culture will understand us and how we can interact with it. Similar to Mead’s “me,” without understanding the cues and signals of the world around us, we cannot think. The last part, the Imaginary builds off of our understanding of the world around us and how we use that to think deeper and connect it with ourselves, specifically our desires. We have expectations, we dream, and we think about the future. These thoughts demonstrate how we try to make sense of reality and desire consistency in both the past events that lead to where we are today and in terms of predicting what will happen in the future. Here, we also look towards the Other in order to fill the gaps we have within our Imaginary and the Real. For example, we may desire a significant other for intimacy and comradery. In terms of our Imaginary, we desire the Other to provide us with the significant other that can make our lives fit the expectations we create after observing the external world and adding Symbolic meaning to it. The Other refers to what is in the world that creates our Symbolic understanding of it, and we look to the Other to make our individual lives fit with the patterns that make our world make sense. We use our understanding of the Other to create a framework and expect characters of the Other to continue to provide us with consistency. When the Other doesn't fit the Imaginary we create with the Symbolic, the Real has access to control our thoughts. When the Real is not contained, we may feel anxious or depressed.

This theoretical understanding of how one's surroundings affects their mental processing can illuminate the aforementioned trend in unhappiness disparities between those who have received college educations and those who have not. Other than the direct result of stress from the economic burden (cost of living, food, healthcare), the images people use in their understanding of the world and the expectations they create can cause emotional turmoil when experiences do not match. There is an expectation to be successful in life that we absorb from “The Other,” the external world that shapes our ideas on what life should look like. What is considered to be success is based on what one sees and associates with success, through both passive observation and active judgment of the trends. Historically, the age group of current white 45 to 55 year olds come from families that saw great increases to their standard of living due to the GI bill allowing for greater economic gain, facilitating class mobility more than it does today. Additionally, in the mid/late twentieth century, it was possible to live the desired lifestyle without a college degree, due to available jobs. Since then, people’s understanding of how the world works is based on what they saw happen, these features became the expectation. Growing up, as they saw different things, they envisioned a future version of themselves fitting the norm and that became what they desired to become. For other age and race groups, similar images of progress and their hope for a better future may have been the Image they created of themselves. Not meeting the expected, imaginary future version of yourself could result in dissonance and feelings of failure.

When the Other — in this case the economic conditions of reality – do not allow for an individual to have the Imaginary life they created for themselves, and the prevailing attitude in the culture continues to neglect the external impacts, people feel inadequate. They feel like it is them who have failed, not the system that was created “For the People, by the People” that is supposed to enrich their lives. This allows for the Real unknowns of life to plague their minds and drive them past the point of return. Stigmas and lack of accessibility to psychological resources (as therapy is costly, with or without insurance) fuel the progression of depression and suicide. These issues are not separate. They come together, along with many more, to create an inescapable discourse of reality that sparks “deaths of despair”.

A similar social trend was analyzed in the phenomena of group suicide by sociologist and journalist Donna Gaines.[14] Four teenagers from working class families in the suburban Bergen County, NJ, commited joint suicide in 1987, even though suicide is normally seen as one of the most intimate, inidivudal decisions one could take. Upon sociological investigation, it was found that teen suicide rates in working class, out-of-city suburban whites had tripled from 1950 to 1980. The changing economic job market made their futures seem bleak as they knew they would not be able to attend college or secure their futures. Being poor in comparison to the rest of their communities, the schools and police treated these teenagers as outcasts. Their only refuge was forming cliques and imagining future versions of themselves as successful punk-rock stars that could surpass the odds. After a while, once the Imaginary was too far away from the Real, the helplessness to fight their fate took control of their perception, and the doubts of the Real controlled their thoughts. A similar link between inability to meet idealized social roles and suicide was found in the mass-practiced old Hindu ritual of Sati.[15] In this practice, women would commit suicide upon their husbands' deaths. The status of widow in this culture and time period held direct consequences of lack in power and indirect emotions of shame and fear. The emotions that may compel one to commit suicide are often tied to extrapersonal institutions and ideas, and thus "when thinking about patterns of suicidality, we must explore how structure and culture condition expectations and obligations, how identity and status performance are intimately driven by these expectations and obligations, and what types of options are available, accessible, and applicable for failing to meet these expectations and obligations." [14] Changes to the social rules, institutions, and norms, are needed to change the patterns that drive one to commit suicide.

Across these situations, the social interactions and the economic limitations could be the driving force behind the psychological turmoil that resulted in the decision to commit suicide. Richer people are not immune to these issues and at times, their mental health could be affected by even more factors, but there is an increased ability to reclaim themselves. It is easier for those with economic privilege to succeed in making changes that could drastically improve their mental health. For those with less economic means and social power, it is harder to see success when one takes the initiative to try and actively bridge the gap between their Imaginary selves and their actual selves. Trying and then failing, or having no option or ability to try, can add to the drowning, inescapable nature of depressive thoughts and push someone into making the decision to kill themselves.

Suicide and mental health will always be a complicated topic to understand. However, the sociological analysis of trends can divulge greater insight into some of the causes of this crisis and by actively trying to change these roots, society can benefit tremendously. Applying an understanding of the terrible economic realities and how they affect people's mental health illuminates this issue and helps foster solutions. For a long term impact, there needs to be a two pronged course of action to alleviate this trend (in addition to increasing access to resources, like therapy, that are normally associated with preventing suicide). First, there needs to be more economic support from the government to allow for class mobility and better life outcomes. Additionally, the government must restructure the social institutions that continue to dramatically make life harder with less income, as one's income is not a direct reflection of their efforts. Whether it's making schools better to ensure equal opportunity, lowering the cost of college, or alleviating the economic burden of survival, if the government wants to improve the lives of its citizens, it must take action. Unless there is major reform in the United States and other nations where the income and standard of living disparities create inescapable conditions that harm an individual's mental health, this trend will continue to grow.

The cultural view of success needs to be more diverse and more cognizant of the socioeconomic “luck” that establishes how futures will look.

References

"Earl Wilson Quotes." Quotes.net. STANDS4 LLC, 2020. Web. 1 Nov. 2020. <https://www.quotes.net/quote/19115>.

Ritter, RJ, Reinhart, and Zacc. “Americans' Perceptions of Success in the U.S.” Gallup.com, Gallup, 29 Oct. 2020, news.gallup.com/opinion/gallup/266927/americans-perceptions-success.aspx.

“Suicide Statistics.” American Foundation for Suicide Prevention, American Foundation for Suicide Prevention, 28 Oct. 2020, afsp.org/suicide-statistics/.

Out of Sight: Stop the Stigma, Start the Conversation. Kyle Mahaney, Aimee Bender, Jessie Minor. Brave Voice Films. 2019. Amazon Prime Video

Aneshensel, C. S., and Phelan, J.C.. Handbook of the Sociology of Mental Health. Kluwer Academic/Plenum Publishers, 1999.

Leonhardt, D, and Thompson, S.A. “How Working-Class Life Is Killing Americans, in Charts.” The New York Times, The New York Times, 6 Mar. 2020, www.nytimes.com/interactive/2020/03/06/opinion/working-class-death-rate.html.

Lareau, A. Unequal Childhoods Class, Race, and Family Life. University of California Press, 2011.

Ehrenreich, B. Nickel And Dimed: On (not) Getting By In America. New York, N.Y. : Henry Holt, 2002. Print.

Whitaker, C. “How Much Cheaper Are The Suburbs?” Forbes, 2016, www.forbes.com/sites/axiometrics/2016/06/30/how-much-cheaper-are-the-suburbs/?sh=59baed047619.

Caspi, Caitlin E et al. “Pricing of Staple Foods at Supermarkets versus Small Food Stores.” International journal of environmental research and public health vol. 14,8 915. 15 Aug. 2017, doi:10.3390/ijerph14080915

Phelan, J. C., Link, B. G., Tehranifar, P. (2010). Social Conditions as fundamental causes of health inequalities: Theory, evidence, and policy implications. Journal of Health and Social Behavior, 51(1_suppl). https://doi.org/10.1177/0022146510383498

Mead, G. H. Mind, Self & Society from the Standpoint of a Social Behaviorist. Chicago, Ill: University of Chicago Press, 1934. Print.

Lacan, J. Anxiety: The Seminar of Jacques Lacan. Translated by A. R. Price.Edición: 1. Cambridge Malden, MA: Polity, 2016.

Gaines, D., Teenage Wasteland : Suburbia's Dead End Kids. New York :Pantheon Books, 1991.

Abrutyn, S. (2017). What Hindu Sati can teach us about the sociocultural and social psychological dynamics of suicide. Journal for the Theory of Social Behaviour, 47(4), 522–539. https://doi.org/10.1111/jtsb.12145

Examining the Credibility and Potential of the Gingipain Hypothesis of Alzheimer’s Pathology

Grace Solomon

Abstract

Alzheimer's Disease (AD) is an age-related, neurodegenerative disease that impairs memory and cognition, and its causes are predominantly unknown. There is no one cause of the disease and in turn, no disease-modifying treatment. This paper argues that the gingipain hypothesis of Alzheimer's pathology is credible and has the potential to lead to disease modifying treatment, by presenting and summarizing relevant studies. The novel gingipain inhibitor, COR388, is identified and described to be a potential disease-modifying treatment, stemming from the gingipain hypothesis. More research is required in order for the gingipain hypothesis to be widely accepted and impactful for AD patients.

Glossary of Terms

Alzheimer's disease (AD): neurodegenerative disease that leads to dementia and brain shrinkage

β-amyloid: protein that builds up abnormally and forms plaques in the AD brain. Hallmark sign of AD

Disease-modifying treatment: treatment that can stop the progression or reverse the effects of a disease

Gingipains: virulence factors that are released by P. gingivalis and work to cleave other proteins in order to help P. gingivalis survive

P. gingivalis: the bacteria that causes periodontal disease, and is hypothesized to build up in the brain and provoke an immune response resulting in AD pathology

Pathology: the effects of a disease on the body

Introduction

Alzheimer’s disease (AD) is a brain disorder related to aging that leads to the development of dementia. Dementia is defined as the loss of cognitive functions, like memory and problem-solving, to the extent that it impairs daily functioning (National Institute on Aging 2021). AD impacts many aging people, with 11.3% of adults over the age of 65 being diagnosed, and women making up to two-thirds of those diagnoses (National Institute on Aging 2021). The disease is most well known for its impact on memory, as AD patients will often forget their family and friends, where they are, or even how to do daily tasks such as brushing their teeth. This cognitive decline occurs because the neurons within the brain deteriorate and can no longer communicate effectively with each other. This leads to brain atrophy, or shrinkage, to the point of biological death. As of now, AD is an incurable disease with minimally effective treatments.

In the field of AD studies, there is a great focus on finding disease-modifying treatment. The novel gingipain hypothesis provides evidence for a previously unidentified risk factor for AD: Periodontitis, or gum disease. Identifying an unexplored cause of AD could lead to the discovery of a treatment that could stop or even reverse the progression of this disease. This treatment potential has led to the gingipain hypothesis gaining traction and credibility within the AD community, with more studies being published in its favor. This paper aims to define AD and its pathology, demonstrate the current state of AD treatments available, and evaluate current hypotheses for the cause of AD. It will introduce and explain the novel gingipain hypothesis, examine its credibility using clinical studies, and determine its potential to lead to a disease modifying treatment for AD.

To thoroughly understand AD and its symptoms, it is necessary to first examine its pathology, or how it physiologically deviates from what is considered normal (Funkhouser 2009). AD can be defined as an age-related neurodegenerative disease that impairs memory and cognition through disrupting neuronal communication. It can be characterized by a complex pathology within the brain, but most researchers focus on neurofibrillary tangles (tau tangles) and β-amyloid plaques. Tau proteins are normally used within the neuron to stabilize microtubules through binding, but in AD they accumulate by binding to each other and forming tangles (Lane et al. 2017). These tangles impair the neuron's transport system, thus harming synaptic communication. β-amyloid proteins collect between neurons, forming a plaque that also harms neuronal communication. They are formed when a larger protein, amyloid precursor protein, is cleaved in three spots by beta and gamma secretases (Makin 2018). These produce β-amyloid proteins 1-40, or 1-42, which are particularly long and tend to clump together and form plaques more readily. Both β-amyloid plaques and tau tangles are particularly prevalent in the hippocampus, the area of the brain associated with learning and memory (Lane et al. 2017). These issues contribute to a greater problem within the Alzheimer's disease patient's brain: inflammation. The glial cells, which normally clear the brain of debris, act abnormally, failing to clear away debris, like β-amyloid plaques and causing additional build up and thus inflammation in the brain (Weiler 2020). The inflammation also worsens with age, as vascular issues often arise and lead to reduced blood flow to the brain and the breakdown of the blood-brain barrier (Lane et al. 2017). The blood-brain barrier protects the brain from harmful molecules by only allowing in small, polar molecules. Thus, when the blood-brain barrier breaks down, it is more difficult for microglia to clear away the increasing amount of debris, which contributes to further inflammation. Ultimately, this destructive cycle continues, as AD is both a cause and effect of it. All of these components of AD pathology lead to eventual neuron death, meaning that the brain eventually shrinks and atrophies, resulting in death.

Current Treatments

Currently, there are no disease-modifying treatments for AD. There are, however, several symptom-modifying treatments designed to improve cognition and memory, but these do not alter the progression of the disease. These treatments are far and few between, with only five being approved by the FDA (Briggs et al. 2016). Three of the five, Donepezil, Rivastigmine, and Galantamine, are cholinesterase inhibitors designed and shown to improve cognition, behavior, and daily activity (Chu 2012). They work by inhibiting acetylcholinesterase, an enzyme that breaks down the neurotransmitter acetylcholine. Inhibiting acetylcholinesterase increases the amount of available acetylcholine in the brain, allowing for better neuronal communication. Deficits in neuronal communication are a prime cause of AD symptoms. Another treatment, Memantine, improves cognition by regulating glutamate activity (Alzheimer's Association 2019). Glutamate is a neurotransmitter involved in memory and learning by triggering NMDA receptors to allow calcium into the cell, aiding information storage. The final treatment is the combination of Memantine and Donepezil, which acts to improve cognition for those with moderate to severe AD. Although these treatments relieve some symptoms, they fail to address the true reality of AD: brain atrophy. To truly combat this degenerative brain disease, finding a disease-modifying treatment is necessary.

Possible Causes of AD

Creating a disease-modifying treatment would require a thorough understanding of what causes Alzheimer’s pathology in the brain. For the last several decades, a prevalent hypothesis in the field of AD studies was the amyloid hypothesis, which credits flaws in the production, accumulation, or disposal of β-amyloid for Alzheimer's pathology (Alzheimer’s Association 2017). The amyloid hypothesis led to a cascade of studies done under the assumption that AD must be caused by issues with the β-amyloid proteins (Makin 2018). This led to numerous clinical trials of anti β-amyloid drugs, but none have been successful in providing a disease-modifying treatment and getting approved by the FDA. Since the field has been dominated by the β-amyloid hypothesis, there has been little room to focus on other possible causes of AD. This leads some to believe that there may be other overlooked causes of AD besides flaws associated with β-amyloid proteins. There have been many studies focusing on identifying risk factors for AD, like lack of sleep, poor nutrition, and lack of mental stimulation, but there have not been any concrete causes identified.

Gingipain Hypothesis

The gingipain hypothesis describes how Alzheimer's pathology may be an immune response to the bacteria, *Porphyromonas gingivalis* (*P. gingivalis*). It is a Gram-negative, anaerobic bacteria involved in periodontal disease, which is an inflammatory gum disease that destroys tissues in the mouth and leads to eventual tooth loss (Mysak et al. 2014). When an aging person develops periodontal disease, and in turn a high bacterial load, *P. gingivalis* can translocate to the bloodstream and then diffuse through the blood-brain barrier (Dominy et al. 2019). From here, *P. gingivalis* hides within the cytoplasm of the neurons and releases sophisticated, toxic proteases called gingipains, which cleave proteins in the brain. The gingipains digest these proteins, thus destabilizing the immune system and simultaneously providing nourishment and hidden cover to *P. gingivalis.* It is theorized that the immune system's response to the presence of *P. gingivalis* in the brain is expressed as Alzheimer's pathology. Ultimately, the gingipain hypothesis states that the *P. gingivalis* infection contributes to Alzheimer's pathology by releasing gingipains and harming neurons.

Gingipains are incredibly sophisticated and play a vital role in the survival of *P. gingivalis.* Gingipains account for 85% of the total proteolytic activity of *P. gingivalis,* demonstrating how important yet destructive they are (Bostanci & Belibasakis 2012). Additionally, gingipains can be divided into arginine-specific (RgpA and RgpB) and lysine-specific (Kgp) types based on what kind of peptide bonds they can cleave. These gingipains attack the molecular components of the immune response, most specifically by digesting T-cell receptors to reduce the cell's immune response. Gingipains also increase the resistance of *P. gingivalis* to antibacterials, allow *P. gingivalis* to bind to host cells, and assist in growth.Thus, gingipains are powerful proteases that play a vital role in the *P. gingivalis* infection.

While there are numerous hypotheses of what puts someone at risk for AD, the gingipain hypothesis is one of the newest. Since 2007, when studies suggesting this connection were first published, the hypothesis has been developing and accumulating supporting evidence. Overall, this paper will argue that the gingipain hypothesis is credible, well-supported, and has the potential to lead to one of the first disease-modifying treatments for Alzheimer's disease.

Poor Dental Hygiene is Associated with Greater Incidence of Dementia

The connection between an infection in the mouth and impacts on the brain needed to be established before the gingipain hypothesis could be fully formed and supported. An early study, revealed the correlation between dental hygiene and dementia incidence, thus providing the initial evidence for the gingipain hypothesis (Stein et al. 2007). It was a longitudinal study that followed 144 aging nuns with extensive dental records, that sought to establish that a person's likelihood of developing dementia can be predicted by the state of their oral health. Specifically, they had 40 years of previous longitudinal dental data, and the study ended with 12 additional years of data with cognitive testing and observations from brain autopsies. The participants were divided into three groups depending on if they had a low, moderate, or high number of teeth, and this was compared to their cognitive assessments, which evaluated dementia incidence. The cognitive assessment was composed of a variety of different tests that evaluated memory, concentration, and language. For a participant to be considered demented they would need to have impairment in memory, social or daily function, and impairment in another area of cognition. In the brain autopsy, they used the stages provided by the Braak and Braak method, which ranks levels of brain deterioration, and compared these results to the participant's number of teeth.

Through this study, researchers found that participants with the fewest teeth had a higher risk of developing dementia (Stein et al. 2007). By the first cognitive exam, 1/3 of participants with 0 to 9 teeth had dementia, and this group ended up being significantly associated with dementia prevalence. The hazard ratio for dementia incidence was 2.20, indicating that participants in the low number of teeth group (0-9) were 2.2 times as likely to develop AD than their counterparts with a moderate number of teeth (10-28). This data suggests that tooth loss may be a risk factor for developing AD. This data provides basic – but not definitive – evidence that poor dental health may be associated with developing dementia, thus providing the foundation for the gingipain hypothesis.

P. Gingivalis Can Translocate to the Brain and Incite AD Pathology in Mice

Building off of the foundational evidence, the Illievski 2018 study uses mice to show the presence of *P. gingivalis* in the brain and relate the pathology to that of AD, in order to support the gingipain hypothesis. The researchers hypothesized that orally administering *P. gingivalis* to wild type mice would result in neuroinflammation, neurodegeneration, and formation of intra and extracellular amyloid plaque and neurofibrillary tangles, otherwise known as Alzhiemer's pathology (Illievski 2018). The 10, 8-week old mice within the experimental group received *P. gingivalis* orally for 22 weeks, while the control group only received a placebo. At 23 weeks the mice were anesthetized and brain tissue samples were collected. The tissues were examined for the presence of *P. gingivalis,* gingipains, and signs of Alzheimer's pathology to determine if *P. gingivalis* had successfully translocated from the mouth to the brain.

Using these methods, the researchers discovered that *P. gingivalis* and gingipains were present in the hippocampi of the mice. It was evident that the brains of mice in the experimental group experienced more extreme neurodegeneration, specifically in the hippocampus (Illievski 2018). Additionally, extracellular Aβ-plaques and neurofibrillary tangles were found in the experimental mice, but not the control. This evidence demonstrates that it is possible for *P. gingivalis* to translocate from the mouth to the brain and incite AD pathology, which supports the points made in the gingipain hypothesis. However, this was done using a model organism, so it is not guaranteed that these conclusions can also be applied to humans.

The Presence of *P. Gingivalis* and a High Gingipain Load in the Brain is Associated with an AD Diagnosis

Another study, published in 2019, used human brain autopsies to show a correlation between high gingipain load and an AD diagnosis. The researchers used tissue microarrays containing brain tissue cores from both control, healthy brains and AD brains (Dominy et al. 2019). They conducted immunohistochemical studies to examine the gingipain load and the tau load within the brain samples. The researchers found that the gingipain load in the AD brains were significantly higher than that in the control brains, with 96% of the AD samples being positive for RgpB compared to the 39% of control brains. This demonstrates that an AD diagnosis may correlate with a high gingipain load within the brain. Additionally, there was a significant positive correlation between gingipain load and tau load. This study shows that the findings from Illievski's 2018 mouse model study may also be applicable to human subjects. To conclude, this study established that there is a correlation between gingipain load and an AD diagnosis, along with gingipain load and tau load.

COR388 is a Possible Disease Modifying Treatment

While the gingipain hypothesis may have data to back it up, it is important to identify how this could lead to disease modifying treatment. If *P. gingivalis* and its gingipains are a risk factor for developing Alzheimer's pathology, how could this be targeted with a drug? *P. gingivalis* is incredibly resistant to antibiotics and can only be suppressed for a few days until it develops a resistance (Ardila et al. 2010). Additionally, sending a broad spectrum antibiotic into the brain could harm the entire microbiome, killing off beneficial bacteria along with *P. gingivalis.* The solution to these issues can be solved by COR388, a small molecule gingipain inhibitor (Fig. 1). COR388 works by hooking onto and permanently attaching itself to the gingipain's binding pocket (S. Dominy, personal communication, March 24, 2021). After this, the gingipain is useless as it can no longer digest proteins within the brain (S. Dominy, personal communication, March 24, 2021). Without successful gingipains, *P. gingivalis* cannot receive nutrition and eventually starves and dies out. Additionally, as the gingipains die out *P. gingivalis* is revealed to the immune system and put under attack (Bostanci & Belibasakis 2012). If COR388 is successful in permanently disabling gingipains, it has the potential to become the first disease-modifying treatment for AD.

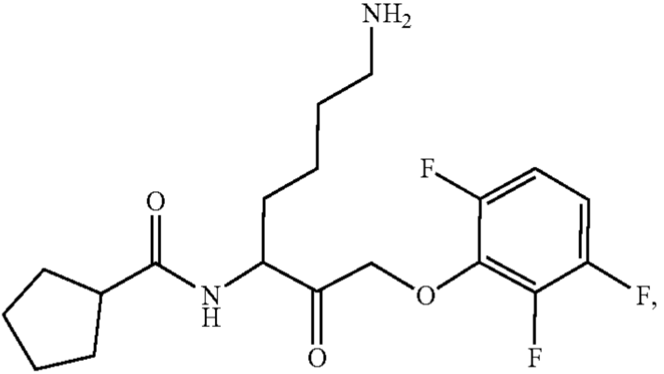

Fig 1. Hypothetical model of COR388 from its patent (Konradi et al. 2020).

COR388 is currently being tested in a stage 2 clinical trial called the GAIN trial (GAIN Trial… 2019). It is a randomized, double-blind, placebo-controlled study that began in March of 2019, and is currently still in progress. The 643 participants were recruited based on whether they had probable dementia based on NIA-AA criteria and AD based on an MRI scan. They are split into three groups: those receiving the placebo, a 40mg dose, or an 80mg dose in order to examine their tolerance. To measure the efficacy of COR388, the researchers are measuring changes in cognitive function using a variety of cognitive tests, determining if COR388 can help relieve AD symptoms. While the cognitive effects of COR388 are the focus of this trial, pocket depth, level of *P. gingivalis* antibodies, and MRI scans will also be evaluated throughout the study, providing more information about the effects on COR388.

All the components of the GAIN trial are working toward establishing causation for the gingipain hypothesis. If COR388 is effective in reversing some of the Alzheimer's pathology, and has beneficial effects on cognition, this could mean that it is the first disease modifying treatment for AD. While this study is still ongoing, it has great potential for producing a disease modifying treatment.

Conclusion

Overall, the gingipain hypothesis is credible and has the potential of leading to a disease modifying treatment for AD. This is supported through the myriad of evidence presented. The Nun study demonstrated the initial correlation between having a low number of teeth and a greater incidence of developing dementia (Stein 2007). This trend was studied further through a mouse model, in which it became apparent that *P. gingivalis* translocated from the mouth to the brain, and incited Alzheimer’s pathology (Illievski 2018). When examining human brains with Alzheimer’s pathology, researchers were able to find a significant positive correlation between gingipain and tau load (Dominy et al. 2019). Now, the ongoing GAIN trial is measuring the efficacy of COR388 in humans, and determining whether it will improve cognition in those with AD (GAIN Trial… 2019). The gingipain hypothesis is clearly well supported and backed up, leading one to believe that it is credible. Further experimental evidence will be needed for it to be fully accepted as a credible hypothesis, and impactful to AD patients. The gingipain inhibitor, COR388, could be the first disease modifying treatment for AD. To conclude, the gingipain hypothesis has incredible potential to make a worthwhile impact on the field of AD studies.

References

Arastu-Kapur S, Nguyen M, Raha D, Ermini F, Haditsch U, Araujo J, De Lannoy IAM, Ryder MI, Dominy SS, Lynch C, et al. Treatment of Porphyromonas gulae infection and downstream pathology in the aged dog by lysine-gingipain inhibitor COR388. Pharmacology research & perspectives. 2020 Feb [accessed 2021 Apr 13]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6990966/

Ardila CM, Granada MI, Guzmán IC. Antibiotic resistance of subgingival species in chronic periodontitis patients. Journal of Periodontal Research. 2010 [accessed 2021 Apr 23]. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-0765.2010.01274.x

Beta-amyloid and the amyloid hypothesis. Alzheimer's Association. 2017 [accessed 2021 Apr 13]. https://www.alz.org/national/documents/topicsheet_betaamyloid.pdf

Beydoun MA;Beydoun HA;Hossain S;El-Hajj ZW;Weiss J;Zonderman AB; Clinical and Bacterial Markers of Periodontitis and Their Association with Incident All-Cause and Alzheimer's Disease Dementia in a Large National Survey. Journal of Alzheimer's disease: JAD. 2020 May 5 [accessed 2021 Apr 13].
https://pubmed.ncbi.nlm.nih.gov/32280099/

Bostanci N, Belibasakis GN. Porphyromonas gingivalis: an invasive and evasive opportunistic oral pathogen. OUP Academic. 2012 Aug 1 [accessed 2021 Apr 13]. https://academic.oup.com/femsle/article/333/1/1/586464

Briggs R, Kennelly SP, O'Neill D. Drug treatments in Alzheimer's disease. Clinical medicine (London, England). 2016 Jun [accessed 2021 Apr 13]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5922703/

Chu LW. Alzheimer's disease: early diagnosis and treatment. Hong Kong Medical Journal. 2015 Jan 17 [accessed 2021 Apr 13]. https://www.hkmj.org/abstracts/v18n3/228.htm

Dominy SS, Lynch C, Ermini F, Benedyk M, Marczyk A, Konradi A, Nguyen M, Haditsch U, Raha D, Griffin C, et al. Porphyromonas gingivalis in Alzheimer's disease brains: Evidence for disease causation and treatment with small-molecule inhibitors. Science Advances. 2019 Jan 1 [accessed 2021 Apr 13]. https://advances.sciencemag.org/content/5/1/eaau3333

Funkhouser WK. Pathology: The clinical description of human disease. Molecular Pathology. 2009:197–207. doi:10.1016/b978-0-12-374419-7.00011-1 GAIN trial: Phase 2/3 study of COR388 in subjects with Alzheimer's disease. (2019, January 30). Retrieved April 21, 2021, from https://clinicaltrials.gov/ct2/show/NCT03823404?term=cortexyme&draw=2&rank=1

Haditsch U, Roth T, Rodriguez L, Hancock S, Cecere T, Nguyen M, Arastu-Kapur S, Broce S, Raha D, Lynch CC, et al. Alzheimer's Disease-Like Neurodegeneration in Porphyromonas gingivalis Infected Neurons with Persistent Expression of Active Gingipains. Journal of Alzheimer's Disease. 2020 Jan 1 [accessed 2021 Apr 13].

https://content.iospress.com/articles/journal-of-alzheimers-disease/jad200393

Ilievski V, Zuchowska PK, Green SJ, Toth PT, Ragozzino ME, Le K, Aljewari HW, O'Brien-Simpson NM, Reynolds EC, Watanabe K. Chronic oral application of a periodontal pathogen results in brain inflammation, neurodegeneration and amyloid beta production in wild type mice. PLOS ONE. [accessed 2021 Apr 13]. https://journals.plos.org/plosone/article?id=10.1371%2Fjournal.pone.0204941

Is Alzheimer's Genetic? Alzheimer's Disease and Dementia. 2021 [accessed 2021 Apr 13]. https://www.alz.org/alzheimers-dementia/what-is-alzheimers/causes-and-risk-factors/genetics

Lane CA, Hardy J, Schott JM. 2017. Alzheimer's disease. European Journal of Neurology. [accessed 2021 Apr 13] https://onlinelibrary.wiley.com/doi/10.1111/ene.13439

Liu Y, Wu Z, Nakanishi Y, Ni J, Hayashi Y, Takayama F, Zhou Y, Kadowaki T, Nakanishi H. Infection of microglia with Porphyromonas gingivalis promotes cell migration and an inflammatory response through the gingipain-mediated activation of protease-activated receptor-2 in mice. Scientific reports. 2017 Sep 18 [accessed 2021 Apr 13]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5603557/

Makin, S. (2018, July 25). The amyloid hypothesis on trial. Retrieved April 21, 2021, from https://www.nature.com/articles/d41586-018-05719-4

May B. FDA Places Partial Clinical Hold on Cortexyme's Alzheimer's Drug Trial. BioSpace. 2021 Feb 16 [accessed 2021 Apr 13].

https://www.biospace.com/article/fda-places-partial-clinical-hold-on-cortexyme-s-alzheimer-s-drug-trial/

Mysak J, Podzimek S, Sommerova P, Lyuya-Mi Y, Bartova J, Janatova T, Prochazkova J, Duskova J. Porphyromonas gingivalis: Major Periodontopathic Pathogen Overview. Journal of Immunology Research. 2014 Mar 25 [accessed 2021 Apr 13]. https://www.hindawi.com/journals/jir/2014/476068/

Nonaka S, Nakanishi H. Secreted gingipains from Porphyromonas gingivalis induce microglia migration through endosomal signaling by protease-activated receptor 2. Neurochemistry International. 2020 Aug 25 [accessed 2021 Apr 13]. https://www.sciencedirect.com/science/article/pii/S019701862030231X?via%3Dihub

Raha, D., Broce, S., Haditsch, U., Rodriguez, L., Ermini, F., Detke, M., . . . Dominy, S. (2020). COR388 (atuzaginstat), a novel gingipain inhibitor, decreases ApoE fragmentation in the CNS of Alzheimer's disease patients. Retrieved April 22, 2021, from https://www.cortexyme.com/wp-content/uploads/2020/07/AAIC_2020_COR388-A-novel-gingipain-inhibitor-decreases-ApoE-fragmentation-in-the-CNS-of-Alzheimers-disease-patients_Poster_070520.pdf

Sparks Stein P, Steffen MJ, Smith C, Jicha G, Ebersole JL, Abner E, Dawson D. Serum antibodies to periodontal pathogens are a risk factor for Alzheimer's disease. Alzheimer's & dementia : the journal of the Alzheimer's Association. 2012 May [accessed 2021 Apr 13]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3712346/

Sienski G, Narayan P, Bonner JM, Kory N, Boland S, Arczewska AA, Ralvenius WT, Akay L, Lockshin E, He L, et al. 2021. APOE4 disrupts intracellular lipid homeostasis in human iPSC-derived glia. Science Translational Medicine. 13(583). doi:10.1126/scitranslmed.aaz4564. [accessed 2021 Jun 1]. https://pubmed.ncbi.nlm.nih.gov/33658354/.

What is dementia? symptoms, types, and diagnosis. National Institute on Aging. [accessed 2022 Feb 13]. https://www.nia.nih.gov/health/what-is-dementia

Weller J, Budson A. Current understanding of Alzheimer's disease diagnosis and treatment. F1000Research. 2018 Jul 31 [accessed 2021 Apr 13]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6073093/

Weiler, N. (2020, February 30). Distinctive Alzheimer's symptoms linked to damaged glial cells. Retrieved April 21, 2021, from https://www.ucsf.edu/news/2020/01/416561/distinctive-alzheimers-symptoms-linked-damaged-glial-cells

Diffuse Idiopathic Skeletal Hyperostosis in a Paleopathological Case Study of 19th-century Remains

Juliet LaVigne

Abstract

This project analyzed the pathology present in the case of an individual labeled RU-029 and looked at the history of daily life during the 1800s in Philadelphia to understand how this individual may have lived. RU-029 was examined in Drew University's osteology lab in Falkner House using equipment provided by Drew University. It was discovered that RU-029 had a condition called diffuse idiopathic skeletal hyperostosis, also known as DISH. This pathology is correlated with obesity and diabetes mellitus, suggesting that this individual may have been from an upper class where they had access to more caloric foods. The osteophytes present on the calcanei are a presentation of DISH and could also suggest excess weight on the individual's heels, supporting the correlation of obesity and diabetes mellitus with DISH. RU-029 can show how diffuse idiopathic skeletal hyperostosis (DISH) may have affected an individual during the 19th century in Philadelphia.

Bioarchaeology is the study of human remains in an archaeological context. This is an important field for understanding and researching past populations and looking at trends over time. Bioarchaeology is a subfield of anthropology and archaeology. It focuses on human remains, human osteology, and odontology. These are important for the understanding of diet and nutrition in the past as well as paleopathology and paleoepidemiology, which all give us a clearer understanding of past civilizations and populations. Most often, the skeletal remains and the dentition are the only parts of the body that survive over long periods of time, so they tend to be what is found in an archaeological context, analyzed by bioarchaeologists, and are therefore considered representative of the entire body and cultural context within which it was embodied.

The Arch Street Project was created when over a hundred sets of human remains were discovered in Philadelphia during a construction project (Arch St. Project). These remains were supposed to have been transported to Mount Moriah Cemetery in Philadelphia in 1860 from the burial grounds of an Old First Baptist Church, established in 1707 (Arch St. Project). During a recent construction project, the construction crew discovered human remains on the site (Arch St. Project). The founders of the Arch St. Project, Kimberlee Moran (Rutgers University), Anna Dhody (Mütter Museum), and Ani Hatza (Rosemont College) were able to convince the developers to give them one week to excavate all of the remains properly. From there, analyses have been conducted on the remains to learn more about the people who were buried there and the context within which they lived and died (Arch St. Project). This site was legally complicated because it was private property and the construction was privately funded which meant that there was little legal ground to stand on to demand the halt of construction for months in order to conduct a thorough and proper excavation. For the purpose of this study, the legal and time complications had no impact on the collection and study of RU-029. These remains give us the chance to study the past population of Philadelphia and learn more about the lives of this community during the mid-1700s to the mid-1800s.

DISH

Diffuse idiopathic skeletal hyperostosis, or DISH, is a pathological condition that primarily affects the vertebrae but can also be seen in extra-spinal entheses and ligaments. DISH is associated specifically with the fusion of four or more thoracic vertebrae from osteophytes on the right side only (Waldron, 2021). This fusion can cause dripping candle wax-like bone formations which are the most extreme and obvious cases of DISH (Rogers and Waldron, 2001). Cases of DISH in an early stage might not have complete fusion and only have bridging osteophytes (Waldron, 2021). The key detail for diagnosing DISH in skeletons is the presence of osteophytes isolated to the right side of the thoracic vertebrae. This is because the anterior longitudinal ligament ossifies since the descending aorta is on the left which was confirmed when there was evidence of DISH in a person with situs inversus (Waldron, 2021). The osteophytes in this case were located on the left side of the thoracic vertebrae since the descending aorta was on the right side in this individual (Waldron, 2021). Another way to determine if the individual being studied has DISH is to identify if they also have extra-spinal entheses and ligaments (Waldron, 2021). This can be osteophytes on the calcanei and enthesophytes on the patellae, for example. When all of these symptoms are present, the conclusion is that DISH can be confidently diagnosed in the individual (Waldron, 2021).

The case of individual RU-029 is the focus of this paper. The alphanumeric code, RU-029, represents the individual that was studied. Studying RU-029 can show how diffuse idiopathic skeletal hyperostosis (DISH) may have affected an individual during the time in Philadelphia.

Materials

The materials used in this research project were the bones of individual RU-029, the inventory of which is shown in Image 1 and is detailed in the table in Appendix 1. Sliding calipers were used to measure the size of the osteophytes on the T10 vertebra as well as the length of the combined osteophytes from T5 to T12 vertebrae. An osteometric board was used to measure the femur for stature estimation.

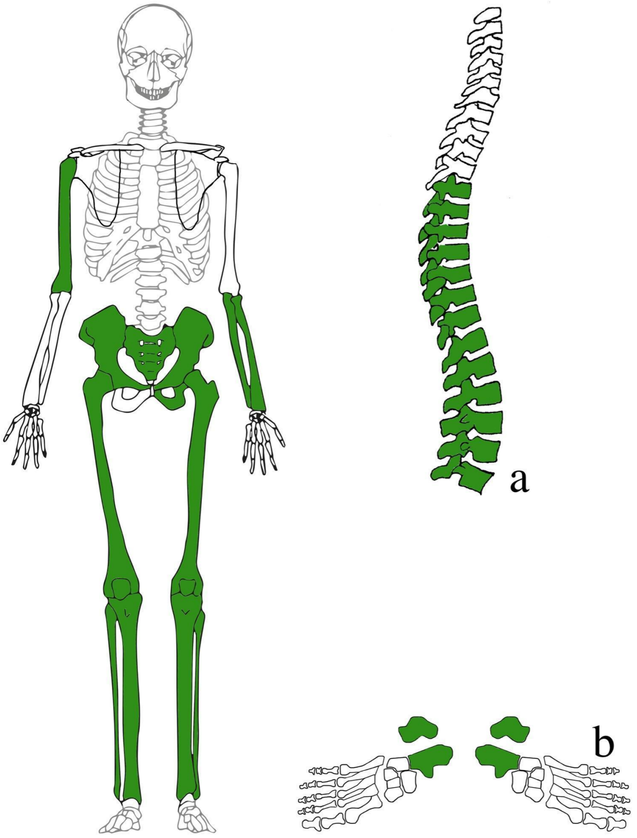

Image 1: Skeletal diagram depicting the present elements in individual RU-029. The ribs were fragmented and not included, but are included in the table in the Appendix. A represents a more detailed image of the vertebrae, and b shows the individual bones of the feet. Diagrams have been

adapted by the author from Buikstra and Ubelaker (1994) and Roksandic (2003).

Methods

The minimum number of individuals was estimated, and the biological profile was established using the following standard methods (Buikstra and Ubelaker, 1994). The biological profile includes sex, age-at-death, stature, and ancestry estimations (Buikstra and Ubelaker, 1994). Ancestry was not estimated in this case. The bones were received in a cardboard box and were mostly clean. Where there was still dirt on the bones, a soft, dry toothbrush was used to wipe it away. After making sure that the bones were clean, they were laid out in anatomical order before starting to establish a biological profile. The Buikstra and Ubelaker (1994) and the Klales et al. (2018) methods were used to score the pelvic features for sex estimation as well as the Walker (2008) method for sex estimation using morphological features of the skull. The Trotter and Gleser (1952) method was used to estimate stature by measuring the length of the femur. The pubic symphysis and the auricular surface of the ilium were analyzed using the Suchey-Brooks (1990) and Buckberry and Chamberlain (2002) methods, respectively for the estimation of age. After establishing the biological profile, the remains were examined for taphonomy, trauma, and pathology.

Results

Biological Profile

The MNI (minimum number of individuals) was determined to be 1 because there were no duplicate bones of the same siding. The pelvis indicates that the remains are female. The ilium, pelvic inlet, ventral arc, sub-pubic concavity, medial ischiopubic ramus, sub-pubic angle, greater sciatic notch, and preauricular sulcus were all analyzed using the Buikstra and Ubelaker (1994) method (see Image 2). The results suggest an estimation of female. The Klales et al. (2018) method was used to score the pubic area. The results were input into Program V1 on morphopasse.com which estimated that the remains were female with a 100% probability. Program VI is an online database where one can input a combination of features from a set of remains and the program compares it to a large collection of known individuals to determine sex estimation. The metric analysis of the femoral head was also used to determine sex estimation. The Spradley and Jantz (2011) reference was used for North American white and black populations since the ancestry of this individual was not determined. Sliding calipers were used to measure the maximum diameter of the femoral head which was 41mm. This showed that with an 86-88% accuracy that the remains are female.

Image 2: The pelvic bones and sacrum

Credit: LaVigne, J. (2021)

Age-at-death was estimated to be between 27.3 and 88 using the Suchey-Brooks (1990) method and the Buckberry and Chamberlain (2002) method. The mean age was 38.2 with a standard deviation of 10.9 for the Suchey-Brooks (1990) method. The Suchey-Brooks (1990) method uses the pubic symphysis in order to determine age-at-death. For the Buckberry and Chamberlain (2002) method, the mean age was 59.94 ±12.95. This method analyzes the auricular surface of the ilium for determining the age-at-death for the individual (Buckberry and Chamberlain, 2002).

For stature estimation, the Trotter and Glesser (1952) method was used for European females and African females. The maximum length of the femur was 395mm and it was measured using an osteometric board. The equation for European females is

2.47 x (femur length) + 54.10,

with a standard error of ±3.72, and for African females, it is

2.28 x (femur length) + 59.76,

with a standard error of ±3.41(Trotter and Glesser, 1952). This means that the range for stature estimation for this individual is 146.41cm-155.39cm.

Taphonomy

Most of the bones showed signs of postmortem breakage or cracking, most likely from excavation and decomposition. Small cracks and other forms of postmortem breakage were present in the ribs. The ribs, vertebrae, pelvic bones, sacrum, radius, tibia, and femurs showed varying degrees of postmortem exfoliation. Taphonomic damage includes decomposition, animal scavenging, plant growth, excavation, and more after death. Taphonomy is important to distinguish from trauma which occurs perimortem or antemortem.

Trauma

The left tibia showed new bone formation on the anterior medial part of the tibia (Images 3 and 4). This bone formation is a fracture callus from an old injury that healed over time. The contour of the bone suggests it may have healed without a rigid cast or splint. The fibula could have acted as a natural splint during the healing process.

Image 3: Fracture callus on left tibia
Credit: LaVigne, J. (2021)

Image 4: Fracture callus on left tibia
Credit: LaVigne, J. (2021)

Pathology

There was continuous spinal osteophytosis from the L1-L5 vertebrae and the T5-T12 vertebrae (Images 5 and 6). The spinal osteophytes were multifocal, unilateral, and local. The osteophytes were localized to the right side of the lumbar and most of the thoracic vertebrae, though the rest of the thoracic and the cervical vertebrae were missing from the collection. The osteophytes from the T5-T12 vertebrae measured 136 mm using sliding calipers, and the largest osteophyte on the T10 vertebrae measured 25.07 mm. The thoracic vertebrae showed signs of bridging between the osteophytes. There was no fusion of the vertebrae, but based on the extent of osteophytes along the right side of the vertebrae, fusion would have likely occurred had the individual lived longer. Enthesophytes were found on both patellae as well as the calcanei (Image 7 and Image 8). Osteophytes were also present in the calcanei which in addition to DISH, can also be associated with exertion and excess exercise or excess weight on the heels of the individual (Smith et al. 2007). Extra-spinal entheses are indicative of DISH when seen in conjunction with spinal osteophytes on the right side of the lumbar vertebrae, but they can also be seen as an activity marker (Waldron, 2021; Smith et al. 2007).

Discussion

The osteophytes and enthesophytes indicate that the individual could be diagnosed with diffuse idiopathic skeletal hyperostosis or DISH (Rogers and Waldron, 2001).

This was determined using the Rogers and Waldron (2001) method of identifying DISH in archaeological remains. This method looks at the candle wax-like ossifications on the vertebrae in later stages as well as enthesophytes in the patellae, calcanei, and ulnae that are associated with the disease in order to form an identification (Rogers and Waldron, 2001). This disease does not have a known etiology, but it is associated with the elderly and with conditions related to lifestyle like obesity and diabetes mellitus (Holgate and Steyn, 2016).

Image 5: Osteophytes on the thoracic vertebrae
Credit: LaVigne, J. (2021)

Image 6: Osteophytes on the lumbar vertebrae
Credit: LaVigne, J. (2021)

Image 7: Enthesophytes on the patellae
Credit: LaVigne, J. (2021)

Image 7: Enthesophytes and osteophytes on the calcanei
Credit: LaVigne, J. (2021)

The case of RU-029 is very intriguing because of the presence of DISH in the individual. It is interesting to observe how this could have affected the life of this individual in Philadelphia in the 1800s. The association of DISH with obesity and diabetes mellitus suggests that this individual might have been of a higher class with access to more caloric foods. DISH has been correlated with high status as well as monastic burials, but this does not indicate causation (Rogers and Waldron, 2001). It is interesting to note that DISH tends to be asymptomatic in the clinical cases found today, so while it may not have caused them any suffering, DISH still informs archaeologists about the individual's life (Waldron, 2021). The possibility of obesity and diabetes is, however, likely because of the industrialization that was taking place in the United States at the time which resulted in a shift away from an agrarian society to an industrial one and this individual was found in a populous city (Nugent, 2010). This resulted in more processed foods as well as a growing wealthy middle class (Nugent, 2010). The osteophytes on the calcanei are a presentation of DISH (Waldron, 2021), but may also suggest either excess exercise or excess weight on the heels of the individual which could support the idea that the individual was obese or had diabetes mellitus which is correlated to DISH (Smith et al. 2007). Though the age range of this individual is broad, it is more likely that the individual was older because DISH is more common in the elderly (Holgate and Steyn, 2016). The fracture to the tibia could have been the result of an old accident, but it is interesting to note because of the change in manual labor from that on a farm to that in a factory in this context (National Geographic). Osteophytes on the vertebrae can also be caused by manual labor and increase with age (Roberts and Manchester, 2012). The osteophytes on the calcanei could also indicate manual labor which would match the intense conditions found in the factories of the time (Smith et al. 2007; Nugent, 2010). DISH is closer correlated to obesity and diabetes mellitus and not manual labor though, which indicates that the first theory is more probable. It is always interesting, however, to examine how these pathological conditions relate back to the time when the individual was alive, which is why it is important to keep an open mind and examine all of the possibilities.

Future Directions and Conclusions

Using all of the remains found at the Arch Street location in Philadelphia, it would be interesting to see if there is a difference between males and females with DISH in the osteophyte distribution on the lumbar and thoracic vertebrae. Previous studies showed that there is no significant difference in the distribution of osteophytes on the lumbar and thoracic vertebrae between males and females with DISH (Holgate and Steyn, 2016). This would be an important study because it can expand the current knowledge of this disease and how these osteophytes affect people differently. The presence of osteophytes can be an effect of aging, or, if present on the vertebrae, can indicate a variety of diseases, among them DISH (Roberts and Manchester, 2001). Looking at DISH in relation to the aging process between males and females could provide insight into how aging and lifestyle affect the body. DISH is less common in females than in males, so looking at possible lifestyle correlations could provide insight into why this occurs (Holgate and Steyn, 2016).

This case of DISH gave an insight into the past and what an early condition of the disease looks like before the fused, candle-wax vertebrae that are the signature of more progressed cases. The case of RU-029 had many interesting features to analyze and further analysis of this case along with others in the future could provide more insight into living conditions, aging, and pathology during the 19th century.

Bibliography

Brooks, S., & Suchey, J. M. (1990). Skeletal age determination based on the os pubis: a comparison of the Acsádi-Nemeskéri And Suchey-Brooks methods. Human Evolution, 5: 227-238.

Buckberry, J., & Chamberlain, AT. (2002). Age estimation from the auricular surface of the ilium: a revised method. American Journal of Physical Anthropology,. 119(3), 231-239.

Digging through history: The arch street project. (n.d.). Retrieved May 05, 2021, from https://fas.camden.rutgers.edu/2017/08/08/digging-through-history-the-arch-street-project/

Haas, J., Buikstra, J. E., Ubelaker, D. H., & Aftandilian, D. (1994). Standards for data collection from human skeletal remains: Proceedings of a seminar at the Field Museum of Natural History, organized by Jonathan Haas. Fayetteville, AR: Arkansas Archeological Survey.

Holgate, R. L., & Steyn, M. (2016). Diffuse idiopathic skeletal hyperostosis: Diagnostic, clinical, and paleopathological considerations. Clinical Anatomy, 29(7), 870-877. doi:10.1002/ca.22716

Nugent, Walter. (2010). Progressivism: A very short introduction. New York: Oxford University Press.

Lee, D., Ko, H., & Son, B. (2018). Extensive heterotopic ossification following anterior cervical fusion in a patient with diffuse idiopathic skeletal hyperostosis. The Nerve, 4(1), 12-15. doi:10.21129/nerve.2018.4.1.12

National Geographic Society. (2019, December 09). Industrialization, labor, and life. Retrieved May 05, 2021, from https://www.nationalgeographic.org/article/industrialization-labor-and-life/

Olivieri, I., D'Angelo, S., Palazzi, C., Padula, A., Mader, R., & Khan, M. A. (2009). Diffuse idiopathic skeletal hyperostosis: Differentiation from ankylosing spondylitis. Current Rheumatology Reports, 11(5), 321-328. doi:10.1007/s11926-009-0046-9

Program V1. (n.d.). Retrieved May 05, 2021, from https://www.morphopasse.com/program.html

Roberts, C. A., & Manchester, K. (2012). The archaeology of disease. Stroud: The History Press.

Rogers, J., & Waldron, T. (2001). Dish and the monastic way of life. International Journal of Osteoarchaeology, 11(5), 357-365. doi:10.1002/oa.574

Smith, S., Tinley, P., Gilheany, M., Grills, B., & Kingsford, A. (2007). The inferior calcaneal spur—anatomical and histological considerations. The Foot, 17(1), 25-31. doi:10.1016/j.foot.2006.10.002

Waldron, T. (2021). Palaeopathology. Cambridge University Press.

Welcome to the ARCH St Project. (n.d.). Retrieved May 05, 2021, from http://archstreetproject.org/

L'enfant et les sortilèges: A Children's Opera for Grown-ups

Cristabella Fortna

Abstract

A time-honored musical tradition, operas are perhaps the oldest form of on-stage story-telling. As most traditions evolve with time, it is no shock that the twentieth century brought about a new sub-genre of operatic entertainment amidst its explosion of musical expression. Eric Champagne asserts that Children's Operas came about in the early eighties with the production of *Where The Wild Things Are*, by Oliver Knussen and libretto by Maurice Sendak. While there is no debate that this is a Children's Opera, this paper argues that it is not the first. This research and musical analysis of Maurice Ravel's opera *L'enfant et les sortileges* explains; why this is indeed a Children's Opera as per criteria explained by Champagne regarding performance length, subject matter, and the use of "children's language"; why this is the first Children's Opera, thereby shifting the date of codification from 1983 to 1925; and why other examples of fantastical operas and fantasie lyriques do not qualify despite their magical nature. In summation, this paper presents why *L'enfant et les sortileges* is the first Children's Opera, one which can be enjoyed by children and parents alike; a Children's Opera for Grown-Ups.

Introduction and Background

A well established musical tradition, opera remains perhaps the oldest genre of music composition and performance. Amidst the musical explosion of the twentieth century, a new sub-genre of this beloved musical tradition began to develop in the 1980s: children's operas (Champagne, 2006, 83). There exists a clear distinction, however, between fantastical operas, also known as fantasie lyriques, and operas which deal with children's subject matter like fairy tales and myths. Of this distinction, the question is raised by Eric Champagne (2006): "[are fairy tales and legends the subject of children's entertainment or a symbolic argument for adults' enjoyment?]" (84). Champagne argues that Ravel's second opera *L'enfant et les sortilèges* sits somewhere between a children's opera and a fantastical opera based on children's subject material, like Humperdinck's 1893 opera, *Hansel und Gretel*. However, upon further analysis of the criteria which dictate a children's opera, the subject matter presented, and the manner in which it is performed on stage, *L'enfant et les sortilèges* should be treated as the first children's opera which birthed the later codified sub-genre. This holistic analysis of Ravel's *L'enfant et les sortileges* asserts that this 1925 operetta should be recognized as the first children's opera on the basis of its performance length, subject matter, the motivation for its creation, and the relationship of these criteria to children as an audience in contrast to other operatic works such as *Hansel und Gretel*.

A well-known and orchestral-standard opera, *Hansel und Gretel* was set to music in 1893 by Engelbert Humperdink, bringing to stage the popular children's fairytale by the same name which was originally published by the Grimm brothers in 1812. This three-hour performance presents two German children who are sent into the woods by their mother to collect dinner for the evening; along the way they meet a witch who attempts to fatten them with candy and bake them into pies. While grim, this tale is standard in many homes then and now. The operatic rendition by Humperdink presents the first example of children's literature in opera, not to be confused with a children's opera. Almost 90 years later, *Where the Wild Things Are* was brought to the stage in 1984 by Knussen and Sendak, providing another example of a children's story brought to the stage through opera. While both works provide examples of child-like fantasy brought to an otherwise grown-up form of entertainment, Ravel's work in 1925 brings to the stage a unique application of fantasy and music, producing the first children's opera.

First performed in 1925 in Monte Carlo, *L'enfant et les sortilèges* is the product of librettist Colette and composer Maurice Ravel. Born in March 1875, Ravel followed a unique music educational path which involved repeated dismissals from courses at La Conservatoire de Paris, despite his evident musical talent and world-renowned contributions to music history (Kelly 2001). During the first world war, Ravel volunteered for service; his tour of duty kept him away from home during the time in which Colette had written her first draft of the opera (Orenstein 1966). Colette's first draft never reached Ravel, but the second draft finally arrived in 1918, still during Ravel's service in the war. However, due to health reasons and perhaps the more pressing issue of a global post-war sentiment, Ravel did not begin his compositional work for *L'enfant et les sortilèges* until the spring of 1920 (Oresntein 1966, 215). Originally titled *Divertissement pour ma fille*, the opera was renamed *L'enfant et les sortilèges* in 1924 (*ibid*) and completed the following year, amassing somewhere over six years of collaboration between these two masterminds, though the two had not met until after the Parisian performance (Smith 2002).

L'enfant et les sortilèges saw great success in both Monte Carlo upon its premiere in 1925, and Paris the following year (Malvano 2017). Ravel and Colette's collaboration "touched on an enduring preoccupation with childhood and fantasy and gave [Ravel] the opportunity to experiment with a range of styles" (Kelly 2001, 4). Colette had written, and Ravel had set to music, the story of a disobedient son who learns the consequences of his actions when the toys and furniture, entirely destroyed during his tantrum, come to life and taunt him until nightfall. The entire plot of this work largely unfolds in the child's room until the spells brought to life "[destroy the walls of the house to materialize the mysterious magic of the night]" (Malvano 2017, 102-103). With this, the spells which animate the inanimate allow the child to "[experience the every day from a new perspective]" (Malvano 2017, 102).

Ravel qualifies this work as "[distinguished by a mix of styles]" (Orenstein 1966, 217), incorporating "18th-century pastiche, mock-oriental writing, and ragtime" (Kelly 2001, 16) in the spirit of an American operetta (Malvano, 2017, p. 100). In a near-Wagnerian leitmotivic manner, where each character bears its own lyrical passage, each character brought to life in L'enfant et les sortileges also bears its own thematic style: the sofa and shepherd doll dance to an unsettling, wholly modernist, tune (4:50); the clock a pounding metric nod to Stravinsky (6:50); the Wedgwood teapot a quite racist almost-rag paired with a faux-oriental tune of the china cup (8:10); the tapestry figures march to a haunting liturgy (13:50); the Princess performs her own French recitative (17:20); the math homework a tormenting polka (23:55). These themes, however, are insignificant to the musical or theatrical function of this operetta and do not reappear throughout the duration of this work, separating them from leitmotives. The only theme assigned to a character that is recurring throughout this opera, thus serving a leitmotivic function and presenting an integral perspective to the world of children's operas, is that of "Mamman."

What Makes a Children's Opera?

Champagne (2006) asserts that children's operas must meet and contain three criteria: a length of approximately fifty minutes, subject matter that is "[specifically designed for children]," and lyrics "[in the language of the young audience]" (85). Similarly, when thinking of children’s operas, “[one imagines a work of fantastical subject, outlined in fairy tales and legends that can amaze the spectator]” (Champagne, 2006, p. 83). The strict and irrefutable time restraint of Champagne is evidently met in the nature of L’enfant et les sortilèges and thus the opera passes preliminary inspection for qualification as a children’s opera with no further analysis. Qualities such as “designed for children” and the use of “children’s language” are perhaps more obscure, as L’enfant et les sortilèges has deeply intertwined the two. To analyze these more obscure qualities, it helps to compare L’enfant et les sortilèges (1925) to Hansel und Gretel (1893) and Where the Wild Things Are (1984).

The subject matter within L’enfant et les sortilèges is firmly created with children in mind, as evidenced by the first working title, Divertissement pour ma fille, cited in letters between Colette and Ravel in 1919 (Orenstein 1966, 216-217). Colette created a children’s story for her daughter, asking Ravel to add music and bring this work to the stage. In contrast, Engelbert Humperdinck did not write the story of Hansel and Gretel–a children’s tale originally published in 1812 by the Grimm brothers–but merely set this popular children's fairytale to music on-stage. This is also the case of the 1983 opera Where the Wild Things Are, a musical setting of the original storybook by Maurice Sendak (Northcott 2002), and therefore does not disqualify Hansel und Gretel from children’s opera classification outright. It does showcase the heightened level of care given to the child audience in the creation of L’enfant et les sortilèges as Colette wrote her own story for her own daughter to then be set to music for other young children to enjoy.

Colette not only wrote an engaging children's story laced with magic and intrigue, but an opera that also brought to the stage fundamental stages of child development as l'enfant begins to learn the consequences of his actions. While the story of L'enfant et les sortileges is fantastical and imaginative, the written libretto showcases standard six-year-old behavior such as throwing a tantrum, pulling a cat's tail, ignoring math homework, and the general defiance of mother in the search to find one's self. Furthermore, and in many aspects most importantly, l'enfant is always on stage. It is this critical aspect of the opera which cements the structural importance of l'enfant in this work of children's media and begins to blur the distinction between "designed for children" and the exemplification of "children's language."

In every scene, l'enfant remains on the stage and in the scene which unfolds before him even when many characters do not speak to him or acknowledge his presence. In fact, it is not until the princess' recitative seventeen minutes into the performance that a spell-animated character engages in conversation with l'enfant; yet he remains on-stage throughout. This is, in effect, the true magic of *L'enfant et les sortileges* and this is what begins to break new ground in the world of children's status in children's media. The audience, independent of age or education, experiences these spells as the child sees them, rather than watching the child experience these spells and emotions as an adult retells them.

In contrast to other operas which deal with fantastical work and other child-like themes, *L'enfant et les sortilèges* presents all aspects of this work with the child onstage, to bring the audience into the situation through the perspective of the child himself. Engelbert Humperdinck's child-like opera *Hansel und Gretel* from 1893 may seem quite similar to the work of Ravel and Colette in the operatic representation of fantasy, but within the first twenty minutes of this near-two hour work, the children are sent off-stage into the woods. This leaves their mother alone on-stage to present a different perspective, and effectively isolates the children, both in the diegesis of the opera and in the audience in reality, from this new level of understanding. In this scene in *Hansel und Gretel*, the mother is painfully singing about her struggle to feed her children and the hurt associated with such hardship. While this is deeply moving and sad, it showcases a key difference between an opera that seems child-like and a children's opera, as it deals with a standard fairy tale but was not designed with children in mind. Despite its plot of fantasy and childish mischief, this dismissal of the children, literal and figurative, in conjunction with the three-hour length of the opera itself, means *Hansel und Gretel* therefore cannot be considered a children's opera.

Furthermore, the plot of *L'enfant et les sortileges* is presented from the perspective of the child using the first-person, a notable shift in the presentation of children's literature in France at the time. Even though *Les malheurs de Sophie* by la Comtesse Sophie de Ségur (1858), a collection of children's stories popularly read then and now, presents four-year-old Sophie as the primary character, the narration is third-person omniscient rather than first-person through Sophie herself. Additionally, the original text of *Hansel und Gretel* written by the Grimm brothers (1812) narrates the main characters' actions and findings through the same third-person omniscient perspective. This is to say that at the time, children's literature presented the child's world through adult's eyes; the magic of a tea party with tap-water and leaves in the twelfth chapter, "*Le thé*," is lost through this third-person presentation of *Les malheurs de Sophie*. Colette, however, has written a sample of children's literature which presents the magic of imagination onstage through the perspective of the child and enchanted toys rather than through the eyes of mamman, who only enters the stage during the final moment of silence (44:41-45:00).

While the final criterion of children's language remains obscure, citing once again that l'enfant himself uses "je" or "[I]" in lieu of narration, *L'enfant et les sortilèges* can therefore be considered written in children's language. In other words, the vocabulary and syntax of the written work presented on stage matches, and does not exceed, that of the six-year-old Mademoiselle Gaulet who was originally cast as L'enfant in 1925 (Orenstein 1966, 216). This use of first-person narration and present-tense verbiage is not seen, however, in Humperdinck's *Hansel* *und Gretel* to the same extent as displayed in *L'enfant et les sortileges* simply because the child, or children, are not on-stage throughout the entire opera. While the different perspective of their mother is helpful to the audience, such a narrative shift approaches the fourth wall as the mother's monologue is directed at the audience, who remain outside the diegesis, rather than to her own children, who remain inside the diegesis of the opera but are now outside the setting of the stage. Once again, *Hansel und Gretel* is therefore not a children's opera as it has failed to adhere to any of the three criteria of Champagne.

Where the Wild Things Are is cited by Champagne as the first instance of a children's opera (Champagne 2006). The original text was written in 1963 by Maurice Sendak, the opera was created with music by Knussen between 1973 and 1983, and finally performed in 1984 (Northcott 2002). This forty-minute performance depicts a young boy sent to bed without dinner due to bad behavior. In his rage, he imagines a world of creatures and playthings within the confines of his bedroom to allow him to escape the control of his mother and the obligations of his real world. However, he eventually realizes that this world of fuzzy monsters still brings fear and terror and he thus returns back to his room to find his mother and apologize (*ibid*). With this summary alone, *Where the Wild Things Are* and *L'enfant et les sortileges* are identical in concept. Further, Champagne explicitly states that *Where the Wild Things Are* is the first of this operatic sub-genre. While it goes without argument or further analysis that this 1984 opera is indeed a children's opera, it cannot be considered the first.

Musical and Structural Analysis of "Mamman" as a Perfect Fourth

Written by a mother for her daughter, and composed by a child who has just lost his mother, the thematic presentation and representation of the bond between a mother and child is a key component of *L'enfant et les sortilèges*. After his own bout with dysentery in 1916, Ravel lost his mother quite suddenly in 1917, approximately a year before receiving the draft of the libretto to begin composing. Despite much speculation regarding Ravel's personal life, "it seems certain that his relationship with his mother was the closest emotional attachment he ever experienced" (Kelly 2001, 4). With such a deep connection to the theme of motherhood, it is therefore noteworthy that such a relationship is presented on-stage in a period where childhood and motherhood may have been lost during the first world war.

The musical representation of "Mamman" is outlined solely with the interval of a fourth. The name, and thus the interval, are expressed only three times throughout the entire work; first when L'enfant cries "*j'ai envire de mettre mamman en penitence*" in the first scene (Figure 1, 2:21), again when crying for his mother out of fear (Figure 2, 38:28) when lost in the garden and taunted by the wildlife therein, and once more as the final call for mamman closes the opera (Figure 4, 44:42). With each iteration, the interval of a fourth is only expressed by l’enfant himself and is only ever in reference to his mother; the function of this interval and the lyrical sentence associated with it, however, is modified with each occurrence. This specific connection between a perfect fourth, mamman, and l’enfant presents a unique perspective on the unbreakable bond between mother and child, an integral component of childhood and thus this operetta.

The opening utterance of “Mamman” (Fig 1) is written as an ascending fourth, signifying the child's want to get away from mamman’s control, and to become his own human in defiance of his mother’s rules.

Figure 1. The first appearance of “Mamman” in L’enfant et les sortilèges. The ascending fourth alludes to the child’s want to get away from Mamman’s control, the search for independence.

The lyrics express the child’s displeasure with his mother, stating that he wants to put Mamman in time-out. With such fervent unrest and emotional turmoil, the rhythmic expansion from 16-notes to eighths gives more weight to the child’s statement, mirroring the emotions that are not uncommon to six-year-old children.

While childish in linguistic expression, the outward-seeking fourth in juxtaposition with “Mamman” presents a taste of the child's journey to find himself through this work. This contextualization of the search for self sets up the beginning of the protagonist's character arc, but more importantly presents a key moment in child development on-stage through the perspective of the child himself. By presenting a universal and critical developmental experience through the child, Ravel opens new doors to the portrayal of children in media of the time. All of this is embedded in an ascending fourth before the magic of the opera has truly begun.

At the time of the opening fourth (Fig 1), Mamman has not yet entered the stage, nor will she enter the stage until the last five minutes of the opera. Between this first appearance and the next, fourths are not heard or written in the score except to represent "Mamman" each time the child calls for her. When L'enfant cries for his mother, rehearsal number 135 (Fig 2), only the second time he has mentioned her by name, the pattern changes to that of a descending fourth. This descent perhaps symbolizes the child's desire to return home as he realizes that he is all alone and forgotten by his playthings.

Figure 2. The second appearance of a perfect fourth, now descending to express L'enfant wanting to return home. Lyrics: [They love each other… they forget me… I am alone… Mom!]

The score notes describe the child’s worry and defeat – “*inquiet, presque sans voix*” [worried, almost voiceless]– describing the manner in which this line should be sung. “[Despite this, he calls]” for his mother, states the final score note. Though it is unclear if such writings in the score are the work of Colette, the writer and therefore lyricist, or Ravel, the composer, such notes corroborate the sense of longing and yearning produced by the descending, tonic-seeking fourth. Perhaps an expression of Ravel’s grief over his mother’s recent passing, illustrated through a young son who also wants to return to his mother’s arms, or perhaps the projection of Colette’s motherly instincts painted over l’enfant’s worries, expressing that she will always be waiting for her own child; in either circumstance, the perfect fourth once again presents an integral facet of childhood on-stage through the perspective of the child, rather than that of an adult who otherwise governs a child’s life.

After this attempt to find Mamman and return home, the child trips and falls; the beasts recognize that they have hurt the child, but they do not know how to help. They, too, begin to cry “Mamman” (Fig 3), but their chorus moves in stepwise motion rather than the true perfect fourth.

Figure 3. The beasts attempt to call for Mamman, but their cries are not in perfect fourths but rather steps.

Thus, though the word "Mamman" is heard more times than the perfect fourths assigned to her namesake, the intervallic representation of her persona is strictly confined to the call of her own child. This is an important musical distinction of *L'enfant et les sortilèges* as the aforementioned connection between mother and child remains unadulterated, though others can also call for the child's parent without expressing the same deep-rooted familial, and here musical, connection that l'enfant and mamman share.

As a demonstration of the musical specificity of a perfect fourth, the final call from L'enfant of "Mamman" is once again a descending fourth to call mamman on stage (Fig 4).

Figure 4. The final cry for "Mamman." Sung by L'enfant, this is once again a descending perfect fourth which ends the entire work.

As in Figure 2, the descending intervallic representation of "Mamman" once again demonstrates the idea of finding one's home. This time, however, mamman is called upon not only to help l'enfant and heal his wounds, but to physically bring him home and end this mad sorcery as "[only an adult could undo the spell of a world which turns against its creator]" (Malvano 2017, 102).

While this paper discusses the status of *L'enfant et les sortileges* as a children's opera, the theoretical analysis of "Mamman" presents one of many profound layers to this work which play to the adult audience and those that are musically educated. This theme of motherhood, and the connection between mother and child, is implied throughout the entirety of this work, but can also be concretely expressed through score analysis as presented here. Further, the strict presentation of an intervallic fourth functions as a music theory representation for, perhaps, the most profound aspect of this opera as it relates to its qualification as the first-ever children's opera: the child's perspective.

Conclusions

Under sixty minutes in length, created with children in mind, and restricted to children's language, Colette and Ravel's 1925 opera *L'enfant et les sortileges* is the first of the operatic sub-genre referred to as children's operas. The analysis presented here does not disqualify the later-performed 1984 *Where the Wild Things Are* from qualification as a children's opera, but it shifts the birth of this sub-genre sixty years prior. This is in contrast to the assertion of Eric Champagne (2002), while adhering fully to his own criteria for distinguishing opera from children's opera. Additionally this research presents why *Hansel und Gretel* is not a children's opera, despite its musical adaptation of a children's fairy tale, on the basis of length, language, and mindfulness of the child audience. In other words, this paper presented that the irrefutable children's opera *Where the Wild Things Are* is not the first of its kind, as *L'enfant et les sortileges* is the original children's opera, and that *Hansel und Gretel* cannot be qualified as a children's opera at all. Furthermore, the categorization of *L'enfant et les sortilèges* as a children's opera should not disqualify this magnificent work as one without deeper levels of analysis. As with much, if not all, children's media, there is a superficial layer of intrigue for the young, but "[the fairy tales can be interpreted and analyzed by the adults through their life experiences]” (Champagne 2006, 85), which oftentimes brings a deeper appreciation for the work as a whole.

References

Champagne, Éric. 2006. “L’opéra pour enfants ou la quête d’identité : commentaire critique sur *L’arche*, d’Isabelle Panneton et Anne Hébert” [“The opera for children or the search for identity: critical commentary on *L’arche* by Isabelle Panneton and Anne Hébert”]. *Circuit* 16 (2): 83–92. https://doi.org/10.7202/902400ar

Grimm, Jacob and Wilhelm. 1857. “*Hänsel und Grethel,*” In *Kinder und Hausmärchen* 1 (15): 79-87. Göttingen: Verlag der Dieterichschen Buchhandlung.

Kelly, Barbara L. (2001) “Ravel, (Joseph) Maurice.” *Grove Music Online*. https://www.oxfordmusiconline.com/grovemusic/view/10.1093/gmo/9781561592630.001.0001/omo-9781561592630-e-0000052145

Malvano, Andrea. 2017. “La chute du voile de tulle. Considérations sur la fonction de la mélodie dans *L’enfant et les sortilèges* de Ravel” [“The fall of the tulle veil. Considerations on the function of the melodie in *L’enfant et les sortilèges* by Ravel”]. *Revue musicale OICRM* 4, (2): 99–117. https://doi-org.ezproxy.drew.edu/10.7202/1043222ar

Northcott, Bayan. 2002. “Where the Wild Things Are.” Grove Music Online. https://www-oxfordmusiconline-com.ezproxy.drew.edu/grovemusic/view/10.1093/gmo/9781561592630.001.0001/omo-9781561592630-e-5000002107.

Orenstein, Arbie. 1966. “*L'enfant et les sortilèges*: correspondance inédite de Ravel et Colette” [“*L’enfant et les sortilèges:* unedited correspondence between Ravel and Colette”]. *Revue de Musicologie*, 52: 215–20.

Ravel, Maurice et Colette. 1925. *L'enfant et les sortilèges*. Paris: Durand.

Segur, Comtesse Sophie de. 1858. *Les malheurs de Sophie.* Paris: Hachette.

Smith, Richard Langham. 2002. "Colette." *Grove Music Online*. https://www-oxfordmusiconline-com.ezproxy.drew.edu/grovemusic/view/10.1093/gmo/9781561592630.001.0001/omo-9781561592630-e-5000005396.

The Neuroethics of Biomedical Research Involving Cognitively Impaired Human Participants

Evan Fairweather

Abstract

To gain useful data, research on novel therapeutic and diagnostic technologies must eventually involve human subjects. For conditions such as Alzheimer's and Parkinson's diseases, it is necessary to enroll participants affected by neurocognitive deficits, which raises concerns over research ethics. Existing guidelines must be considered using a modified ethical framework. Due to their vulnerability, special considerations are needed to preserve the rights and autonomy of these individuals, while also gaining the knowledge necessary to further biomedical research. The fair selection of subjects, risk vs. benefit analysis, and informed consent are all complicated by the progressive cognitive impairment associated with these diseases. While proposed solutions such as surrogate decision-makers and research advance directives have emerged, they each have shortcomings that highlight the challenges involved with reconciling the interests of research subjects, their families, healthcare providers, and scientists. As such, there is a need for both standardization of laws and interdisciplinary shared decision-making.

The ultimate goal of biomedical research is to help people. Through the generation of data, researchers are able to inform clinical care and improve diagnostic or therapeutic technologies, leading to better patient outcomes (Hurst, 2011). Whether investigators are looking to understand the molecular mechanisms underlying Parkinson's disease or develop novel drug therapies for Alzheimer's disease, studies that begin in the laboratory must eventually involve patients afflicted by the disorder (Hurst, 2011). For these patients to benefit from said studies, participants must be recruited from vulnerable or impaired populations (Hurst, 2011). Results generated from neurotypical populations are often not generalizable, diminishing the validity of the research. Individuals considered "vulnerable" must be included to fulfill the purpose of such studies. However, the effects of these diseases on cognitive function raise concerns about autonomy and informed consent, thereby fundamentally changing the approach researchers would otherwise take with populations not affected by degenerative diseases. Care must be taken to ensure that one is "still treated with the dignity that [they] should have as a human being" (Sorrell, 1999). Such circumstances necessitate special considerations beyond those routinely employed in research to preserve the rights and autonomy of subjects, whilst also maintaining the utility and value of human studies.

Prior to exploring the neuroethical implications of research involving cognitively impaired patients, it is necessary to understand the pathology and neurocognitive impacts of these conditions. Alzheimer’s disease (AD) is a progressive neurodegenerative disorder that leads to deficits in memory, language, visuospatial skills, and executive function (Castellani et al., 2010; Horng, 2017). Alzheimer’s disease researcher Dr. Jeanne Sorrell (1999) recounts the case of Josie from her husband Robert’s point of view:

> [My wife] was only 47 when she started becoming symptomatic, and they really didn't know what it was. We actually went to four different neurologists. One thing led to another, and the next thing I know, I'm in an Alzheimer's study.

Symptom onset occurs gradually, beginning with mild cognitive impairment in the early stages of the disease. As time passes, individuals begin exhibiting more dramatic neurocognitive changes, losing the ability to perform everyday tasks. The rate of symptom progression and cognitive decline varies between individuals.

Parkinson’s Disease (PD), the second most common neurodegenerative disorder, is commonly thought of as only a neuromotor condition. However, it also has a neurocognitive component (Horng, 2017). Patients may present with cognitive deficits in executive function, memory, and attention. Referred to as Parkinson’s Disease Dementia (PDD), this collection of symptoms typically occurs as a late complication of the disease, with 75-90%

of patients experiencing neurocognitive deficits by 10 years post-diagnosis (Gratwicke et al., 2015). However, research has shown that executive function deficits can manifest early in the course of the disease as a prodromal symptom, progressively worsening with time. These can present as difficulties in problem-solving, rule-shifting, task-switching, and working memory. Since Alzheimer's and Parkinson's diseases are the most common neurodegenerative diseases, they are of significant interest to researchers investigating pathophysiology, diagnostic technologies, and therapies. However, the variable progression of cognitive deficits complicates the fair and ethical recruitment of subjects in these studies. Thus, it is important to develop a neuroethical framework to critically examine and improve research practices.

Current best practices for research involving human subjects were developed in response to the Tuskegee Syphilis Study (1932-1972), where researchers sought to study the natural course of syphilis in a group of African American men. Despite the emergence of Penicillin as an effective therapy during the trial, it was withheld from the participants (they were not even informed of the potential treatment), presenting numerous ethical concerns. As a result of a government inquiry, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research released the Belmont report (1979). The principles of respect for persons, beneficence, and justice have become fundamental guides to the responsible conduct of research. Respect for persons centers around recognizing and respecting an individual’s autonomy (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979). This also dictates that those with compromised autonomy, whether that is due to age or state of disease, require specialized protections to protect their wellbeing. The principle of beneficence promotes the wellbeing of others, making the ultimate goal of research to provide benefits to persons. This is distinct from, though related to the idea of Primum non nocere (first, do no harm) that underlies the practice of medicine. The principle of justice dictates that both the benefits of discoveries, as well as the risks of research, should be equitably distributed to avoid placing an undue burden on one group. Other established principles guide the ethical conduct of research as well. Among them are ethics board approval, social value, scientific validity, independent review, informed consent, and respect for enrolled participants (Hurst, 2011; Bracken-Roche et al., 2017). Of particular concern when involving cognitively impaired participants are the principles of fair subject selection, risk/benefit analysis, informed consent, and respect for persons.

The Belmont principles are applied to research conduct in a myriad of ways. The concept of informed consent, which embodies the principle of respect for persons, is deeply ingrained in clinical research.The assessment of risks and benefits, a continuous process that begins during study design, embodies the principle of beneficence by ensuring that there any risk to the participant is worth the potential benefits associated with new scientific advances. The process of subject selection is driven by the principle of justice, as fair subject selection confers scientific legitimacy and an equitable distribution of risk. While researchers face challenges with informed consent, risk vs. benefit analysis, and subject selection even when employing neurotypical, non-vulnerable populations, research involving those with cognitive impairment presents greater challenges.

Once more, consider the case of Josie, which illustrates the challenges of working with those affected by AD (Sorrell, 1999). In discussion with a nurse, Josie's husband Robert describes her cognitive decline:

> The first thing that she lost was her ability to pay the bills. She'd get so confused, and I couldn't figure out what was going on. Everything just happened so gradually that little by little I found myself, like doing the driving, 'cause she used to do all the driving, even when we went on vacation […]. One hard thing is that Josie was always such a gentle person, and now sometimes when she wants to resist things, it's like looking into the eyes of the devil. It's scary. I had never seen such hate and anger. (Sorrell, 1999)

Before delving into the neuroethical complications of her case, consider how her situation would differ if she was enrolling in a research study after a cancer diagnosis. Despite a disease such as cancer leading to progressive physical decline, the cognitive abilities of those affected remain largely uncompromised. Though fear, depression, or anxiety may be observed in these individuals, their abilities to engage in rational decision making are not compromised to the same degree as in an individual with Alzhimer's or Parkinson's diseases. As such, her decisional capacity would remain relatively constant. It would be relatively uncomplicated for researchers to maintain respect for autonomy, for she remains capable of expressing (or revoking) informed consent. However, Josie has early-onset Alzheimer's disease, and her cognitive abilities progressively decline, diminishing her decisional capacity. In such a case, it becomes challenging to reconcile her wishes and the goals of the researchers in a way that does not violate her rights or autonomy.

Before exploring the specific precautions to take when involving vulnerable populations in research, it is important to define "vulnerability." This concept originated in the Belmont report, but there is still no consensus on the criteria by which vulnerability is defined (Bracken-Roche et al., 2017). Some base the criteria on the idea of justice, where vulnerability originates from the failure to fairly recruit participants or distribute burdens and benefits (Bracken-Roche et al., 2017). Others base these criteria on the principles of autonomy and respect for persons, as individuals unable to voluntarily provide informed consent cannot protect their interests (Bracken-Roche et al., 2017).

Due to this, it is incumbent upon the researcher to protect the interests of participants. Justice, autonomy, and respect for persons must all be ensured, as failure to do so jeopardizes the legitimacy of the research being conducted. To protect participants, it is important to identify potential wrongs, as well as possible victims (Hurst, 2011). Specifically, the risks of coercion and exploitation can emerge from the inability to provide informed consent. Coercion is defined as "credible and strong threat exerted by a person that limits the options in a negative way available to another person" (Hurst, 2011, p. 2), while exploitation is defined as the “unfair distribution of the benefits and burdens of a transaction” (Hurst, 2011, p. 3). By this definition, exploitation may not be completely avoidable, as the patients involved in trials for diagnostic technologies or novel drugs do not always benefit from participation in the same way that future users of this novel technology will. However, it is still vital to minimize undue exploitation of participants. Vulnerability is both “relational” and “dynamic,” determined by the circumstances of the study in which one is participating (Bracken-Roche et al., 2017). Vulnerability is “relational” as one’s degree of vulnerability is dependent upon both their cognitive state, as well as the specifics of the study. These variables cannot be considered independently. Furthermore, as the cognitive abilities of individuals with neurodegenerative diseases change, so does their level of vulnerability. As such, one of the greatest challenges in protecting vulnerable participants is first identifying them.

Individuals may be vulnerable based on reduced autonomy, susceptibility to external influence, or likelihood of harm (Bracken-Roche et al., 2017). Individuals that are unable to express their wishes, rely on surrogates to make decisions due to cognitive decline, or are medically fragile are all considered vulnerable

Current standards surrounding the protection of vulnerable research participants can be broken down into two overarching categories: when to enroll and how to enroll (Hurst, 2011). When to enroll encompasses the fair recruitment of participants to ensure representativeness and generalizability (Hurst, 2011). This includes recruiting patients at various stages of disease progression, which presents its own set of ethical and logistical challenges for researchers. In the early stages of drug trials, participants typically are at a more advanced stage of disease progression and have tried other available treatments without improvement (Barker and Coles, 2011). This is due in part to patient/caregiver desperation and the hope of finding an effective "last-ditch" treatment effort (Hurst, 2011). As the safety of a drug is established, the clinical trial sample is expanded to encompass a greater range of patients and the researchers must explain the trial's risks, benefits, and disease prognosis (Barker and Coles, 2011). This phenomenon poses several ethical concerns, as these advanced state patients are often also affected by cognitive impairments that can affect the informed consent process. How to enroll encompasses the protections afforded to study participants (Hurst, 2011). These include monitoring for adverse effects and generally ensuring the safety and wellbeing of patients. The neuropsychological deficits associated with diseases such as Parkinson's disease and Alzheimer's disease threaten one's autonomy, diminishing the ability to make informed decisions (Hurst, 2011). Researchers must therefore strike a balance between patient protection and participation. Should one be rendered incapable of providing informed consent, they should be disqualified from participation unless consent can be provided by a legal proxy or research advance directive.

Informed consent is defined by the United States Food and Drug Administration (2018) as

> Providing a potential participant with: adequate information to allow for an informed decision about participation in the clinical investigation, facilitating the potential participant's understanding of the information, an appropriate amount of time to ask questions and to discuss with family and friends the research protocol and whether you should participate, obtaining the potential participant's voluntary agreement to participate, and continuing to provide information as the clinical investigation progresses or as the subject or situation requires.

Of particular interest to the discussion of cognitively impaired subjects are the aspects of informed decision and voluntary agreement, both of which are affected by neurodegenerative diseases such as Alzheimer's and Parkinson's disease. Making an informed decision requires the capacity to understand and integrate information, as well as to weigh risks and benefits. Voluntarily consenting to participate necessitates that one is free from coercion, compulsion, or constraint. By failing to meet any of these requirements, one may be deemed lacking decision-making capacity. Thus, determining decisional capacity is a challenging task for researchers, as it places them in the position to potentially violate another's autonomy. It would be somewhat extreme to exclude all potential participants on the grounds of cognitive impairment, especially if they stand to benefit from the results of the research. However, their inclusion must come with additional protections, with the level of safeguards proportional to that of the level of risk. The University of California San Francisco Human Research Protection Program (2018) posits that the assessment of decision-making capacity should be the first line of protection for these vulnerable populations . By their standards, adequate decisional capacity is marked by the understanding of the "nature of the research and the information relevant to his/her participation, consequences of participation for the subject's own situation, especially concerning the subject's health condition, and consequences of the alternatives to participation" (Human Research Protection Program, 2018). As such, it is possible that one can have the capacity to consent to low-risk research but be unable to consent to high-risk research or make decisions under duress.

Many factors can influence one's decision-making capacity. Deficits in language, memory, and executive function associated with Alzheimer's disease can both limit one's understanding of information provided by investigators and affect one's decision making. Parkinson's disease, as well as the drugs used to treat it, can affect personality and cognition to a degree that may detrimentally influence decision making (Appel-Cresswell and Stoessl, 2011). Parkinsonian dementia can have an effect like that of Alzheimer's disease, negatively impacting memory and other cognitive functions. Dopaminergic drugs used to treat the motor symptoms of Parkinson's disease also act on other areas of the brain, including the mesolimbic dopamine pathways. This has the potential to affect one's ability to weigh risks and benefits (Appel-Cresswell and Stoessl, 2011). This is because a possible side effect of taking these drugs is difficulty learning from negative outcomes, which can affect one's decision to withdraw their participation. This must be considered by researchers, and they must educate the patient, proxies, and caregivers in the process of determining decisional capacity.

Inextricably linked to autonomy is the concept of legacy (Hart, 2021). This is defined as "the part of the patient that will persist into the future, even after death" (Hart, 2021, p. 2). Legacy is an important consideration in developing an ethical framework with which to examine research involving those with cognitive deficits, as it relates both autonomy and consent. Failure to emphasize consent and autonomy can deprive one of control over their future and legacy. To understand why, it is important to make the distinction between the “person of the lifetime” and “the person of the moment” (Hart, 2021, p. 2). The former embodies one’s identity created by a lifetime of experiences and values, whereas the latter is the new identity created as a result of memory loss. Consider the dichotomy between the “old” Josie that Robert knew, and the “new” Josie created by her AD. These distinct identities, or “personhoods” in the words of bioethicist Dean Hart, must both be considered when examining one’s willingness to participate in biomedical research (Hart, 2021). The reconciliation of the values and desires of these two entities presents an ethical and legal challenge. We must first and foremost recognize that the “person of the moment has value and can enjoy the pursuit of happiness” (Hart, 2021, p. 2). As such, their assent to participation is still necessary, even if they are unable to provide proper informed consent. Failing to acknowledge the “person of the moment” dehumanizes the individual and constitutes a violation of the principle of “respect for persons.” The importance of the “person of the lifetime” must also be acknowledged. Decisions made by third parties trying to act in the best interests of the “person of the moment” can disrespect one’s legacy (Hart, 2021). Hart claims that “autonomy can be increased by permitting Alzheimer’s patients to document their legacy and wishes prior to significant cognitive impairment” (Hart, 2021, p. 2). The use of research advance directives can eliminate or greatly reduce the conflict between the interests of one's legacy, the "person of the moment," and one's next of kin.

The gradual cognitive decline associated with Alzheimer's and Parkinson's diseases may eventually render one incapable of making their own decisions, thereby necessitating that a surrogate decision maker or proxy assumes such responsibilities. In research contexts, if an individual has impaired decisional capacity and is thus unable to provide informed consent, a "legally authorized representative" can provide "surrogate-based consent" (Herault et al., 2018, p. 11). While such provisions facilitate studies using participants affected by diseases such as Alzheimer's and Parkinson's, they can also create legal and ethical challenges. Identifying a proxy is a major source of these. Laws regarding medical and research proxies vary by state. While the United States Code of Federal Regulations provides some guidance on the selection of proxies, this guidance is directed towards Veterans Affairs-operated healthcare institutions, though it remains a useful framework for the evaluation of such legal and ethical situations. An appointed healthcare agent, designated by the patient, is the first choice (Informed consent and advance directives, 2007). However, if an individual has not already designated their proxy prior to loss of decision-making capacity, the law then dictates the order of priority for proxy selection. The individual's legal guardian is given highest priority, followed by their next of kin (in the order of spouse, child, parent, sibling, grandparent/grandchild), and, in the absence of any family, a close friend. The potential for conflict exists if this hierarchy is inconsistent with the wishes of the individual or the rest of the family. The inherently invasive nature of an individual exerting control over another's medical affairs also has the potential to compromise confidentiality and autonomy (Hurst, 2011). Having a proxy presiding over one's decision making requires an individual to forfeit a degree of privacy that would otherwise be afforded to cognitively unimpaired individuals. This, Hurst (2011) argues, underscores the importance of thoroughly evaluating one's decisional capacity prior to appointing a proxy.

Even in cases where an individual names their own surrogate, their wishes still may not be followed. Ideally, decisions are solely based on the values and preferences of the prospective participant. However, the proxy's decision making may be constrained or compelled by their own beliefs, or exogenous factors such as societal interests and social norms (Hurst, 2011). In the interest of protecting dignity and preventing suffering, based on either individual or group morality, one's surrogate may decide against enrollment in a research study. This is similar to Robert's challenges, as he considers his wife's future:

> Intellectually for me, I still feel that Josie is a human being and I've tried to ensure that she has a quality of life. When I go visit her sometimes, she slips in and out of being normal. I would always hope that she's still

> treated with the dignity that she should have as a human being. (Sorrell, 1999)

It is also possible for a surrogate to be unaware of or misunderstand one's wishes. In a 2012 study that compared the wishes of patients and surrogates, 20% of patients would have been excluded from study participation despite a desire to enroll (Herault et al., 2018). Another 10-20% would have been enrolled against their wishes. This disconnect has been attributed to the difficulty that the proxy may have weighing risks and benefits. Other studies have found that with low-risk studies, proxies are biased towards over enrollment, while the opposite is true for high-risk studies (Hougham et al., 2003). This emphasizes the need for communication between patients, family, and healthcare providers, as well as clear documentation of one's wishes.

Research advance directives have the potential to address some of the shortcomings of proxies and surrogates (Hart, 2021). According to Hart (2021), these documents may present an answer to the question of "how can we obtain informed consent from a person unable to weigh different options and risks/rewards properly?" (p. 3). These documents, drafted during the prodromal phase of disease when one still possesses full decisional capacity, spell out what research one would or would not be willing to participate in (Hurst, 2013; Hart, 2021). They detail one's wishes regarding acceptable levels of risk, degree of invasiveness, type of study, etc. While research advance directives do present advantages by explicitly outlining one's desires, they are an imperfect solution. This is primarily due to their legal ambiguity (Hart, 2021). There are wide variations in state law regarding advance directives, especially regarding research. The Patient Self Determination Act, a federal statute governing Medicare and Medicaid, requires adherence to medical advance directives. However, it does not address the issue of "continuity of person" (Hart, 2021, p. 3). Because of this, the wishes of the "person of the lifetime" may not be followed, as the "person of the moment" is treated as a distinct individual not subject to the other's desires. The "person of the moment" must also retain the ability to withdraw participation, as they still have autonomy. Thus, even in cases where consent is provided through an advance directive, participant assent is necessary. Despite the wishes of the "person of the lifetime," it is very possible that the "person of the moment" will prohibit research participation by not providing assent. Such situations illustrate how advance directives, though helpful, are merely a tool in a continuous, complex ethical decision-making process.

In an effort to resolve some of these ambiguities, ethicists and scientists have begun engaging in empirical research to develop and refine ethical frameworks upon which to base such processes and policies. This reflects a substantial change in the field of Bioethics, straying away from basing guidance on intuition alone (Hougham et al., 2003). Over the past two decades, several studies have been conducted to compare the congruence of belief between patients and proxies, to understand decision making by cognitively impaired individuals, and to improve the informed consent process. With these, their aim has been to reconile the wishes of the "person of the lifetime," the "person of the moment," and what the proxy believes these wishes to be. Based on findings from such work, Hougham et al. (2003) propose several recommendations for the ethical conduct of research involving impaired human participants. The first is that informed consent must be treated as a continuous process, rather than an event, which begins well before the participant signs any paperwork (Hougham et al., 2003). This plays into the time dimension of neurodegenerative disorders, whereby research must respect the wishes of the "person of the lifetime" whilst also respecting the autonomy and personhood of the "person of the moment." In Josie's case, this would involve gaining an understanding of her wishes before she continues to decline and continually re-evaluating her as she undergoes cognitive changes that may alter her personality and desires. Hougham et al. (2003) also argue that our conception of the participant-investigator or proxy-investigator dynamic is too simplistic, often neglecting the importance of involving participants, proxies, and other stakeholders such as those conducting the research in a shared decision-making process.

Lack of process standardization is also a commonly cited concern surrounding the issue of consent, though Hougham et al. (2003) specifically focus on the lack of standardized frameworks in the assessment of decisional capacity. Even with a standardized framework different disciplines (e.g., geriatrics, neuropsychology, and neurology) focus on different aspects of capacity and informed consent (Hougham et al. 2003). As a result, there is a need for multidisciplinary teams in both clinical practice and the conduct of research, aligning with the theme of shared decision making. Therefore, the need for standardization encompasses the legal recognition of advance directives as well. Policy changes on the national level can support the increased utilization of research advance directives, thus helping to reduce conflicts over legacy and autonomy. Furthermore, they can alleviate ethical and moral concerns among proxies, families, and researchers by reducing ambiguity surrounding an individual's wishes.

The fields of neuroscience and neuroethics are constantly changing, evidenced by the newfound integration of empirical research into the development of ethical frameworks, as well as the increased importance of neuroethical considerations in research conduct. As new challenges and ethical dilemmas emerge, so must new solutions. Advancements of biomedical research into neurodegenerative diseases such as Alzheimer's and Parkinson's have necessitated the recruitment of inherently vulnerable populations. Without their participation, the development of diagnostic and treatment technologies for these conditions will be stalled. Thus, it is vital that scientists, ethicists, and jurists work together to protect the autonomy and respect the legacy of these individuals.

Through collaborative, interdisciplinary decision making, thorough assessment of decisional capacity, and adoption of research advance directives as a standard practice, we can conduct human research in an ethically sound manner.

References

Appel-Cresswell, S., & Stoessl, A. J. (2011). Ethical issues in the management of parkinson's disease. In J. Illes & B. J. Sahakian (Eds.), Oxford Handbook of Neuroethics Oxford University Press.

Barker, R. A., & Coles, A. (2011). The ethical issues of Trials of neural grafting in patients with neurodegenerative conditions. In J. Illes & B. J. Sahakian (Eds.), Oxford Handbook of Neuroethics. Oxford University Press.

Bracken-Roche, D., Bell, E., Macdonald, M. E., & Racine, E. (2017). Erratum to: The concept of 'vulnerability' in research ethics: an in-depth analysis of policies and guidelines. Health Research Policy and Systems, 15(1). https://doi.org/10.1186/s12961-017-0186-8

Castellani, R. J., Rolston, R. K., & Smith, M. A. (2010). Alzheimer disease. Disease-a-Month, 56(9), 484–546. https://doi.org/10.1016/j.disamonth.2010.06.001

Gratwicke, J., Jahanshahi, M., & Foltynie, T. (2015). Parkinson's disease dementia: a neural networks perspective. Brain: A Journal of Neurology, 138(Pt 6), 1454–1476. https://doi.org/10.1093/brain/awv104

Hart, D. E. (2021). Advance directives and research advance directives. Voices in Bioethics, 7. https://doi.org/10.52214/vib.v7i.8594

Hérault, É., Bravo, G., & Trottier, L. (2018). Advance directives for research: How do they compare with surrogates' predictions of older adults' preferences? Ethics & Human Research, 40(5), 11–19. https://doi.org/10.1002/eahr.405002

Horng, S. (2017). Impairments in moral decision making due to neurodegenerative disease: Ethical and practical considerations for clinicians. Journal of Hospital Ethics, 4(2), 65–73.

Hougham, G. W., Sachs, G. A., Danner, D., Mintz, J., Patterson, M., Roberts, L. W., Siminoff, L. A., Sugarman, J., Whitehouse, P. J., & Wirshing, D. (2003). Empirical research on informed consent with the cognitively impaired. IRB: Ethics & Human Research, 25(5), S26–S32. https://doi.org/10.2307/3564119

Human Research Protection Program. (2021, August 30). Enrolling individuals with cognitive impairments and assessing decisional capacity. University of California San Francisco Institutional Review Board. https://irb.ucsf.edu/enrolling-individuals-cognitive-impairments-and-assessing-decisional-capacity

Hurst, S. (2011). Clinical research on conditions affecting cognitive capacity. In J. Illes & B. J. Sahakian (Eds.), The Oxford handbook of neuroethics. (pp. 513–528). Oxford University Press

Informed consent and advance directives, 38 CFR § 17.32 (2007).

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1979). The Belmont report: Ethical principles and guidelines for the protection of human subjects of research. U.S. Department of Health and Human Services.

Sorrell, J. (1999). Ethical concerns in the care of individuals with Alzheimer’s disease. Age in Action, 14(2), 1-5.

United States Food and Drug Administration. (2018, January 4). Informed consent for clinical trials. https://www.fda.gov/patients/clinical-trials-what-patients-need-know/informed-consent-clinical-trials

Visiting a Soft Free Will

Natalia Jamiolkowski

Abstract

Free will is a socially protected concept that holds much weight in our psyche on who we are. Yet such personhood and control that is connected to free will is challenged when a neuroscientific perspective enters the discourse. Based on Benjamin Libet's study in the 1960s that measured surface-level brain activity preceding awareness of deciding to move, the ill-informed and premature conclusion was made that free will does not exist. Yet what can it be? Yes, there is a personal importance placed on an unlimited and unrestrained libertarian free will. Yet neuroscience, though also limited in scope, observes that something precedes the thought to act. Rather than a strictly 'yes' or 'no' debate, a middle ground must be reached to position free will as on a spectrum. In a collection of interdisciplinary literature that encompasses a scientific, theoretical, and metaphysical approach, I argue that the stance of free will is not defined in a limited and polarizing matter. People follow a causal nature, yet the nature of the source and its nuanced implications must be included in debate. An agent - a person - is subject to a soft determinism that allows for an interactive discourse between science and society in which they are not at odds.

The field of neuroscience aims to understand the complexities of the human brain. The results and interpretations of neuroscience research are largely unquestioned by a general audience as they demand utmost attention. Yet when neuroscience encroaches onto the validity of free will, the objective is challenged, becoming uncomfortable to deal with. Free will, as defined by Patrick Haggard (2013) in "Neuroethics of Free Will", sees conscious decisions and conscious intentions as the cause of specific actions a person chooses from. This conception depends on the libertarian view of consciousness – the basis of our thought and being. The debate of whether or not free will exists, strictly divided between determinism and indeterminism, began with the studies performed by Benjamin Libet in the 1960s. Libet, measuring the electroencephalography (EEG)–the measurement of electric activity on the scalp of the surface-level brain activity–noted traces of the brain as associated with action of free will. This action can be something as inconsequential as a flick of the wrist. From this observation, Libet interpreted that brain activity preceded the awareness of deciding to move. The brain's unconscious decision, Libet argued, was a neuronal determinism that rendered conscious decisions causally inefficacious**.** In other words, the brain causes the action before the person can even decide it. This is a direct contrast to the libertarian free will where determinism indicates that "human beings are subject to the very same regularities we observe in the natural world" (Baertschi and

Mauron, 2013)**.** Essentially, what the reductionist argues is that people never had the free will to act. Their brains did the work before they had any conscious thought of it. This assertion, especially when presented to a public that values their free will, sparks controversy and debate. What must be noted, however, is that the two sides of the free will spectrum do not have to be polar opposites. The previous subjective value of a consistent and indeterministic free will does not crumble under Libet's ill-considered hypothesis of strict determinism. Despite the polarized nature of the determinism debate, we cannot leave the foundation of personhood, which rests on free will, up for debate. Determinism is not strict; it reaches a middle ground that encompasses the objective causal nature of neuroscience, while also taking into account the flexibility of an individual's narrative.

The opposite nature of determinism versus indeterminism must be further explored, especially when studying what underlies the alleged determining mechanisms of human behaviors. Bernard Baertschi and Andre Mauron (2013), in "Genetic Determinism, Neuronal Determinism, and Determinism Tout Court," connect a strict determinist framework to how human beings are included in the causal behavior of the natural world. Determinism, being "strict", is resistant and in direct contrast to a libertarian view of free will that is completely free and uncaused. Yet part of this libertarian view is similar to a neuro reductionist view where, instead of the brain being the sole provider of behavior, it is the "soul" (seen in complete contrast and separation from the physical brain). As natural beings, humans cannot be exempt from the causal patterns that exist within their neural and environmental mechanisms. Genetic and biological determinism, though a causal influence on human behavior, is not the sole explanation for human traits. This is an oversimplification of human behavior that does not take into account neuroplasticity and the flexible dynamic of human behavior. To incorporate neuronal determinism in the context of determinism tout court–a physical determinism of cause and effect (Baertschi and Mauron, 2013)–the existing structures of free will must be revisited. Without such revisions, what is left of the debate is the assertion that "free will is an illusion" (De Ridder et al., 2013). Neuronal determinism, taking into account the adaptive mechanisms of the brain that allow flexible behavioral decision making, must connect free will to the causal and changing patterns of the human neuronal effect and the natural world's effect. These ideas are not entirely antagonistic if free will is rewritten in a compatibilist view that accepts determinism tout court. This does not uproot free will entirely. Unlike Patrick Haggard (2013) in his "Neuroethics of Free Will"–in which he claims the causal laws of the brain leaves no place for freedom–the revaluation of free will to include the nature of causal patterns bridges the deterministic nature of the brain and its interaction with the mind and environment. Brain determinism "only adds a set of factors that sometimes constrains our decisions and behaviors" (Baertschi and

Mauron, 2013). Determinism, in this sense, exists as a means of providing context rather than complete constraint. Free will, the essence of our consciousness and foundation of moral responsibility, cannot be a retrospective illusion. It must be reconciled with the causal nature of determinism to bring into light the compatibilist perspective.

To evaluate the nuance of the free will debate, we must look beyond the seemingly contradictory tango of science and philosophy. As there is discourse between the fields, there is also contestation within them. The scientific field brings in a view that finds a more tested approach to free will. Bjorn Brembs (2011), in "Towards a Scientific Concept of Free Will as a Biological Trait," detracts from the philosophical discussion and posits free will as a scientific concept. The opposite of determinism is physical indeterminism–or free will–where there is no predetermined path. Yet Brembs (2011) does not frame the debate from the individual perspective; rather, it is viewed from the concept of evolution where "selection pressures favor unpredictability" (p. 931). Rationalizing this line of thought, to be efficient in living as a species, one needs to be unpredictable. To be predictable–or deterministic–means to be in a dilemma in a natural world that values natural selection. Survival is to expect the unexpected, not to wait for a guaranteed behavior. If predators were to learn someone's every move and reaction with accuracy, there would be no survival. The determinism debate follows an idea that expects linearity in reaction to stimuli. Yet the variability and unpredictability of human, and overall biological behavior, requires nonlinearity that simultaneously rejects libertarian free will and hard determinism (Brembs, 2011). Though there is discomfort in quantitatively defining an abstract concept, it is important to bridge the two. Free will is not solely attributed to a view outside of science and must reach the middle ground between objective and subjective.

As a set idea, soft determinism/compatibilism acts as the connector between polarized views of determinism and indeterminism (the libertarian vision of free will). Free will is not impeded by the physical causal nature of determinism tout court (Baertschi and Mauron, 2013) because it is hindered more by certain causes rather than others. These certain causes encompass a direct and external force that is coercive and manipulative–not simply including the environment and social processes in which one lives in and is shaped by. This causal and circular interaction that makes determinism soft was first proposed by Walter Glannon (2009) in “Our Brains Are Not Us.” To distinguish between the mind and the brain and describe their connections revises the definition of free will in a causal setting. For neuronal determinism to be seen as compatible with soft determinism, the neuro-reductionist view that people are one and the same as their brains must be challenged. The concept of an embodied and embedded mind, interacting with the external features of the body and situating a person in the natural and social environment, encompasses a circular causation feedback loop. This is not a top-down approach where everything is located in the brain; this is a set of interactions that posits the brain as a relational organ (Glannon, 2009). Different environments result in different meanings of experience and memory, but this does not contradict the capacity for the mind to be embedded and embodied. However Lawrence R. Tancredi (2007), in “The Neuroscience of ‘Free Will’”, argues that brains make the mind. This mechanical concept of free will–limiting the mind to be solely subject to the brain–does not encompass the complexity of the interactions of the mind beyond the brain. The brain allows for the *capacity* for the mind, yet does not solely and entirely define it.

In return, the relationships between brain, body, and environment make it so that the mind makes the brain. An important mechanism for the brain is its neuroplasticity for human behavior, leaving moral judgements to be flexible in accordance with the circular causation interaction model. The difference must be made between seeing the brain as relational or as an in-a-vat thought experiment. Can cognition exist in the same degree with neuronal functions if we take away the body? It is implausible to view cognition, a prerequisite of free will, as only a product of the central nervous system. The brain that enables that mind is “not only shaped by our bodies but also by the environment in which we are embedded” (Glannon, 2009, p. 324). Free will, a product of our cognition, requires the body and environment. For the concept to be solely attributed to the brain is to ignore the content and meaning of a person’s narrative.

Moral judgements and the capacity for free will must also be analyzed in a philosophical sense to posit free will in both a qualitative and quantitative view. In order to do so, the brain must be seen as a relational organ in respect to those subjective aspects. Michael Gazzaniga (2005) in *The Ethical Brain* approaches soft determinism in a societal sense, demanding the "need to distinguish among brains, minds, and personhood" (p. 89). Gazzaniga argues the brain will always be viewed and studied in a mechanical conception; free will and moral responsibility should not be limited to those fields, though. The deterministic and indeterministic view of free will aims to search for a neurological basis of the concept. Yes, brains are determined in the mechanical sense. But the mind, the essence of personhood and free will, is a "public concept" (Gazzaniga, 2005, p.90) that can be accepted even in the presence of mechanical causes (Tancredi, 2007). Soft determinism defines actions as free as long as they are not constrained and are dependent not on the *existence* of a cause but the *source* of it (Gazzaniga, 2005). A person, either viewed as a mechanical brain or a moral mind, does not exist in a vacuum–a libertarian viewpoint that escapes the causal nature of the natural world. Even with preexisting causes, an action caused by the agent's beliefs and desires is free and responsible. Nancy Holstrum (1977) in "Firming Up Soft Determinism" takes this philosophical debate of causal patterns to multiple orders of volitions and places free will on a continuum. In order for a person to be free, the desires of the actor must not be coerced, the second order of volition (the source of those desires and beliefs) must not be in contrast to the action, and must connect to their integrated set of desires and beliefs (Holstrom, 1977). The first order of volition is the desires and beliefs of an actor; the second order of volition is the source of those desires and beliefs. The higher orders of volition continue to follow the causal line of thought. Though this leaves room to an infinite regression of a causal pattern, the personal identification towards the cause of one's beliefs (second order of volition) overtakes the source of the multiple higher orders of volition. Free will, being seen as a nuanced concept, encompasses the means in which the volitions are caused. This is not a ‘yes’ or ‘no’ question; it is dependent on how much control and identification you have with the motivations that impact actions. No matter what, there will be the existence of a cause. Yet the source that Holstrom alludes to defines where someone lies on the free will spectrum. Whether it be a metaphysical or an empirically debated concept, free will must be modified to be a nuanced compatibilism. Through this modification, free will, as in relation to our consciousness and responsibility, will be protected.

In the actual application of the free will debate, stemming from the monumental but controversial Libet experiment, soft determinism becomes empirically and theoretically protected. The claims against free will and the premature interpretations of experiment results leave room for question and skepticism. Andrew C. Papanicolaou’s “The Myth of the Neuroscience of Will” (2017) directly challenges the conclusions drawn from Libet-like experiments. Free will as an “illusion” will remain a hypothesis since there is doubt that there is enough identification of the neuronal causes or correlates of will (Papanicolaou, 2017). Specifically, with Libet, the focus on inconsequential acts was seen as applicable to “all acts trivial and significant alike” (Papanicolaou, 2017, p. 312). The lifting of a finger is equivalent in the experiment to a highly contested course of action in the neurophysiological events that precede them. Yet that is the only thing that can be agreed upon: something precedes a reported experience of initiation of movement. These experiments heavily relied on assumptions of patients being passive and impartial to their own mental states (Papanicolaou, 2017), leaving room for interpretational error. There is no evidence of a neuronal mechanism for free will. Libet’s interpretation and analysis of such results can lead to unintended detriments when taken to the public sphere. As Brun G. Breitmeyer (2017) presents in “What's All the Recent Free Will Ado About?,” the popularity of Libet should not be a goal when taking a valued concept and inefficiently translating or debunking it. The free will debate should not be reduced to whether it entirely exists or not, but, rather, to positing whether the source of the causes in compatibilism undermine the capacity of free will.

Neuronal determinism undermines free will in a nuanced fashion when it comes to conditions and diseases of the mind. Looking at addiction, “decision making and behavioral control are severely impaired” (Hyman, 2011).

The source of the cause significantly remodels the nervous system and takes advantage of the neuroplasticity of brains. Bringing back Nancy Holstrom's line of logic, the second order of volition–the source of an actors' desires and beliefs–of the addicted individual are the manipulated desires by the neuronal re-modification of adaptation. As this is more coercive in nature, the actor and act are not free. Addiction has a direct and coercive force that rewires the neurological mechanism to adapt. The individual "pathologically overvalues drugs" because of the "potent signals produced by addictive drugs" (Hyman, 2011, p. 212). This sense of coercion and personal demand follows a linear cause and effect scenario: the dopamine signals of addictive drugs directly modify the brain to unwillingly value the substance as a means of survival. In comparing addiction with adolescence, it is questionable to demonstrate solely through neuroscience that free will is impaired (Luciana, 2011). The adolescent has the same capacity for rationality as an adult, but is less efficient under conditions of high demand. Through this rational cohesion, the desires and beliefs of an adolescent can be viewed as an integrated and consistent volition. The implementation for this group is limited through neural capacity that cannot entirely take into account the embedded and embodied mind. The adolescent as an embedded and embodied mind is hyper-reactive to external and peer pressures. This does not, however, follow a linear line of reasoning like that of addiction. The reactivity of the adolescent is not a direct or manipulative neuronal process;

this is a nonlinear line of action and reaction where the source of the beliefs is not automatically compromised. The adolescent will, more or less, remain the same person despite the neural limitations of their capacities to act on their cohesive beliefs and desires. Addiction entirely violates the free will of the individual when it comes to the topic of drugs. This is compatibilism at work as the capacity for free will continues to exist despite the neuronal determinism of addiction and adolescence.

As the conversations play out on neuroscience's inclusion into free will, people at large should not feel the immediate need to compromise their own beliefs. Chris Kaposy (2010), in his article "The Supposed Obligation to Change One's Beliefs About Ethics Because of Discoveries in Neuroscience," argues that it is more rational to preserve free will and personhood than it is to neglect these concepts in the light of dramatized and premature studies. Despite studies in neuroscience that aim to debunk the validity of free will, it must not be the responsibility of the audience to willingly and completely accept these claims. People of every field follow their own ethical considerations that are shaped by socially and personally agreed upon norms. Kaposy relays the disconnect between studies in neuroscience and ethics by noting that "evidence from neuroscience does not identify the concept of free will [...] for the purpose of ethics, but as deficient for the purposes of neuroscience" (Kaposy, 2010, p.29). Though there can be a certain merit attached to scientific studies, especially in valuing the search for the "truth," it cannot be seen as rationally acceptable if the truth detests the significant value that free will has in our lives. Instead of the divide between neuroscience and ethics that Kaposy proposes, a compatibilist framework that accepts neuroscience into the rational debate of free will must be strengthened and solidified. Neuroscience does not have to be purely at contestation with free will if we are to make the two consistent. In order to preserve the rationality of truth and free will, the contested concept must be redefined in a way that values its indispensable nature to the moral worldview as compatible with neuroscientific evidence (Kaposy, 2010). This takes into account the previous considerations of compatibilism where the deterministic and causal manner of the natural world is aligned with the intentionality and choice behind free will.

It is crucial to bridge the divide between determinism and indeterminism in order to respect ethical considerations in neuroscience. As there is a significant value of free will in our lives, we must preserve the concept in order to fundamentally maintain our social and personal order. The interactions between science and society would be compromised, leaving previous ethical considerations on autonomy and consent up to question in the light of debates about free will. To completely reject free will is to neglect the rational obligation to protect and keep our desires and beliefs. Libet’s experiment is monumental for the wrong reasons in which it prematurely worked to undermine free will, a concept that is contingent in our social practices (Haggard, 2013). Yet free will as its original conception must not stand as it treats its subjects as exceptions to the laws of nature. The natural world follows a causal pattern; people must follow suit. What must be considered is the nature of the source and how nuanced its implications are for the application of free will. Is it right to claim that those who were raised in separate settings were conditioned to have the same capacity for free will? The connection between the brain, body, and the environment for each individual leaves them with their own spectrum of freedom, yet it does not leave the person unfree. Soft determinism, taken in a scientific and societal standpoint, provides space for further deliberation on the patterns and shifts within free will. Moving away from the conversation on whether free will is a ‘yes’ or ‘no’ subject leaves space to further focus on means of enhancing and enforcing a greater degree of freedom at the institutional level.

References

Baertschi, B., & Mauron, A. (2013). Genetic determinism, neuronal determinism, and determinism tout court. In J. Illes & B. J. Sahakian (Eds.), The Oxford handbook of neuroethics. (pp. 151–160). Oxford University Press.

Breitmeyer, B. G. (2017). What's all the recent free-will ado about? Psychology of Consciousness: Theory, Research, and Practice, 4(3), 330–333. https://doi.org/10.1037/cns0000132

Brembs, B. (2011). Towards a scientific concept of free will as a biological trait: Spontaneous actions and decision-making in invertebrates. Royal Society, 930–939. https://doi.org/10.1098/rspb.2010.2325

De Ridder, D., Verplaetse J., & Vanneste, S. (2013). The predictive brain and the free will illusion. Frontiers in Psychology, 4. https://doi.org/10.3389/fpsyg.2013.00131

Gazzaniga, M. S. (2005). My brain made me do it. In The Ethical Brain (pp. 87–102). Dana Press.

Glannon, W. (2009). Our brains are not us. Bioethics, 23(6), 321–329. https://doi.org/10.1111/j.1467-8519.2009.01727.x

Haggard, P. (2013). Neuroethics of free will. In J. Illes & B. J. Sahakian (Eds.), The Oxford handbook of neuroethics. (pp. 219–226). Oxford University Press.

Holmstrom, N. (1977). Firming up soft determinism. Personalist, 58, 39–51.

Hyman, S. E. (2011). The Neurobiology of Addiction: Implications for voluntary control of behavior. In J. Illes & B. J. Sahakian (Eds.), Oxford Handbook of Neuroethics. Oxford University Press.

Kaposy, C. (2010). The supposed obligation to change one's beliefs about ethics because of discoveries in neuroscience. AJOB Neuroscience, 1(4), 23–30. https://doi.org/10.1080/21507740.2010.510820

Luciana A. (2011). Development of the adolescent brain. In J. Illes & B. J. Sahakian (Eds.), Oxford Handbook of Neuroethics (pp. 59-82). Oxford University Press. https://doi.org/10.1093/oxfordhb/9780199570706.013.0058

Papanicolaou, A. C. (2017). The myth of the neuroscience of will. Psychology of Consciousness: Theory, Research, and Practice, 4(3), 310–320. https://doi.org/10.1037/cns0000116

Tancredi, L. R. (2007). The neuroscience of free will. Behavioral Sciences & the Law, 25(2), 295–308.